Horizontal Interactions in Cat Striate Cortex: III. Ectopic Receptive Fields and Transient Exuberance of Tangential Interactions

H. J. Luhmann¹, J. M. Greuel² and W. Singer³
¹Universität Köln, Physiologisches Institut, Albertus-Magnus-Platz, D-5000 Köln 41, FRG
²Tropenwerke GmbH, Berliner Str. 156, Postfach 80 10 60, 5000 Köln 80, FRG
³Max-Planck-Institut für Hirnforschung, Deutschordenstr. 46, D-6000 Frankfurt a.M. 71, FRG

Key words: visual cortex, receptive fields, development, deprivation

Abstract
In this study the developmental changes of intracortical connectivity are related to changes of cortical receptor fields (RFs). The RFs of striate cortex neurons of 4- to 8.5-week-old kittens, reared under normal conditions (NR) or in a selective visual environment (SE), were analysed quantitatively and compared with adult cats. To unmask weak inputs from outside the conventional RF (CRF), cell excitability was raised by iontophoretic application of glutamate (GLU) and/or bicuculline methiodide (BIC) or by light stimulation of the CRF. Both the dominant discharge region (DDR) and the total RF (TRF) area were significantly larger in NR and SE kittens than in adult cats. Moreover, in kittens 18% of the cells had additional ectopic fields that were excitatory, had similar orientation preferences as the CRF, and ranged 4° to 23° from the centre of the CRF. In 74% of the cases the ectopic fields were direction-selective and 70% of them preferred stimuli moving toward the CRF. Ectopic fields occurred mainly in supragranular cells, were similarly frequent in simple and complex cells and slightly more frequent in SE (20.7%) than in NR (13.3%) kittens. In adult cats only one of 83 cells tested had an ectopic field. It is concluded that the age-dependent decrease in the RF size, the laminar distribution of cells having an ectopic RF, and the numerical reduction of these cells with age correlate well with the organization and postnatal pruning of tangential projections, suggesting that these contribute to the elaboration of specific response properties. Moreover, the authors infer from the early presence and from the selectivity of ectopic fields that the system of horizontal intrinsic connections mediates far-reaching, excitatory interactions between cortical neurons with similar functional properties and serves as a substrate for the processing of global aspects of visual patterns.

Introduction
The existence of far-reaching tangential connections in striate cortex suggests that the area in the visual field from which neuronal responses can be influenced exceeds that predicted by the spatial overlap of thalamo-cortical terminal arbors (for review see Ferster and Lindström, 1984; Nelson and Frost, 1985). Therefore, influences mediated by intrinsic tangential connections ought to come from regions outside the conventional receptive field (CRF). Such long range effects have been searched for in numerous studies, but most authors agree that they are weak and infrequent. The peripheral stimuli either had to be very large and moving or they had to be presented in conjunction with stimuli placed within the CRF in order to show an inhibitor or facilitatory influence on the cellular activity (Fries and Albus, 1973; Gulyás et al., 1987; Hammond and MacKay, 1981; Jones, 1970; Maffei and Fiorentini, 1976; Nelson and Frost, 1985; Orban et al., 1987; Rizzolatti and Camarda, 1977). It has been further suggested that some of the very large CRFs can only be accounted for if one assumes a contribution of far-reaching tangential connections. This has been proposed to be the case for the very elongated fields of layer VI cells (Gilbert, 1977; Gilbert and Wiesel, 1983) and particularly for wide RFs consisting of several excitatory subregions (Nelson and Frost, 1985; Pollen and Ronner, 1975). In the preceding two papers (Luhmann et al., 1990a, b), the author presented data which indicate that tangential connections are more numerous and mediate excitatory synaptic actions more effectively over larger distances in kittens than in adult cats. This suggests that remote influences on cortical responses might be more readily detectable in striate cortex of kittens. This conjecture receives direct support from an earlier study that was performed in kittens raised with selective visual experience (Singer and Tretter, 1976). In this study

Correspondence to: W. Singer, as above
Received 11 April 1989, revised 5 December 1989, accepted 11 December 1989
neurons were encountered which possessed, in addition to the CRF, further ectopic regions clearly separated by 10° to 20°C from the centre of the CRF. These ectopic fields produced strong responses even when stimulated alone and based on theoretical arguments it was concluded that they resulted from experience-dependent selective stabilization of intracortical connections (Singer, 1985a, b).

