J. Physiol. (Paris) 94 (2000) 525–537

PII: S0928-4257(00)01104-9/REV

How can squint change the spacing of ocular dominance columns?

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Abstract – The pattern of ocular dominance columns in primary visual cortex of mammals such as cats and macaque monkeys arises during development by the activity-dependent refinement of thalamocortical connections. Manipulating visual experience in kittens by the induction of squint leads to the emergence of ocular dominance columns with a larger size and larger column-to-column spacing than in normally raised animals. The mechanism underlying this phenomenon is presently unknown. Theory suggests that experience cannot influence the spacing of columns if the development proceeds through purely Hebbian mechanisms. Here we study a developmental model in which Hebbian mechanisms are complemented by activity-dependent regulation of the total strength of afferent synapses converging onto a cortical neurone. We show that this model implies an influence of visual experience on the spacing of ocular dominance columns and provides a conceptually simple explanation for the emergence of larger sized columns in squinting animals. Assuming that during development cortical neurones become active in local groups, which we call co-activated cortical domains (CCDs), ocular dominance segregation is controlled by the size of these groups: (1) Size and spacing of ocular dominance columns are proportional to the size σ of CCDs. (2) There is a critical size σ^* of CCDs such that ocular dominance columns form if $\sigma < \sigma^*$ but do not form spontaneously if $\sigma > \sigma^*$. This critical size of CCDs is determined by the correlation functions of activity patterns in the two eyes and specifies the influence of experience on ocular dominance segregation. We show that σ^* is larger with squint than with normal visual experience. Since experimental evidence indicates that the size of CCDs decreases during development, ocular dominance columns are predicted to form earlier and with a larger spacing in squinters compared to normal animals. © 2000 Éditions scientifiques et médicales Elsevier SAS

Area 17 / development / experience-dependence / cortical maps / self-organization

1. Introduction

In layer IV of primary visual cortex, afferents from the left and right eye are segregated into spatially distinct domains called ocular dominance columns (ODCs) [30, 48]. Neurones in individual domains preferentially respond to stimulation of either the left or the right eye [23, 24]. In the primary visual cortex of cats, ODCs form a roughly repetitive pattern [1, 33, 48, 49]. During development the initially overlapping thalamocortical afferents of the two eyes gradually segregate into alternating patches between the third and sixth postnatal week [31, 49]. Functionally, however, ocular dominance columns can be visualized already between the second and third postnatal week [10, 44]. Many lines of evidence indicate that ocular dominance segregation is driven by activity-dependent competition for cortical territory between the geniculocortical afferents serving the two eyes [9, 20, 52]. At the level of individual neurones and synapses this competition presumably results from an activity-dependent refinement of synaptic connections whereby 'improper' connections are removed and 'appropriate' connections are elaborated [8, 26, 51]. It was shown previously that the spacing of ODCs in squinting cats was significantly larger than in normally raised animals [32] (*figure 1*). This dependence of ODC spacing on visual experience has also been suggested from model simulations [19] and similar observations have meanwhile been reported from cats that were raised with alternating monocular occlusion [56].

Because a global change in columnar spacing cannot be easily produced by shifting ocular dominance borders in a pre-existing grid these experimental observations rather indicate that the initially emerging pattern of ODCs forms spontaneously and is not determined by a yet unobserved pre-pattern.

The actual mechanism by which squint leads to a larger spacing of ODCs is presently unknown. Indeed the phenomenon that ODC spacing changes in response to a manipulation of visual experience seems to be at odds with a basic principle governing pattern formation in mathematical models of visual development. In a large class of models for the formation of ocular dominance

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patterns, it has been demonstrated mathematically that the spacing of ODCs is (1) determined by the range of lateral interactions within the cortical layer and (2) is independent of the degree of correlation among afferent activity patterns from the two eyes [39, 40, 54]. In particular, Miller has shown that (1) and (2) hold if activity-dependent rearrangement of synaptic connections follows a generalized Hebbian rule, i.e. is driven by the correlation of arbitrary functions of pre- and post-synaptic activity [34]. Because manipulating visual experience must be assumed to primarily affect the correlations among afferent activity patterns, the above observations [32, 56] appear rather surprising from a theoretical point of view. For reasons that are either mathematically or biologically not well understood some models for the formation of ocular dominance patterns appear to exhibit a dependence of column spacing on afferent activity patterns [4, 13, 19, 47].

In this paper we argue that the observed experience-dependence of the spacing of ODCs is readily explicable if the occurrence of ODC segregation is controlled by the range of intracortical interactions. Our mathematical analysis indicates that the range of intracortical interactions may not only determine the spacing of the emerging ODCs but also control ODC segregation in the sense that segregation can only occur if this range is below a threshold value.

Two assumptions appear essential for such a qualitative dependence of ODC segregation on intracortical interactions. (A1) Cortical activity patterns take the shape of locally co-activated domains. (A2) The total strength of synaptic connections is dynamically regulated by an activity-dependent mechanism.