In the present study we investigated the possibility that these far-reaching tangential interactions are also more readily demonstrable in NR kittens than in adult cats. For that purpose we quantitatively analysed the receptive fields (RFs) of a large number of cells in striate cortex of NR kittens, of kittens reared with selective visual experience, and of NR adult cats.

Part of this work has been presented in abstract form (Luhmann et al., 1987).

Materials and methods

**Animals and procedure**

This study is based on 20 cats. Their respective ages and rearing conditions are summarized in Table 1.

Eight kittens (NR-A – NR-H) and five adult cats (NR-J – NR-M) were bred in our cat colony and reared under normal conditions. Seven more kittens (SE-A – SE-G) were transferred into a dark room before natural eye opening and from the middle of the fifth postnatal week onwards were exposed selectively to vertical gratings of constant spatial frequency. For that purpose kittens were transferred every day for 1–6 h to a 2 m wide and 1.1 m high cylinder, which was covered inside with a high contrast pattern of vertically oriented black and white stripes. During exposure kittens wore masks constructed of polyurethane foam which were fixed to the arms of a carousel similar to that described by Held and Hein (1963). This procedure prevented the kittens from seeing their paws and the horizontal border of the vertical pattern and assured constant viewing distance of 36 cm from the cylinder. At this distance, the black bars covered a visual angle of 3° and the distance between them was 5°. Total exposure time ranged from 31 to 67 h (Table 1). To minimize the influence of any other visual stimulation, animals were transported from the dark room to the exposure apparatus in a small light-impermeable box and masks were fixed on the kittens’ heads in complete darkness. All animals reared in a selective visual environment (SE-A – SE-G), were anaesthetized in the dark room and then prepared for electrophysiological recordings.

**Preparation and electrophysiology**

For surgical preparation, animals received i.m. injections of 0.01 mg atropine sulphate and a mixture of 30 mg/kg ketamine hydrochloride and 15 mg/kg xylazine hydrochloride. During further preparation and recording, anaesthesia was maintained by artificial ventilation with a mixture of N₂O/O₂ (70:30) and by a continuous i.v. infusion of 6% pentobarbital (1.8 mg/kg h) or by adding 0.2–0.4% halothane. At the end of all surgical procedures, the animals were paralyzed with an i.v. infusion of 0.7 mg/kg h hexacarboncholine bromide. A 5% glucose-Ringer’s solution (5:1) was given continuously at a rate of 3–6 ml/h through an orally inserted gastric catheter. During recording, EEG, heart rate, body temperature and the expiratory CO₂ were monitored continuously. Rectal temperature was held constant at 37.5°C and tidal volume and rate of respiration were adjusted to yield end-tidal CO₂ concentrations between 3.5 and 4%. The pupils were dilated with atropine, the nictitating membranes retracted with neosynephrine and the corneas protected with contact lenses containing artificial pupils of 2 mm diameter. The refractive state of both eyes was determined by a refractometer and refractive errors were corrected by appropriate spectacle lenses. With a fundus camera, the retinal landmarks were plotted on a tangent screen located 1.14 m in front of the cat’s eye plane. Single cell activity was recorded with a micropipette containing 1.5 M potassium citrate. For iontophoretic application of drugs, a seven-barrelled micropipette was glued to the recording electrode. The cortex was covered with silicone or 4% agar and the skull opening sealed with bone wax to avoid drying out and to minimize pulsations. Multibarrelled electrodes were filled with 0.1 M glutamate (GLU), pH 8.5, 5 mM bicuculline methiodide (BIC), pH 3.0, and 2.0 M NaCl which served as balance. DC resistance of the recording electrodes ranged from 10 to 30 MΩ and electrode signals were fed into a conventional PET-equipped input stage of an amplifier system.