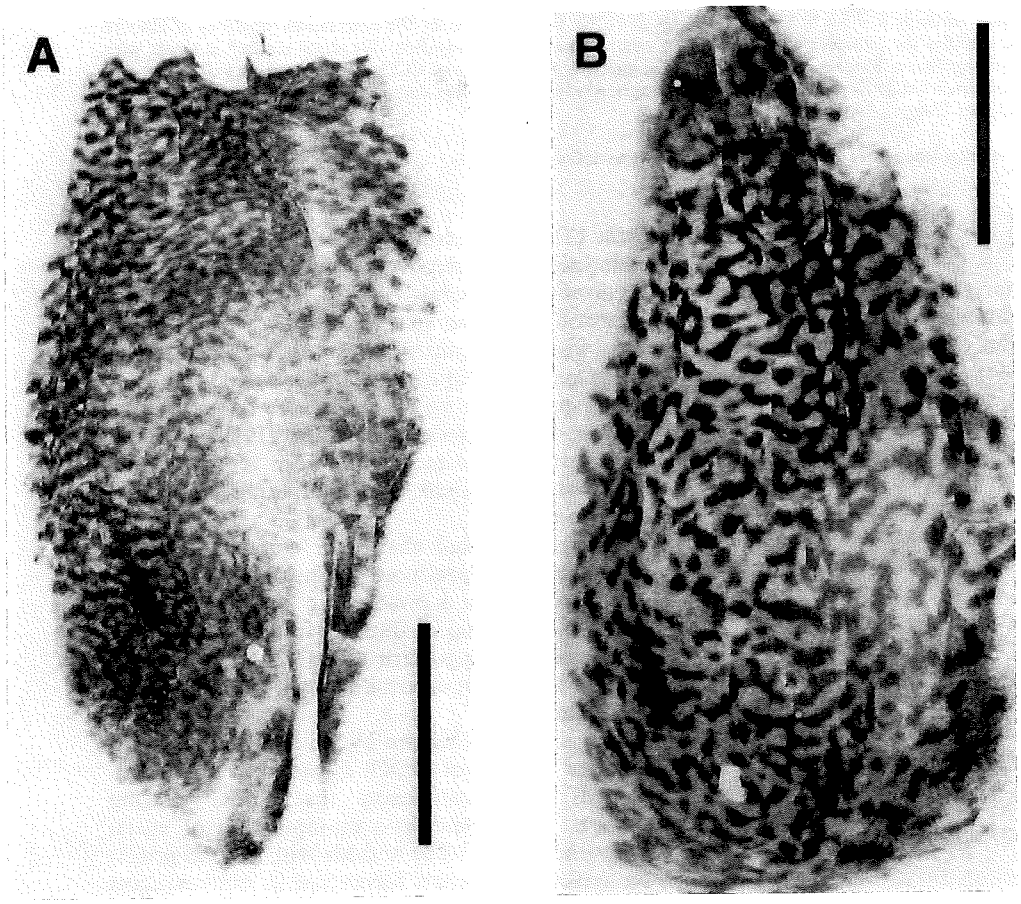

Figure 1. Pattern of ODCs in the visual cortex of a normally raised cat (**A**) and a cat raised with artificially induced squint (**B**). ODCs in squinting cats exhibit a larger column-to-column spacing than ODCs in normally raised cats. The pattern was visualized by proline labelling. Scale bars 10 mm. (Modified from [32]).

In order to investigate how a changing range of intracortical interactions influences the segregation of afferent connections, we analysed a simple phenomenological model equation for ODC development which idealizes assumptions (A1) and (A2). In the following, we will first discuss the behaviour of this model assuming that the cortical response to an afferent activity pattern consists of a single co-activated domain. We will then show that the basic properties of this simple model persist when cortical activity patterns are a general nonlinear functional of afferent input. Our results demonstrate that the size σ of CCDs is a decisive parameter in the considered model. We show that under a wide range of conditions there exists a critical size σ^* of CCDs such that ODCs can only form if σ is smaller than σ^*. Furthermore, if ODCs do form their spacing is proportional to σ. Since evidence suggests that the size of CCDs decreases during development [2, 6, 12, 14, 17, 53], this implies that (1) ODCs arise by a symmetry breaking bifurcation that takes place as σ decreases below the critical value σ^* (see also [21]) and (2) the spacing of ODCs is proportional to the size of CCDs when symmetry is broken. We show that the critical size σ^* depends on the correlations between activity patterns in the two eyes and should be larger in squinting compared to normally raised animals. This dependency of the bifurcation threshold on afferent activity patterns yields a conceptually simple and experimentally testable mechanism for the development of larger sized columns in squinters.

ODCs are predicted to form earlier in squinting animals, i.e. at a time when co-activated domains are still of a larger size. As a consequence they exhibit a larger spacing in these animals. This should however only be the case if squint is induced before the emergence of ODCs. Ways to experimentally test the validity of the proposed mechanism are suggested.

2. The model

It is convenient to discuss the formation of the pattern of ODCs during development in terms of an abstract order parameter field $o(\mathbf{x})$ where $\mathbf{x}$ denotes the location within the cortical layer and the regions defined by $o(\mathbf{x}) > 0$ and $o(\mathbf{x}) < 0$ represent the left and right eye columns respectively [54].

Here and in the following, bold characters represent 2-dimensional vectors that denote positions in a cortical layer and LGN layers representing the two eyes. Our primary aim is the dynamics of $o(\mathbf{x})$ which governs the emergence of the pattern of ODCs from a homogeneous initial state, and in particular its dependence on parameters describing visual experience. Such a dynamics is derived from a dynamics of synaptic strengths which models basic learning mechanisms. In the following we will first construct a simple, phenomenological synaptic dynamics which is driven by Hebbian modifications and through which the total strength of synapses onto a cortical neurone is stabilized by an activity-dependent dynamic process. Using a set of idealizing assumptions on the shape of cortical activity patterns we will then derive a dynamics for the order parameter field $o(\mathbf{x})$.

In a stabilized Hebbian dynamics, the elementary learning rule for the synaptic strength $W(\mathbf{r},\mathbf{x})$ that link a neurone at location $\mathbf{r}$ in a model LGN layer to a neurone at location $\mathbf{x}$ in the model cortex is composed of a Hebbian term modelling how synaptic strengths change as a function of correlated pre- and post-synaptic activity and non-Hebbian terms which ensure that a measure of total synaptic strength is conserved. Since all variants of Hebbian rules suffer from the same fundamental instability problem we restrict our attention to the most simple term given by

$$\delta W(\mathbf{r},\mathbf{x}) \propto [a(\mathbf{r})e(\mathbf{x}) - f(W(\mathbf{r},\mathbf{x}),e(\mathbf{x}))] \qquad (1)$$

where $\delta W(\mathbf{r},\mathbf{x})$ is the modification of synaptic strength induced by an afferent activity pattern $a(\mathbf{r})$ and $e(\mathbf{x})$, the activity pattern that forms as a response to $a(\mathbf{r})$ in the cortical target layer. It is easy to see that the first term considered in isolation is unstable. Since the activities $a(\mathbf{r})$ and $e(\mathbf{x})$ are both positive, synaptic strength can only increase through the first term and in general will diverge as time proceeds. This implies that additional influences must exist which stabilize the synaptic dynamics. In Eq. (1) we assumed that these influences are synaptically local, i.e. for every individual synaptic connection the stabilizing component $f(\cdot)$ depends only on the present strength of the synapse $W(\mathbf{r},\mathbf{x})$ and on the postsynaptic activity of the cortical neurone under consideration $e(\mathbf{x})$.

If $W(\mathbf{r},\mathbf{x})$ changes slowly through the cumulative effect of a large number of activity patterns its temporal evolution follows the dynamics

$$\frac{\partial}{\partial t} W(\mathbf{r},\mathbf{x}) = \langle a(\mathbf{r})e(\mathbf{x}) - f(W(\mathbf{r},\mathbf{x}),e(\mathbf{x}))\rangle \qquad (2)$$

where t denotes time and $\langle\ \rangle$ represents the average over an ensemble of afferent activity patterns. The most simple dynamics of the form (2) that dynamically leads to the conservation of total synaptic strength is identified by expanding $f(W(\mathbf{r},\mathbf{x}),e(\mathbf{x}))$ in a power series

$$f(W(\mathbf{r},\mathbf{x}),e(\mathbf{x})) = f_0 + f_1^W W(\mathbf{r},\mathbf{x}) + f_1^e e(\mathbf{x}) + f_2^{We} W(\mathbf{r},\mathbf{x}) e(\mathbf{x}) + \cdots \quad (3)$$

and asking which of the successively more complicated terms is sufficient to stabilize the synaptic dynamics. It is easy to convince oneself that the first three terms cannot stabilize the dynamics. The forth term however is in itself sufficient to stabilize Eq. (1) and leads to a dynamic regulation of the total synaptic strength. Firstly, with

$$f(W(\mathbf{r},\mathbf{x}),e(\mathbf{x})) = f_2^{We} W(\mathbf{r},\mathbf{x}) e(\mathbf{x}) \quad (4)$$