**Visual stimulation and iontophoresis**

Receptive fields were qualitatively analysed with hand projected light stimuli of variable width and length. The background luminance was 0.2 cd/m² and the stimulus luminance 22 cd/m². For detailed quantitative investigation, the authors used electronically controlled light stimulators and peristimulus-time histograms (PSTHs) were computed on-line from responses to repeated stimulus presentations. Neurons with little or no spontaneous activity were often detected by moving a stimulus with properties preferred by the last recorded cell continuously over the tangent screen. In order to reveal subliminal facilitatory and inhibitory inputs to the recorded cells and to detect remote influences from outside the CRF, the authors used the dual stimulation technique (Bishop et al., 1971a; Orban et al., 1979) or

<table>
<thead>
<tr>
<th>Animal</th>
<th>Age [weeks]</th>
<th>Visual experience [hours]</th>
<th>Number of qualitatively analysed cells</th>
<th>Number of quantitatively analysed cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR-A</td>
<td>4</td>
<td>–</td>
<td>31</td>
<td>9</td>
</tr>
<tr>
<td>NR-B</td>
<td>4.5</td>
<td>–</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>NR-C</td>
<td>5</td>
<td>–</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>NR-D</td>
<td>5</td>
<td>–</td>
<td>33</td>
<td>18</td>
</tr>
<tr>
<td>NR-E</td>
<td>5</td>
<td>–</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>NR-F</td>
<td>5</td>
<td>–</td>
<td>25</td>
<td>5, 7†</td>
</tr>
<tr>
<td>NR-G</td>
<td>5.5</td>
<td>–</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>NR-H</td>
<td>7</td>
<td>–</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>NR-I</td>
<td>adult</td>
<td>–</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>NR-J</td>
<td>adult</td>
<td>–</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>NR-K</td>
<td>adult</td>
<td>–</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>NR-L</td>
<td>adult</td>
<td>–</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>NR-M</td>
<td>adult</td>
<td>–</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>SE-A</td>
<td>6</td>
<td>31</td>
<td>56</td>
<td>7</td>
</tr>
<tr>
<td>SE-B</td>
<td>6.5</td>
<td>40</td>
<td>60</td>
<td>16</td>
</tr>
<tr>
<td>SE-C</td>
<td>7</td>
<td>10</td>
<td>49</td>
<td>14</td>
</tr>
<tr>
<td>SE-D</td>
<td>7</td>
<td>46</td>
<td>49</td>
<td>7</td>
</tr>
<tr>
<td>SE-E</td>
<td>7</td>
<td>50</td>
<td>65</td>
<td>15</td>
</tr>
<tr>
<td>SE-F</td>
<td>8</td>
<td>60</td>
<td>35</td>
<td>12</td>
</tr>
<tr>
<td>SE-G</td>
<td>8.5</td>
<td>67</td>
<td>67</td>
<td>11</td>
</tr>
</tbody>
</table>

The age of normally reared (NR) animals and kittens raised in a selective visual environment (SE) at the time of recording is given in weeks. Cuts older than 6 months were classified as adult. For animals reared in a restricted visual environment, the total exposure time is indicated in hours. The last two columns give the number of qualitatively and quantitatively analysed cells for each animal. Units, which were investigated with stationary stimuli, are indicated by * (see kitten NR-F).
iontophoretically applied GLU (Hess and Murata, 1974) and/or BIC (Sillitio, 1975) through one or several of the iontophoresis barrels. The retaining current for GLU was +10 nA and for BIC ~10 nA. Ejection currents ranged from −5 to −20 nA for GLU and from +5 to +50 nA for BIC.

**Cell classification and quantitative analysis**

Whenever a neuron was isolated, the following parameters were routinely determined: (i) recording depth from cortical surface; (ii) the cell’s spontaneous activity; (iii) the orientation, the movement velocity and direction, and the length of the stimulus that gave maximal responses; (iv) the vigour of the left and right eye response to an optimal stimulus, using the criteria of Greuel et al. (1987) for classification; (v) the ocular dominance (OD) according to a scale of 5 classes (1 and 5: monocular; 2 and 4: binocular with unilateral bias; 3: binocular without bias); (vi) the spatial structure of the RF (simple/complex) as determined from responses to stationary stimuli of optimal orientation; (vii) the orientation tuning in steps of 22.5°; and (viii) the size of the RF. Once this analysis was completed, visual stimuli of different lengths and orientation were moved over a wide area of the visual field in search for any remote influences on the cell’s discharge behaviour. Moving stimuli were used because they provide a more accurate estimate of the spatial organization of the RF (Kulikowski and Bishop, 1981) and are more successful in revealing remote responses from outside the CRF than stationary stimuli (Andrews and Pollen, 1979). However, in seven neurons (Table 1, kiten NR-F) the authors also analysed in detail the RFs with stationary stimuli positioned at different locations in the visual field. To reveal weak influences, responses were averaged from up to 50 stimulus passages. The following RF dimensions were defined for quantitative comparison: (i) width of the excitatory dominant discharge region (DDR) which gave the strongest response in the PTH; (ii) width of the total receptive field (TRF) including all excitatory and inhibitory subregions; and (iii) existence of an ectopic field. The criteria were that the additional field was clearly segregated from the CRF and separated by more than 4° from the CRF (Singer and Tretter, 1976).