the synaptic strength $W(\mathbf{r},\mathbf{x})$ cannot leave the region defined by

$$0 \le W(\mathbf{r},\mathbf{x}) < a_{\max}/f_2^{We} \quad (5)$$

where $a_{\max}$ is the maximal activity value in the ensemble of afferent activity patterns. Secondly, the total afferent synaptic strength converging onto a cortical neurone

$$w_{tot}(\mathbf{x}) = \int d^2r\, W(\mathbf{r},\mathbf{x}) \quad (6)$$

develops according to the equation

$$\frac{\partial}{\partial t} w_{tot}(\mathbf{x}) = \left\langle \int d^2r\, a(\mathbf{r}) e(\mathbf{x}) - f_2^{We} e(\mathbf{x}) w_{tot}(\mathbf{x}) \right\rangle \quad (7)$$

and therefore converges towards

$$w_{tot}^{\infty}(\mathbf{x}) = \frac{\left\langle e(\mathbf{x}) \int d^2r\, a(\mathbf{r}) \right\rangle}{f_2^{We} \langle e(\mathbf{x}) \rangle} \quad (8)$$

when the dynamics (2) settles into a stationary state. Assuming the total afferent activity $\int d^2r\, a(\mathbf{r})$ to be constant in the ensemble of afferent activity patterns, Eq. (8) implies that the total synaptic strength converges to the same value $\int d^2r\, a(\mathbf{r})/f_2^{We}$ for every cortical neurone. Even if afferent activity patterns differ in their total activity $w_{\text{tot}}(\mathbf{x})$ will in general assume a well defined equilibrium value for every cortical neurone.

The most simple stabilized Hebbian dynamics therefore takes the form

$$\frac{\partial}{\partial t} W(\mathbf{r},\mathbf{x}) = \langle a(\mathbf{r}) e(\mathbf{x}) - W(\mathbf{r},\mathbf{x}) e(\mathbf{x}) \rangle \quad (9)$$

where f_2^{We} is set to unity without lose of generality. Eq. (9) represents a generalization of models previously called competitive-Hebbian models (see [15, 55]). The dynamic normalization of total synaptic strength in such models was first pointed out by Ritter and Schulten [45].

In order to model ocular dominance segregation we must consider connections $W_L(\mathbf{r}_L,\mathbf{x})$ and $W_R(\mathbf{r}_R,\mathbf{x})$ from the left and right eye LGN layers respectively. The order parameter $o(\mathbf{x})$ describing the pattern of ocular dominance columns can be defined in terms of these connections as

$$o(\mathbf{x}) = \int d^2r (W_L(\mathbf{r},\mathbf{x}) - W_R(\mathbf{r},\mathbf{x})) \quad (10)$$

where a common co-ordinate system in the two LGN layers is assumed. Eq. (9) then implies a dynamics for the field $o(\mathbf{x})$ itself

$$\frac{\partial}{\partial t} o(\mathbf{x}) = \left\langle \left(\int d^2r (a_L(\mathbf{r}) - a_R(\mathbf{r})) - \int d^2r (W_L(\mathbf{r},\mathbf{x}) - W_R(\mathbf{r},\mathbf{x})) \right) e(\mathbf{x}) \right\rangle = \langle (s - o(\mathbf{x})) e(\mathbf{x}) \rangle \quad (11)$$

where the activity patterns $a_L(\mathbf{r})$ and $a_R(\mathbf{r})$ in the left and right eye LGN layers define a formal ocular dominance stimulus $s = \int d^2r (a_L(\mathbf{r}) - a_R(\mathbf{r}))$.

To complete the definition of the model we must finally specify the cortical activity pattern $e(\mathbf{x})$ in response to an individual afferent stimulus. Here we assume that the activity pattern $e(\mathbf{x})$ is dominantly shaped by interactions within the cortical layer. If neighbouring units in the cortical layer are linked such that excitation spreads locally within the layer then cortical activity patterns will be composed of local domains of co-activated neurones.

As a mathematical idealization of this behaviour we assume, following Kohonen [29], that the cortical activity pattern is given by a stereotyped activity blob

$$e(\mathbf{x}) = \frac{1}{2\pi} \exp\left(-\frac{|\mathbf{x} - \mathbf{x}^*|^2}{2\sigma^2} \right) \quad (12)$$

where $\mathbf{x}^*$ is the position of the most activated neurone $\mathbf{x}^*$ and σ measures the size of a CCD. Given this idealization, afferent stimuli determine only the position $\mathbf{x}^*$ of the CCD but not its shape and size. The location of the CCD is therefore a functional of the stimulus and of the present synaptic strengths

$$\mathbf{x}^* = \mathbf{x}^*(a_L(\cdot), a_R(\cdot), W_L(\cdot), W_R(\cdot)) \quad (13)$$

Assuming a single activated domain, like in Eq. (12) is justified if we restrict the afferent activity patterns $a_L(\mathbf{r}),a_R(\mathbf{r})$ to be localized. The activity centre $\mathbf{x}^*$ will then be located in the vicinity of the cortical position, which corresponds to the centre

$$\mathrm{r}_s = \frac{\int d^2r\ \mathbf{r}\ (a_L(\mathbf{r}) + a_R(\mathbf{r}))}{\int d^2r (a_L(\mathbf{r}) + a_R(\mathbf{r}))} \tag{14}$$

of the afferent stimulus. In the following we assume that the retinotopic organization is isotopic, homogeneous, and identical, i.e. that

$$\mathbf{R}_L(\mathbf{x}) = \mathbf{R}_R(\mathbf{x}) = \mathbf{x} \tag{15}$$

with $\mathbf{R}_i(\mathbf{x}) = \int d^2r\mathbf{r}W_i(\mathbf{r},\mathbf{x})$ $(i = L,R)$ denoting the receptive field centre positions.

In order to keep the model simple our aim is to identify a plausible choice of $\mathbf{x}^*(a_L(\cdot),a_R(\cdot),o(\cdot))$ that leads to a closed form of the dynamics (11) and is capable of describing the development of a pattern of ODCs. We consider an ensemble of stimuli with variable parameters s localized at variable locations $\mathbf{r}_s$ in the LGN layers. With the most simple choice $\mathbf{x}^* = \mathbf{r}_s$ the dynamics (11) reduces to

$$\frac{\partial}{\partial t} o(\mathbf{x}) = \langle s \rangle - o(\mathbf{x}) \tag{16}$$

and a pattern of ODCs cannot form. In general, however, the emerging pattern of ODC will modify the position of the activity centre $\mathbf{x}^*$. A generalization of $\mathbf{x}^* = \mathbf{r}_s$ is given by

$$\mathbf{x}^* = \mathrm{argmin}(|s - o(\mathbf{x})|^2 + |\mathbf{r} - \mathbf{x}|^2) \tag{17}$$

through which the activity centre $\mathbf{x}^*$ is shifted towards the neighbouring column dominated by the eye which is currently more active.