**Statistical analysis**

A Lilliefors-test (Lilliefors, 1967) on normality and a linear or nonlinear regression analysis were performed to analyse the relation between RF size and RF eccentricity. The significance of the correlation coefficient was tested with a t-test. Groups were compared with a χ²-test or a nonparametric Wilcoxon-Mann-Whitney U-test with different significance levels.

**Results**

**Comparison of RF size in kittens and adult cats**

The authors analysed a total of 608 neurons in the primary visual cortex of eight NR kittens, five NR adult cats and seven SE kittens (Table 2).

A detailed quantitative analysis of the RF dimensions was carried out on 204 units. In 144 cells (71%), the RF structure was examined only with moving light bars. Stationary stimuli were used in another seven of the investigated neurons (3%). In order to increase the probability of detecting weak influences from outside the CRF the authors applied iontophoretically BIC to 18 of the cells (9%) and a combination of GLU and BIC to 27 units (13%). In eight neurons (4%), the cell’s activity was increased by continuously moving a conditioning stimulus within the CRF. The CRFs of all units were located within 20° of the area centralis.

In NR kittens the mean width of the DDR was significantly smaller (U-test, p < 0.001) in simple (2.8 ± 1.4° SD, n = 9) than in complex cells (5.7 ± 1.8° SD, n = 20). No significant difference was found between the two cell groups with respect to the mean width of the TRF (p < 0.01 level; TRF width of simple cells: 5.9 ± 4.5° SD, n = 10; TRF width of complex cells: 6.2 ± 1.8° SD, n = 21). In SE kittens, the DDR width was also significantly smaller (p < 0.001) in simple cells (1.5 ± 0.9° SD, n = 34) than in complex cells (3.0 ± 2.1° SD, n = 47); however in contrast to NR kittens, the mean width of the TRF was also significantly smaller (p < 0.001) in simple (2.7 ± 1.9° SD, n = 34) than in complex cells (4.7 ± 2.8° SD, n = 47). In SE kittens, all parameters referring to RF size of both simple and complex cells gave significantly smaller values than in NR kittens. For simple cells the DDR and TRF values were different at the p < 0.01 level; for complex cells DDR values differed at the p < 0.001 level and TRF values at the p < 0.01 level. Iontophoretic application of GLU and BIC caused only a small increase in the mean width of the DDR and TRF, which neither in simple nor in complex cells reached the level of statistical significance (for all parameters: p > 0.1).

In NR adult cats, DDR and TRF widths were smaller than in NR kittens both for simple and complex cells. The DDR and the TRF of simple cells measured 1.3 ± 0° SD (n=23) and 2.6 ± 1.7° SD (n=23), respectively and differed from the corresponding values in NR kittens at the p<0.01 level. For complex cells of adult cats, the width of the DDR and TRF are taken as identical, because the authors were not able to demonstrate multiple excitatory subregions, or inhibitory sidebands, as they have been described for a small number of complex cells by other authors (Albus and Fries, 1980). The fields of complex cells in adult cats measured 3.6 ± 1.6° SD (n=16) and differed from those in NR kittens at the p<0.01 (DDR) and p<0.001 (TRF) level.

**Responses from outside the conventional receptive field**

Responses separated by more than 4° from the centre of the CRF were detectable only with moving stimuli. In seven neurons, the region around the CRF was thoroughly explored with stationary stimuli, but none of these cells showed a response to ectopic stimuli.

In kitten striate cortex, 18% (n=28) of the units had one or two
ectopic fields. The percentage of neurons with an ectopic response was higher in SE kittens (20.7%, n=17) than in NR kittens (13.3%, n=11), but this difference was not significant (p>0.05, χ²-test). Of the cells with an ectopic field, ten (36%) had a CRF of the simple and 18 (64%) of the complex type. One simple and two complex cells had two ectopic fields. In 45 quantitatively analysed neurons in SE and NR kittens, the authors raised the discharge level with iontophoretic application of GLU and BIC or with continuous stimulation of the CRF in order to detect remote inhibitory influences. However, in no case could they demonstrate any far-reaching suppressive effects from regions outside the CRF. All ectopic fields were excitatory.