The model defined by Eqs. (11), (12) and (17) has a homogeneous stationary solution

$$o_0(\mathbf{x}) = \langle s \rangle \tag{18}$$

which in the presence of left-right eye symmetry reduces to $o_0(\mathbf{x}) = 0$.

In the following we will show that the stability of this solution depends on the statistical structure of the afferent activity-patterns and on the size σ of CCDs.

3. Dynamics of ocular dominance segregation

To understand the mechanism of ocular dominance segregation the primary question is whether the homogeneous solution identified above is stable or unstable against spatially periodic perturbations. In the later case, ODCs will in general arise spontaneously from homogeneous initial conditions. To determine this stability we linearize the dynamics of $o(\mathbf{x})$ around the homogeneous solution. Because the resulting linear equation must be translation invariant in the cortical layer its eigenfunctions are plane waves. It therefore suffices to study the stability of the model in 1 spatial dimension

$$\frac{\partial}{\partial t} o(x) = \frac{1}{2\pi}\left\langle (s - o(x))\exp\left(-\frac{|x - x^*(s,r,o(\cdot))|^2}{2\sigma^2}\right)\right\rangle \tag{19}$$

$$= \frac{1}{2\pi}\int dsdrP(s,r)(s - o(x)) \times \exp\left(-\frac{|x - x^*(s,r,o(\cdot))|^2}{2\sigma^2}\right) \tag{20}$$

where $P(s,r)$ is the probability density of stimuli. For simplicity we further assume $P(s,r)$ to be independent of position $P(s,r) = P(s)$. To eliminate the implicit dependence of the activity centre x^* on the stimulus parameters and $o(x)$ we perform a change of co-ordinates to new state dependent stimulus co-ordinates y,p defined by

$$r(p,y) = y + \frac{p}{\sqrt{1 + o_x(y)^{-2}}} \tag{21}$$

$$s(p,y) = o(y) - \frac{p}{o_x(y)\sqrt{1 + o_x(y)^{-2}}} \tag{22}$$

where $o_x(y) = (\partial/\partial x)o(x)|_y$. As a function of the new stimulus co-ordinates p and y the activity centre is located at $x^* = y$. The stimulus co-ordinate system (21,22) defines a unique reparameterization of (s,r) for $|s - \langle s \rangle| < p_{\max} \propto \max(\partial_x^2 o(x))^{-1}$. Because the probability density of s must have finite support there is always a non-zero amplitude $\max(o(x))$ up to which the co-ordinates p,y sample the stimulus set completely and uniquely. The dynamics close to the homogeneous stationary state, i.e. for $o(x) \approx s$ can therefore be written as

$$\frac{\partial}{\partial t} o(x) = \frac{1}{2\pi}\int dydp\hat{P}(p,y)J(p,o_x(y),o_{xx}(y))(s(p,y) - o(x)) \times \exp\left(-\frac{|x - y|^2}{2\sigma^2}\right) \tag{23}$$

where

$$J(p,o_x(y),o_{xx}(y)) = (1+o_x(y)^2)\times \left[\frac{1}{o_x(y)\sqrt{1+1/o_x(y)^2}} + \frac{po_{xx}(y)}{o_x(y)^4(1+1/o_x(y)^2)^2}\right] \quad (24)$$

with $o_{xx}(y) = (\partial^2/\partial x^2)o(x)|_y$ is the Jacobian of the co-ordinate transform defined above and $\hat{P}(p,y) = P(s(p,y))$. The right hand side of the integro-differential Eq. (13) can be linearized by linearizing the integrand and yields

$$\frac{\partial}{\partial t}\hat{o}(x) = -\sigma^2\hat{o}(x) + \frac{\langle p^2\rangle}{2\pi}\int dy\hat{o}_{xx}(y)\exp\left(-\frac{|x-y|^2}{2\pi\sigma^2}\right) \quad (25)$$

after performing the p integration. Here $\hat{o}(x) = o(x) - \langle s\rangle$ and

$$\langle p^2\rangle = \langle (s-\langle s\rangle)^2\rangle \quad (26)$$

The growth rates of $\hat{o}(x)$, i.e. the eigenvalues of the rhs operator

$$\lambda(k) = \left(-1+\langle p^2\rangle k^2\exp\left(-\frac{k^2\sigma^2}{2}\right)\right)\sigma^2 \quad (27)$$

are found by Fourier transformation. The maximal eigenvalue belongs to

$$k_{\max} = \sqrt{2}/\sigma \quad (28)$$

and is positive for

$$\sigma < \sigma^* = \sqrt{\frac{2\langle p^2\rangle}{e}} \quad (29)$$

(*figure 2*). As a consequence, the homogeneous solution $o_0(x)$ looses stability when the size of CCDs is below the threshold value σ^*. This leads to the emergence of an ocular dominance pattern with characteristic wavelength

$$\Lambda = \sqrt{2}\pi\sigma \quad (30)$$

One should note that according to this result the same microscopic rules of synaptic plasticity can either lead to the emergence of ODCs or suppress ocular dominance segregation depending on the size of CCDs.

4. Experience-dependence of ODC spacing

The above analysis shows that different afferent patterns of activity can influence the emergence of ODCs only through the instability threshold $\sigma^* = \sqrt{2\langle p^2\rangle}/e$. Once σ^* is given the dynamics of ocular dominance segregation from a homogeneous

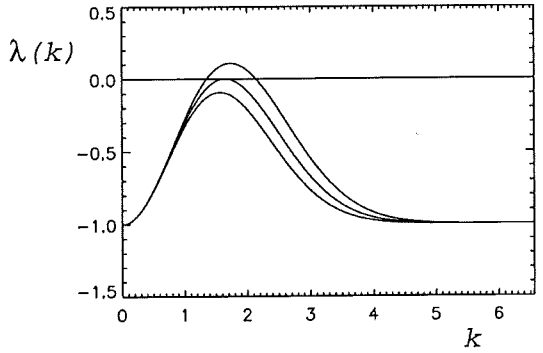

Figure 2. Spectrum of growth rates $\lambda(k)$ for $\langle p^2\rangle = 1$ and $\sigma = 1.05\sigma^*$, σ^*, $0.95\ \sigma^*$ from bottom to top. For σ larger than σ^* the largest growth rate is positive which leads to the emergence of a finite wavelength pattern.

initial state is defined. To show that this influence can in fact explain the observed wavelength change we rewrite the instability threshold in terms of the correlation functions

$$C_L(\mathbf{q}) = \langle a_L(\mathbf{r})a_L(\mathbf{r}+\mathbf{q})\rangle - \langle a_L(\mathbf{r})\rangle^2$$
$$C_R(\mathbf{q}) = \langle a_R(\mathbf{r})a_R(\mathbf{r}+\mathbf{q})\rangle - \langle a_R(\mathbf{r})\rangle^2$$
$$C_{LR}(\mathbf{q}) = \langle a_L(\mathbf{r})a_R(\mathbf{r}+\mathbf{q})\rangle - \langle a_L(\mathbf{r})\rangle\langle a_R(\mathbf{r})\rangle \quad (31)$$