An example of a simple cell with a one direction-selective ectopic field is shown in Figure 1. The ectopic field (open arrow in Fig. 1A) had a diameter of 4.7° and was located 14.8° below the centre of the CRF. The optimal stimulus of the CRF was a horizontal oriented bar, but during the application of iontophoretically applied BIC, responses to an orthogonal, vertical stimulus could also be obtained (Figure 1B). The ectopic field was strongly orientation- and direction-selective and responded only to a horizontal stimulus moving toward the CRF (Fig. 1A).

As illustrated in Figure 2, a cell could also have two ectopic fields. This cell had a complex CRF, responded strongest to an upward moving horizontal bar (PSHT A in Fig. 2), and was broadly tuned. The CRF was 15.5° wide, 12° long and located at an eccentricity of 17°. The spatial organization of the RF was investigated quantitatively during iontophoretic application of BIC (+5 nA) and by stimulation with optimal and nonoptimal oriented bars of different lengths. In addition to the CRF, the neuron had two ectopic fields, which were located 16° left (field 1 in RF plot of Fig. 2) and 13° right (field 3) from the centre of the CRF (field 2). Ectopic field 1 had a diameter of 4.5°.
and its centre was situated 5° from the area centralis. Ectopic field 3 was 2° wide and located at an eccentricity of 30°. Both ectopic fields were highly direction-selective and both responded only to a vertical stimulus, which moved in the direction toward the CRF. The size of the ectopic fields ranged from 0.3 to 5.8° (mean: 2.2 ± 1.4° SD, n = 31) and did not differ for cells with simple or complex CRFs. Of the 31 ectopic fields, 84% (n = 26) were orientation selective and 88% (n = 23) of these had the same orientation preference as the CRF. In the remaining three cells, the orientation preferences between the ectopic and the conventional field differed between 45° and 90°. Seventy-four percent (n = 23) of the ectopic fields had a pronounced direction selectivity and 70% (n = 16) of these preferred stimulus movements towards the CRF. The CRFs of the 28 cells with an ectopic field showed direction selectivity in 71% (n = 20), and in 45% of these units, the CRF preferred the same stimulus direction as the ectopic field. Ocular dominance was determined for ten ectopic fields and in seven of these was found to be similar to that of the CRF.

The distances between ectopic fields and the CRF are plotted in Figure 3A as a function of the retinal eccentricity of the CRF. Statistical analysis revealed no significant linear relationship between the two parameters (r-test for correlation, p > 0.1). There was, however, an indication that particularly distant ectopic fields were more frequent in cells with complex rather than simple CRFs. The mean distance of ectopic responses was significantly larger (U-Wilcoxon-test, p < 0.05) in cells with complex CRFs (12.2 ± 1.1° SD) than in cells with simple CRFs (7.9 ± 3.1° SD). Moreover, the data indicate that iontophoretic application of BIC and GLU increased the probability to detect remote influences (Fig. 3B). Ectopic fields of cells, treated with BIC and/or GLU were on the average located more distant from the centre of the CRF (cells with simple CRF: 11.3 ± 3.2° SD; cells with complex CRF: 15.5 ± 1.8° SD) than in untreated neurons (cells with simple CRF: 6.7 ± 2.0° SD; cells with complex CRF: 11.1 ± 5.0° SD). However, this difference only reached the level of significance in cells with simple CRF (U-Wilcoxon-test, p < 0.05).

Cells with ectopic receptive fields were encountered preferentially within the first 800 μm of each penetration, suggesting that they are located mainly in supragranular layers. Of all the units analysed between 200 and 800 μm, which corresponds approximately to layers II and III, 11% had an ectopic field, while this was the case for only 5% of the cells recorded between 800 and 1400 μm. The responses obtained from the ectopic fields were more variable than those elicited from the CRF. Occasionally even strong responses from ectopic fields would suddenly disappear for a few minutes and reappear as unpredictably as they vanished. These temporal variations were unrelated to any external parameters that the authors could control such as the level of halothane anaesthesia.

In primary visual cortex of adult cats, only one of 83 investigated neurons had an ectopic field (Fig. 4). This ectopic field was located 14° from the centre of the CRF and had a diameter of 2°. The CRF and the ectopic field both preferred a horizontal stimulus (PSTH B–E
in Fig. 4). Stimuli that were orthogonal to the preferred orientation evoked no response from the ectopic field and only an inhibitory response from the CRF (see arrows in PSTH G of Fig. 4). This suppressive influence on the cell’s resting discharge level by a nonoptimal oriented stimulus passing over the CRF has been reported previously (Sillito, 1979) and might be mediated by local inhibitory lateral interactions between neighbouring cells having different orientation preferences (‘cross-orientation inhibition’; for review see Sillito, 1984). The ectopic field and the CRF differed in their direction selectivity. Whereas a response from the CRF could be evoked only with a downward moving stimulus (PSTH C–E), the ectopic field showed a preference for an upwards moving bar. Thus, as in kittens, this ectopic field also responded preferentially to a stimulus moving toward the CRF (PSTH B).

Discussion

Postnatal changes in receptive field dimensions

The mean values of the RF dimensions found in the present study are in agreement with those described in earlier reports both for kitten (Albus and Wolf, 1984; Braastad and Hegelund, 1985; Imbert and Buissere, 1975) and adult cat visual cortex (Albus, 1975; Hegelund, 1981a, b; Palmer and Davis, 1981; Rose, 1977). Also in agreement with earlier reports (Braastad and Hegelund, 1985; Hubel and Wiesel, 1962; Palmer and Davis, 1981), the mean width of the DDR was found to be larger in complex than in simple cells. However, this was not true for the TRF. The authors propose that this is because simple fields often possess distinct inhibitory headbands, which contribute to the TRF but not to the DDR (Bishop et al., 1971b, 1973), while complex cells often lack an inhibitory headband or subregion. Then DDR and TRF often coincide (but see also Albus and Fries, 1980). Comparisons of RF sizes in kittens and adult cats revealed that the DDR and TRF of simple and complex cells were significantly larger in the former than in the latter. The DDR and TRF width of simple cells was about twice as large in NR kittens as in adults and the respective factor for complex cells was 1.6 (see Table 2). This age-dependent decrease in RF size may have several causes. It could result from pruning of thalamo-cortical axonal arbor that occurs during the early postnatal development (LeVay et al., 1978). It could also be a consequence of the reduction of intracortical long-range connections for which the authors obtained indications in previous studies (Luhmann et al., 1986, 1990a). Finally, increased inhibitory interactions could also contribute to a reduction of RF size. At the present stage the authors cannot decide between these possibilities, but several arguments suggest that the readaptation of tangential intracortical connections may be causally related to the reduction of RF size. The size of cortical RFs often exceeds considerably the scatter of the geniculocortical projection, which led Ferster and Lindström (1984) to suggest an involvement of horizontal intrinsic connections in the formation of large RFs. If increased inhibition were the sole cause of changes in RF size, one would expect that the decrease occurred mainly for the DDR and not for the TRF, because the latter comprises both excitatory and inhibitory subregions. Because this was not the case, changes in cortical inhibition are probably not alone responsible for the size changes. Furthermore, our analyses of the RF dimensions in kitten striate cortex showed that both the mean widths of the DDR and the TRF were significantly smaller in kittens with restricted visual experience than in NR kittens (Table 2). This difference may result partially from the fact that the SE kittens were on average about 2 weeks older at the time of recording than the NR kittens. However, it appears unlikely that the large differences of 1.3–3.2 in the mean widths of the DDR and TRF between NR and SE kittens were solely age-dependent (Albus and Wolf, 1984; Braastad and Hegelund, 1985). Plots of RF size versus eccentricity indicate that the differences in mean RF width between these groups were especially pronounced in the more peripheral representation of the visual field at eccentricities beyond 5°, and less distinct at an eccentricity between 0° and 5°. Thus, restricting visual experience seems to affect the central and peripheral representations to a different extent. A similar conclusion has been reached by Flood and Coleman (1979) on the basis of anatomical studies.