Here we assume that the ensemble of activity patterns in both eyes is statistically translation invariant. The expression for the instability threshold follows from the identity

$$\begin{aligned}\langle p^2\rangle &= \left\langle\left(\int d^2r a_L(\mathbf{r}) - \langle a_L(\mathbf{r})\rangle - (a_R(\mathbf{r}) - \langle a_R(\mathbf{r})\rangle)\right)^2\right\rangle \\ &= \left\langle\left(\int d^2r a_L(\mathbf{r}) - \langle a_L(\mathbf{r})\rangle^2\right)\right\rangle + \left\langle\left(\int d^2r a_R(\mathbf{r}) - \langle a_R(\mathbf{r})\rangle^2\right)\right\rangle - \\ &\quad 2\left\langle\left(\int d^2r a_L(\mathbf{r}) - \langle a_L(\mathbf{r})\rangle\right)\times\left(\int d^2r a_R(\mathbf{r}) - \langle a_R(\mathbf{r})\rangle\right)\right\rangle \\ &= \int d^2r d^2q\langle a_L(\mathbf{r})a_L(\mathbf{q})\rangle - \langle a_L(\mathbf{r})\rangle^2 + \int d^2r d^2q\langle a_R(\mathbf{r})a_R(\mathbf{q})\rangle - \langle a_R(\mathbf{r})\rangle^2 -\end{aligned}$$

$$2\left(\int d^2r d^2q \langle a_L(\mathbf{r}) a_R(\mathbf{q})\rangle - \langle a_L(\mathbf{r})\rangle\langle a_R(\mathbf{r})\rangle\right)$$
$$= \int d^2q C_L(\mathbf{q}) + C_R(\mathbf{q}) - 2C_{LR}(\mathbf{q})$$

where the area of the LGN layers is $\int d^2r = 1$. This identity determines the instability threshold

$$\sigma^* = \sqrt{\frac{2}{e}\int d^2q C_L(\mathbf{q}) + C_R(\mathbf{q}) - 2C_{LR}(\mathbf{q})} \qquad (32)$$

as a functional of the correlation functions of afferent activity patterns.

Squint reduces correlations between activity in the two eyes ($C^{sq}_{LR} < C^{norm}_{LR}$) but leaves the correlations within an eye similar to normal vision. Because

$$\int d^2q C_L(\mathbf{q}) + C_R(\mathbf{q}) > 0 \qquad (33)$$

and inter-eye correlations are presumably positive [40] the instability threshold will in general be larger in squinters

$$\sigma^*_{sq} > \sigma^*_{\text{norm}} \qquad (34)$$

compared to normal animals. In contrast monocular deprivation reduces not only the inter-eye correlations but also the activity and as a consequence the correlations in the deprived eye. Therefore

$$\sigma^*_{\text{sq}} > \sigma^*_{MD} \qquad (35)$$

while the ordering of σ^*_{MD} and σ^*_{norm} depends on details of the correlation functions and no general statements can be made.

If we suppose that the size of CCDs decreases from a value initially larger than σ^*_{norm} during development it is easy to see that the dependence of the instability threshold on inter-eye correlations leads to larger columns in squinting animals. In this case, σ will reach the threshold $\sigma^*_{sq} > \sigma^*_{norm}$ earlier in squinters than in normal animals. Because the wavelength Λ is proportional to σ when the homogeneous solution becomes unstable this will in turn cause the emergence of ODCs with a larger spacing (*figure 3*).

5. General conditions for the existence of σ^*

The previous analysis rests upon a set of idealizing assumptions: (1) At any time there is only one active domain within the cortical layer. (2) The shape and size of the cortical activity patterns is rigidly stereotyped. (3) Afferent activity patterns are localized in LGN layers. (4) The position of the CCD is determined by a simple rule neglecting most details of the present synaptic organization. These assumptions enable a complete analytical treatment of the model. However, one expects that our central findings – the existence of σ^* and its dependence of afferent correlations – characterize the behaviour of a large class of models.

In this section we will analyse the existence of a critical size of CCDs under more general assumptions. In particular we will show that a critical size σ^* exists and depends on afferent correlations in a similar manner as in the simple model studied above as long as the area of cortex that is activated on average decreases sufficiently fast when the range of intracortical interactions is decreased. We will consider only the case of statistically equivalent patterns of activity from the two eyes, i.e. $\langle s\rangle = 0$ and $C_R(\mathbf{q}) = C_L(\mathbf{q})$. These results can be easily generalized to the asymmetric case at the cost of notational complexity.

In order to discuss the segregation of ODCs for a synaptic dynamics of the general form Eq. (9), we consider the dynamics for the difference between the strength of synapses from the left and right eye

$$W^D(\mathbf{r},\mathbf{x}) = W_L(\mathbf{r},\mathbf{x}) - W_R(\mathbf{r},\mathbf{x}) \qquad (36)$$

This dynamics is given by

$$\frac{\partial}{\partial t} W^D(\mathbf{r},\mathbf{x}) = \langle a^D(\mathbf{r}) e(\mathbf{x}) - W^D(\mathbf{r},\mathbf{x}) e(\mathbf{x})\rangle \qquad (37)$$

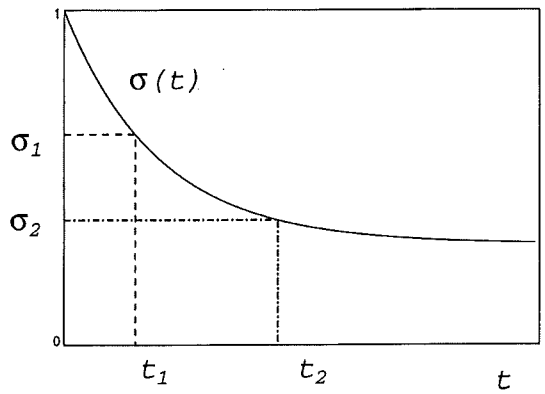

Figure 3. Relation between visual experience, developmental timing, and pattern wave-length in ocular dominance segregation. Solid line size of co-activated domains as a function of time during development (schematic). Dashed and dash-dotted lines mark the level of σ^*_{sq} and σ^*_{norm} and the corresponding points in time at which the segregation of ODCs starts respectively. If σ decreases during development the critical size σ^* determines timing and wavelength of ocular dominance segregation. A larger value of σ^* with squint then leads to an earlier segregation of larger spaced columns.