Far-reaching lateral interactions

The systematic analysis of regions in the visual field remote from the CRF revealed that in both NR and SE kittens a fraction of cells possess ectopic RFs which were clearly separated from the CRF. Responses from far outside the CRF were more readily obtained during iontophotic application of BIC and GLU (Fig. 3). Earlier reports by Hess and Murata (1974) and Sillito (1975) already showed that such treatment helps to reveal subliminal inhibitory or excitatory inputs to cortical cells in vivo, and Miles and Wong (1987) demonstrated in the in vitro guinea pig hippocampal slice preparation, that suppression of inhibition with picrotoxin reveals excitatory connections between two cells appearing as unconnected prior to treatment. The intracortical long-range connections predominantly contact the distal parts of the apical dendrite of pyramidal cells (see Luhmann et al., 1990b) and BIC could uncover these remote inputs. However, in 21 out of 28 cells with an ectopic field, remote influences could also be detected without application of GLU or BIC. Ectopic RFs have been found previously in striate cortical neurons of kittens that had selective visual experience with vertically oriented gratings (Singer and Tretter, 1976). The present results extend these findings to NR kittens. The percentage of cells possessing ectopic RFs and their laminar distribution is similar to that described in the earlier study. Although the authors did not observe a significant difference in the number of cells with an ectopic field between SE and NR kittens, there was a tendency for a higher percentage of ectopic fields in the former (20.7%) as compared to the latter (13.3%). This trend is to be expected if, as proposed previously, tangential intracortical connections are stabilized selectively by patterned visual stimuli (Singer, 1985a). The conjecture is that exposure to a simple, periodic visual pattern would lead to selective stabilization of widespread lateral connections between cells that are often activated simultaneously by the stripes of the grating.

The substrate of long-range interactions

To test the plausibility of the assumption that these ectopic responses are mediated by intrinsic horizontal connections the authors estimated the distance that these connections must span, by transferring the positions of the CRF and of the ectopic fields on to a topographic map of area 17 (Fig. 5A).

These measurements suggest that about 65% (n=20) of the 31 ectopic fields required tangential projections spanning from 2 to 6 mm, the extreme cases necessitating interactions over as much as 10 mm (Fig. 5B). Such large distances cannot be spanned by the arborization of thalamic afferents (Ferster and LeVay, 1978). The long-range interactions, thus, must be attributed either to intra-areal tangential connections or to feedback projections originating in other cortical areas. The authors discuss the first possibility first. The RF properties
of the ectopic fields are fully compatible with the assumption that the remote input is provided by other striate cortex cells. The spatial spread of tangential connections in kitten area 17 is also sufficient to mediate interactions over distances such as are suggested by the present results. As shown previously, they can span distances of up to 10.5 mm (Luhmann et al., 1990a). Evidence is further available from electron microscopic studies (Gabbott et al., 1987; Kisvárdai et al., 1986) and from the authors' previous CSD analysis (Luhmann et al., 1990b) that the far-reaching intracortical connections are excitatory. Finally, there are good correlations between the laminar distribution of tangential fibres and the location of cells with ectopic fields, and between the age-dependent pruning of tangential connections and the reduction of cells with ectopic fields in adult animals. The far-reaching tangential connections were most prominent in supragranular layers and their number (Luhmann et al., 1986, 1990a) as well as the spatial extent of excitatory effects mediated by these connections (Luhmann et al., 1990b) becomes reduced with age. Available evidence is thus, without exception, compatible with the hypothesis that the ectopic RFs result from tangential interactions within striate cortex. However, we cannot exclude the contribution of feedback connections from other cortical areas, which are also exuberant during development (Price and Blakemore, 1985) and thus could also mediate far-reaching interactions between retinotopically noncorresponding loci.

The selectivity of tangential interactions

About three quarters of the ectopic fields had the same orientation preference as the CRF. This suggests either that the remote input is provided selectively and predominantly by cortical cells which have the same orientation preference as the target cells, or that the remote response is nonorientated and that orientation selective responses are generated within the column, which contains the target cell. The authors consider the latter possibility unlikely, because of the cases where the orientation preferences of ectopic and classical RF did not match. Rather, it appears that the ectopic inputs were derived from orientation selective neurons. The implication is that the majority of the excitatory long-range connections selectively couple cells with similar orientation preference. This hypothesis is in agreement with observations of Maffei and Fiorentini (1976) and Nelson and Frost (1985). These authors reported facilitatory or disinhibitory effects from regions outside the CRF which were strongest when the remote stimuli had the same orientation as that preferred by the CRF. Further support for the hypothesis of orientation matched input comes from three recent observations. Firstly, the cross-correlation analysis of Ts'o et al. (1986) shows in adult cats selective excitatory coupling between cells with similar orientation preference located in distant cortical columns. Secondly, the investigation of stimulus dependent oscillatory responses with multi-electrode arrays revealed that remote columns synchronize their oscillatory activity if they have similar orientation preferences and are activated with coherently moving stimuli (Gray et al., 1989). Thirdly, a recent double labelling study by Gilbert and Wiesel (1989) using 2-deoxyglucose autoradiography to visualize orientation columns and injections of rhodamine-filled latex beads to label horizontal intrinsic connections indicates that long-range lateral projections relate columns of similar orientation specificity.