where

$$a_D(\mathbf{r}) = a_L(\mathbf{r}) - a_R(\mathbf{r}) \tag{38}$$

is the difference between the afferent activity patterns from the left and right eye. We are interested in the linearized dynamics of $W^D(\mathbf{r},\mathbf{x})$ in the vicinity of $W^D(\mathbf{r},\mathbf{x}) = 0$ and for $W_L(\mathbf{r},\mathbf{x}) \approx W_R(\mathbf{r},\mathbf{x})$ close to a stationary solution $W^\infty(\mathbf{r},\mathbf{x})$ of Eq. (9). The stability of this solution is determined by the linearized dynamics of $W^D(\mathbf{r},\mathbf{x})$. It takes the form

$$\frac{\partial}{\partial t} W^D(\mathbf{r},\mathbf{x}) = -\langle e(\mathbf{x})\rangle W^D(\mathbf{r},\mathbf{x}) + \int d^2y d^2s C^D(\mathbf{s}-\mathbf{r}) I(\mathbf{y}-\mathbf{x}) W^D(\mathbf{s},\mathbf{y}) \tag{39}$$

where

$$C^D(\mathbf{s}-\mathbf{r}) = C_L(\mathbf{s}-\mathbf{r}) - C_{LR}(\mathbf{s}-\mathbf{r}) \tag{40}$$

is defined by the correlation functions of afferent activity patterns and $I(\mathbf{y}-\mathbf{x})$ describes interactions among adjacent columns. The first term of the rhs in Eq. (39) is derived from the respective term in Eq. (37) by linearizing of $e(\mathbf{x})$ in $W^D(\mathbf{s},\mathbf{y})$ and averaging over afferent activity patterns. It is a special case of a more general expression derived in [34]. The second term follows directly from Eq. (37). Again, Eq. (39) implies a simple dynamics for the ocular dominance field $o(\mathbf{x}) = \int d^2r W^D(\mathbf{r},\mathbf{x})$

$$\frac{\partial}{\partial t} o(\mathbf{x}) = -\langle e(\mathbf{x})\rangle o(\mathbf{x}) + c^D \int d^2y I(\mathbf{y}-\mathbf{x}) o(\mathbf{y}) \tag{41}$$

where

$$c^D = \int d^2s C^D(\mathbf{s}-\mathbf{r}) \tag{42}$$

is independent of the co-ordinate $\mathbf{r}$ by translation invariance. Eq. (25) is a special case of equation Eq. (41) because $c^D = \langle p^2\rangle/2$ and $\langle e(\mathbf{x})\rangle = \sigma^2$.

According to Eq. (41), the dynamics of $o(\mathbf{x})$ depends critically on c^D. Since $\langle e(\mathbf{x})\rangle > 0$ there is always a critical value c^{*D} such that $o(\mathbf{x}) = 0$ is stable for $c^D < c^{*D}$ if the Fourier transform of $I(\mathbf{y}-\mathbf{x})$ is bounded from above and exhibits a positive maximum value. Biologically, this means that if correlations among activity patterns from the two eyes are increased beyond a certain threshold then ODCs cannot form or — when initially present — should desegregated with time.

To access how ocular dominance segregation depends on the range of intracortical interactions, we denote the range of intracortical interactions shaping the cortical response $e(\mathbf{x})$ by σ as in the simple example analysed above. If $e(\mathbf{x}) = e^\sigma(\mathbf{x})$ depends on σ then also the cortical interaction function $I(\mathbf{y}-\mathbf{x}) = I^\sigma(\mathbf{y}-\mathbf{x})$ and the average cortical activity $\langle e^\sigma(\mathbf{x})\rangle = \gamma(\sigma)$ must depend on this parameter. Whether a critical range of intracortical interactions σ^* exists is determined by the qualitative nature of this dependency.

Lets denote the maximum of the Fourier transform of $I^\sigma(\mathbf{y}-\mathbf{x})$ by $\alpha(\sigma)$. The maximal growth rate of the rhs of Eq. (41) then equals

$$\lambda_{\max} = c^D\alpha(\sigma) - \gamma(\sigma) \tag{43}$$

If $\hat{\gamma}(\sigma) = \gamma(\sigma)/\alpha(\sigma)$ is an increasing function of σ and there is a σ^* satisfying $\hat{\gamma}(\sigma^*) = c^D$ segregation will only occur if $\sigma < \sigma^*$. Furthermore the value of σ^* then increases when c^D is increased and therefore should be larger in squinters compared to normally raised animals.

It is easy to see that these conditions are typically fulfilled if cortical activity patterns are composed of locally co-activated domains shaped by intracortical interactions. First, consider the case of the model Eqs. (11), (12) and (17). In this case $\alpha(\sigma) \propto \sigma^0$ and $\gamma(\sigma) \propto \alpha\sigma^2$. As a consequence $\hat{\gamma}(\sigma^*)$ increases unbounded and $\sigma^* \propto \sqrt{c^D}$ depends on between eye correlations. If we assume $\alpha(\sigma) \propto \sigma^0$ then σ^* will exists in general if the average cortical activity $\gamma(\sigma)$ increases with increasing σ. In the model Eqs. (11), (12) and (17) this is fulfilled because the average cortical activity is proportional to the area of cortex activated by each stimulus. $\gamma(\sigma)$ will in general increase with σ if the average cortical activity is proportional to the average area of cortex activated and if this area increases with increasing σ. If intracortical interactions shape cortical activity patterns into the form of locally co-activated domains this will typically occur if the dimensions of the domains are proportional to the range of intracortical interactions. Hence σ^* will typically exist and depend on c^D if $\alpha(\sigma)$ depends only weakly on σ.

In order to complete the argument we must therefore show that a weak dependence of $\alpha(\sigma)$ on σ is expected in general and not a special feature of the model Eqs. (11), (12) and (17). To this end it is useful to revisit Miller's derivation [34] of the Hebbian term in Eq. (39). This term is obtained by linearizing the cortical response $e^\sigma(x)$ in $W^D(\mathbf{s},\mathbf{y})$. Assuming that the cortical response is a unique and differentiable functional

$$e^\sigma(\mathbf{x}) = N^\sigma[\mathbf{x}|i(\mathbf{y})] \tag{44}$$

of the pattern of afferent input

$$i(\mathbf{y}) = \int d^2s a_L(\mathbf{s}) W_L(\mathbf{y},\mathbf{s}) + a_R(\mathbf{s}) W_R(\mathbf{y},\mathbf{s}) \tag{45}$$

this yields

$$\begin{aligned} e^\sigma(\mathbf{x}) &= N^\sigma[\mathbf{x}|i_0(\mathbf{y})] + \\ &\quad \int d^2y L^\sigma_{i_0(z)}(\mathbf{x},\mathbf{y}-\mathbf{x})(i(\mathbf{y}) - i_0(\mathbf{y})) + \dots \\ &= N^\sigma[\mathbf{x}|i_0(\mathbf{y})] + \\ &\quad \int d^2y L^\sigma_{i_0(z)}(\mathbf{x},\mathbf{y}-\mathbf{x}) \int d^2s a^D(\mathbf{s}) W^D(\mathbf{s},\mathbf{y}) + \dots \end{aligned} \tag{46}$$

where

$$i_0(\mathbf{y}) = \frac{1}{2} \int d^2s (a_L(\mathbf{s}) + a_R(\mathbf{s}))(W_L(\mathbf{s},\mathbf{y}) + W_R(\mathbf{s},\mathbf{y})) \tag{47}$$

is the pattern of afferent input if $W_L(\mathbf{s},\mathbf{y}) = W_R(\mathbf{s},\mathbf{y})$ and $i(\mathbf{y})-i_0(\mathbf{y})$ is the deviation from this pattern resulting from $W_D(\mathbf{s},\mathbf{y}) \neq 0$. The second term in the expansion Eq. (46) represents a general, space-variant, linear operator which depends itself on the symmetrized input $i_0(\mathbf{y})$. Approximating $e^\sigma(\mathbf{x})$ in $\langle a(\mathbf{r}) e^\sigma(\mathbf{x})\rangle$ by the first two terms in the expansion Eq. (46) one finds

$$\langle a(\mathbf{r}) e^\sigma(\mathbf{x})\rangle \approx \frac{1}{2}\left\langle \int d^2s d^2y a^D(\mathbf{r}) a^D(\mathbf{s}) L^\sigma_{i_0(z)}(\mathbf{x},\mathbf{y}-\mathbf{x}) W^D(\mathbf{s},\mathbf{y}) \right\rangle \tag{48}$$

If $a^D(\mathbf{r})$ and $a^S(\mathbf{r}) = a_L(\mathbf{r}) + a_R(\mathbf{r})$ are statistically independent this reduces to the first term in the rhs of Eq. (39) where

$$I^\sigma(\mathbf{y}-\mathbf{x}) = \frac{1}{2}\langle L^\sigma_{i_0(z)}(\mathbf{x},\mathbf{y}-\mathbf{x})\rangle \tag{49}$$

Eq. (49) determines the dependence of $I(\mathbf{y}-\mathbf{x})$ on σ, the range of intracortical interactions, given the mapping of afferent inputs $i(\mathbf{y})$ onto cortical activity patterns and the statistics of symmetrized patterns of input $i_0(\mathbf{z})$. In order to analyse this dependence we must specify what it means to change only the range of intracortical interactions while leaving all other aspects of the intracortical propagation of activity unaltered. We define such a change of the cortical response by the requirement that when the range of intracortical interactions is changed from σ_1 to σ_2 then the new response to an arbitrary pattern of inputs should resemble the former response to the spatially rescaled pattern of inputs. More precisely we require

$$N^{\sigma_2}\left[\frac{\sigma_1}{\sigma_2}\mathbf{x}|i(\mathbf{y})\right] = N^{\sigma_1}[\mathbf{x}|i(\sigma_1/\sigma_2\mathbf{y})] \tag{50}$$

which ensures in particular that changing the range of interactions leaves the dynamic range of cortical responses unaffected. The expansion Eq. (46) can fulfill this requirement in general if and only if

$$L^\sigma_{i_0(z)}(\mathbf{x},\mathbf{y}-\mathbf{x}) = \frac{1}{\sigma_2} L^\sigma_{i_0(z/\sigma)}\left(\frac{\mathbf{x}}{\sigma}, \frac{\mathbf{y}-\mathbf{x}}{\sigma}\right) \tag{51}$$

which implies that $I^\sigma(\mathbf{y}-\mathbf{x})$ satisfies

$$I^\sigma(\mathbf{y}-\mathbf{x}) = \frac{1}{2}\frac{1}{\sigma_2}\left\langle L^1_{i_0(z/\sigma)}\left(\frac{\mathbf{x}}{\sigma}, \frac{\mathbf{y}-\mathbf{x}}{\sigma}\right)\right\rangle \tag{52}$$

Eq. (52) determines the behavior of $\alpha(\sigma)$. First, let us assume that symmetrized, afferent input patterns that are spatially scaled versions of one another have equal probability density. Then the interaction function satisfies

$$I^\sigma(\mathbf{y}-\mathbf{x}) = \frac{1}{\sigma_2} I^1\left(\frac{\mathbf{y}-\mathbf{x}}{\sigma}\right) \tag{53}$$

and its Fourier transform fulfills

$$\tilde{I}^\sigma(k) = \tilde{I}^1(\sigma k) \tag{54}$$

i.e. $\alpha(\sigma) \propto \sigma^0$. In general $\alpha(\sigma)$ may exhibit a nontrivial dependence on the range of intracortical interactions. However, Eq. (52) still implies that for a large class of ensembles of afferent activity patterns for which the probability density of input patterns weakly depends on their spatial scale $\alpha(\sigma)$ will only weakly depend on σ.

We therefore conclude that the existence of a critical range of intracortical interactions σ^* and its dependence on correlations between afferent activity patterns found in the model Eqs. (11), (12) and (17) is representative for a large class of models. The critical dependence of ODC segregation on the range of intracortical interactions basically reflects that the strength of Hebbian and non-Hebbian synaptic modifications will in general scale differently with the range of intracortical interactions.

6. Discussion and conclusions

We have analysed a model for the emergence of patterns of ODCs during development of the primary visual cortex. In this model, the dynamics of ocular dominance segregation is controlled by the size σ of CCDs. If this quantity is larger than a critical value ODCs do not form. The occurrence of a critical size of CCDs reflects the interplay of

Hebbian and non-Hebbian, activity-dependent synaptic modifications which induce the preservation of the total synaptic strength onto a given cortical neurone and is characteristic for a large class of such models. The critical size of CCDs itself depends on parameters of visual experience and is predicted to be larger with squint than with normal visual experience. This dependence implies the emergence of larger spaced columns in squinters compared to normally raised cats, if the size of CCDs decreases during development.

The critical dependence of the model on the size of CCDs has a simple intuitive interpretation. The existence of a critical size of CCDs derives from the fact that in activity-dependent development, lateral co-operation has a homogenizing influence on single neurone selectivities. Because a single cell is forced to develop similar specificities as the cells within the range of a typical CCD, domains of a large size make it harder for an individual neurone to specialize in detecting any particular stimulus feature. If one considers an extreme situation in which CCDs are so large that either the whole visual cortex is homogeneously active or inactive ODCs cannot form.

Our quantitative theory shows that the transition to a situation in which columns do form is not gradual but occurs at a discrete instability at a critical size of CCDs. The critical size of CCDs measures the strength of the tendency of individual neurones to specialize in processing information from only one eye, by the minimal range of co-operative interactions that is sufficient to keep any individual neurone from breaking the symmetry between left and right eye inputs. Since with squint the tendency of individual neurones to specialize in processing information from only one eye must be much stronger than under normal conditions only a stronger homogenizing force, i.e. a larger range co-operative interaction, is capable of keeping any individual neurone from specializing in a single eye. Hence σ^* is larger with squint.

Our analysis demonstrates that this qualitative behaviour is to be expected as long as cortical activity patterns are strongly shaped by intracortical interactions. A discrete instability of the kind that underlies the present theory was first studied by Ritter and Schulten [46] for an abstract mapping between spaces of different dimensionalities (see also [42]). The spatio-temporal continuous stability analysis employed in the present study was developed previously [58, 47] and generalizes and simplifies the stochastic approach used in [46]. It gives results that are valid independently of the particular ensemble of stimuli and enables to calculate the instability threshold as a function of afferent correlations. Bauer and coworkers recently explored a complementary method to characterize the behaviour of models for the formation of column patterns [3, 4]. Their results also indicated that discrete instabilities are ubiquitous in models of neural pattern formation.