Another remarkable property of ectopic fields was that the majority preferred stimuli moving toward the CRF. Such direction-selective influences from outside the CRF have been reported previously (Fries and Albus, 1973; Maffei and Fiorentini, 1976; Nelson and Frost, 1978; Orban et al., 1987) and have been suggested to play an important role in figure-ground discrimination or pre-attentive vision (see below). Finally, the authors’ results suggest selectivity of tangential interactions with respect to ocular dominance also, as in 7 of 10 ectopic fields tested for this property the eye dominance of the ectopic and the classical RF was similar.

Functional implications

Our observations indicate that during early postnatal development, neurons in kitten striate cortex receive excitatory input from areas in the visual field more than 20° away from the location of the CRF, suggesting that remote inputs might have a special function in integrating information over several columns within the visual cortex. Selective lateral excitatory connections between visual cortical neurons with spatially separate, but otherwise similar RF properties have been proposed as substrate for visual processes requiring a global analysis of visual scenes, such as figure-ground discrimination (for review see Allman et al., 1985; Julesz, 1984). Selective and co-operative interactions between groups of cortical neurons coding for the same features at different locations in the visual field have been suggested as suitable mechanisms for the detection of coherencies in the feature domain (Marr and Poggio, 1976; Poggio et al., 1985; Singer, 1987; von der Malsburg and Schneider, 1986; von der Malsburg and Singer, 1988). The authors propose here that the ectopic fields reflect the development of connections, which later serve such global scene analysis. Specifically, the authors suggest that the appearance of ectopic fields results from an initial exuberance of intracortical horizontal connections, and that their later disappearance is the consequence of a pruning process, which enhances the selectivity of coupling by selectively stabilizing only those subsets of connections which link cells that are frequently co-activated. Therefore widespread lateral connections are probably not a transiently expressed epiphenomena with no specific functional role, but more likely represent the necessary substrate for the manifestation and experience-dependent modification of these global aspects of information processing. The results described in this and the two preceding studies are without exception compatible with this interpretation. The anatomical data indicated a transient
exuberance of intrinsic tangential connections, and the current source-density analysis confirmed that excitatory interactions were stronger and more far-reaching in kittens than in adult cats. Both phenomena coincide in time with the occurrence of ectopic fields. The high correlation between the RF properties of the ectopic and the classical fields indicates preferential coupling between neurons with similar RF properties. The finding that dark-rearing led to a reduction of tangential connections beyond the normal level suggests that visual activity has a stabilizing function. This, in turn, is compatible with the authors’ proposal that pruning of tangential connections occurs under the influence of neuronal activity. The authors have no direct evidence for the hypothesis that those connections which link cells with correlated activity patterns are stabilized selectively. However, such a process has been shown to occur during the development of other cortical pathways, e.g., for the pruning and selective stabilization of binocular connections (for review see Singer, 1985a, b, 1987; Stryker, 1982).

The finding that ectopic fields disappear in the adult suggests that the persistent horizontal connections are not effective enough to generate cell discharges by themselves. This, however, is not required if, as demonstrated recently (Gray et al., 1989), coherent activation of remote columns is expressed by the synchronization of their respective oscillatory responses. In that case, tangential interactions must only have a synchronizing effect, which can probably be assured with weak interactions that by themselves do not have to elicit cell discharges.

Acknowledgements
We are most grateful to Holga Duckstein and Christa Ziegler for their skillful technical assistance, to Gisela Knott and Gabriele Trauten-Luhmann for excellent editorial support, and to Dr G. A. Orban for his helpful comments on the results of this study. This report is part of the PhD thesis of H. J. Luhmann, presented to the University of Bremen.

Abbreviations
BIC bicuculline methiodide
CRF conventional receptive field
DDR dominant discharge region
EEG electroencephalogram
FET field effect transistor
GABA γ-aminobutyric acid
GLU glutamate
NR normally reared
OD ocular dominance
PSTH peristimulus-time histogram
RF receptive field
SD standard deviation
SE reared in selective environment
TRF total receptive field

References