Presently, there is only indirect experimental evidence on the nature of cortical activity patterns during development. Nevertheless, it is likely that activity patterns in the developing visual cortex take the shape of locally co-activated domains. It has been established that during development cortical neurones form a dense network of lateral connections early on. The developing cortical network initially appears to be linked electrically and chemically through gap junctions [25]. Later, interactions are increasingly mediated by chemical synapses whereby the development of excitatory connections precedes the development of inhibitory connections [17, 53]. Furthermore, Katz et al. have shown in a slice preparation that at the time of eye opening focal activation of cortical neurones initiates a lateral spreading of activity over distances of several hundred μm [41]. All of this is consistent with the assumption that neurones in the developing visual cortex are typically not activated in isolation but participate in the concurrent activity of locally defined groups. Preliminary evidence that this might indeed be the case comes from a recent analysis of spontaneous activity in the developing primary visual cortex in ferrets: Chiu and Weliky [7] were able to demonstrate that patterns of correlated activity are present before the formation of cortical maps and that their centre to centre spacing is in the order of 1 mm.

Furthermore, several independent lines of evidence indicate that the size of CCDs decreases during development. For instance, the experiments of Katz et al. indicate that the range over which activation spreads within developing cortical circuits decreases after the time of eye opening [12]. In kitten visual cortex, the receptive field sizes of neurones decrease during the first weeks of life [6, 14]. Because in retinotopically organized areas, receptive field size and the size of CCDs are proportional to each other this suggests that σ decreases during development. Second, the range of local intracortical connections linking a neurone to cells in its immediate vicinity (in contrast to long-range intracortical connections) also appears to

decrease during development [12]. Because these connections probably mediate a lateral spreading of activity within cortex, decreasing their range should lead to a decreasing size of CCDs. Third, inhibitory intracortical interactions mature later than excitatory interactions [17, 53]. Because inhibitory interactions rather lead to more localized activity patterns this observation is also compatible with the assumption that σ effectively decreases during development. Fourth, in area 17 of cat visual cortex, the range of thalamocortical axon arborizations significantly decreases during the first few weeks of development [2]. This may also contribute to a decreasing size of CCDs. In this respect, it is a very interesting observation that area 18 in which geniculocortical axon arbours expand (rather than decrease) during development [16] does not exhibit a different spacing of ODCs in squinting compared to normal cats [32]. Since the decrease of cortical receptive field size, the range of local intracortical interaction, and the extend of thalamocortical axon arborizations probably all derive from an activity-dependent refinement of connections within the cortex [26] our theory suggests that the refinement of cortical circuitry itself drives the network through the collective instability analysed in the previous sections.

Concerning the mechanisms which regulate the total synaptic strength of afferent connections in the developing cortex experimental evidence is also sparse. Theoretically, it has long been noted that purely Hebbian rules of synaptic plasticity are intrinsically unstable and in mathematical models typically lead to an unbounded growth of synaptic strengths [5, 37, 38]. A variety of mechanisms has been proposed to stabilize the synaptic dynamics by additional non-Hebbian components (reviewed in [35, 37]). In the developing cortex, one attractive possibility is that a competition of afferent axons for cortically released trophic factors constrains the total strength of afferent connections (see [43]). Another interesting proposal states that a sliding threshold level of activity determines whether synapses undergo long-term potentiation (LTP) or long-term depression (LTD). If this threshold is itself regulated by the past history of activity such a mechanism can in principle stabilize the total synaptic strength [5, 37]. As a third possibility the dependence of LTD- and LTP-induction on the precise timing of pre- and post-synaptic spike activity may lead to an emergent stabilization of total synaptic strength [27, 50]. However, the exact nature of the interactions which stabilize synaptic strength in the developing visual cortex has still to be identified and it seems likely that the biological system relies on a multiplicity of functionally redundant processes. We have therefore not attempted to model a particular mechanism for synaptic stabilization in detail.

Contrasting the observation that a basic parameter of visual cortical organization, the spacing of ODCs, depends on visual experience, a series of recent experimental observations suggest that the role of experience in the development of cortical columns is more limited than previously expected [10, 11, 18, 28]. Observations by Bonhoeffer and coworkers [18, 28] in area 18 and also a recent study by Crair et al. in area 17 [10] indicate that visual experience is not necessary for interocularly matched orientation preference maps in the visual cortex. In addition, Crowley and Katz [11] demonstrated that in binocularly enucleated ferrets thalamocortical afferents form patches in area 17, suggesting an ocular-dominance-segregation-like process in the absence of retinal input. It is important to realize that our explanation of the experience-dependent selection of ODC spacing is fully consistent with these observations. Theoretical analyses as the one presented here show that the formation of cortical columns by mechanism of synaptic plasticity is primarily determined by the correlational structure of afferent activity patterns (for review see [36]). The observed patterning of visual cortical columns in the absence of visual input can therefore be explained by the occurrence of structured patterns of spontaneous activity at the LGN level. Indeed, Weliky and Katz recently demonstrated that the LGN generates a richly structured ensemble of spontaneous activity patterns [57]. In the absence of retinal input, the frequency of spontaneous bursts can even increase suggesting a compensation for the missing retinal input. Taken together, these results rather indicate that visually driven patterns of neuronal activity are complemented and may even be substituted by spontaneously generated activity patterns than imply that the formation of columnar patterns is independent of afferent activity patterns including those mediated by visual stimuli. The ensemble of activity patterns that presumably guide the development of ODCs in the brains of normal and squinting animals is therefore suggested to be composed of both spontaneous and visually driven activity.

The mechanism for changing ODC spacing in squinting animals identified here can be tested experimentally in several independent ways. First, the central result of our theory is that a larger

spacing of ODCs is achieved by an earlier emergence of the columnar structure. Therefore the most direct test is to compare the kinetics of ocular dominance segregation in normal and squinting animals. A first study comparing the kinetics of ocular dominance segregation in normal and squinting animals found that under both conditions a pattern of functional ODCs is present at an age of 3 weeks but appears absent one week earlier [44]. This indicates that the timing difference to be detected is in the order of days. Second, our proposed mechanism implies hysteresis. If squint is induced after ODCs have formed, the spacing should be the same as in normal animals. By the same token, squint should not cause a comparable change of ODC spacing in macaque monkey visual cortex since in this species the pattern of ODC appears to be fairly developed at birth [22]. Also it will be important to directly test whether the size of CCDs actually decreases during development. This can be done by chronic multielectrode recording as demonstrated by Chiu and Weliky [7].

Acknowledgements

It is a pleasure for us to thank K. Miller, W. Singer and our colleague H.-U. Bauer for fruitful discussions. This work was supported by the 'Deutsche Forschungsgemeinschaft', the 'Wissenschaftsgemeinschaft-Gottfried-Wilhelm-Leibniz', and the 'Max-Planck-Gesellschaft'.

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