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PROPERTIES OF THE EVOKED POTENTIAL GENERATORS: CURRENT SOURCE-DENSITY ANALYSIS OF VISUALLY EVOKED POTENTIALS IN THE CAT CORTEX

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The depth profiles of visually evoked field potentials were recorded in areas 17 and 18 of the cat visual cortex. For comparison, potential profiles evoked by electrical stimulation of the primary afferents and of the nonspecific reticular system were also recorded. From these profiles the current source-density (CSD) distributions were calculated using the one-dimensional CSD method. CSD distributions evoked by the different types of stimuli differ in their amplitudes and time courses by approximately one and two orders of magnitude. Qualitatively, however, they are very similar. Thus, the CSDs can be interpreted as reflecting the same basic pattern of excitatory synaptic activations. This pattern consists of early activation components in the input layers, followed by excitatory synaptic activations in layer III, then in layer II, and in layer V. The basic pattern of cortical activation was found to be modulated by specific features of the visual stimuli. Modulations reflecting contour- versus contrast-contents as well as those reflecting characteristic features of moving patterns have been identified. Most of the CSD components of the cortical activation sequence were obtained from regions extending well beyond the cellular receptive fields in visual cortex. Thus, they reflect nonretinotopic activities. Parameters other than specific features of the visual stimuli have profound influence on cortical CSDs. Nonspecific parameters which have been considered are the general state of cortical excitability, the temporal interactions of successive activities (which are predominantly facilitatory), and the lateral interactions of simultaneous activations from different regions of the visual field (predominantly inhibitory).

Keywords: visual cortex, field potentials, current source-density analysis, retinotopy

Electrically evoked field potentials in the visual cortex of the cat have been previously investigated using the method of one-dimensional current source-density (CSD) analysis (Mitzdorf & Singer, 1978). This method reveals the current sinks and sources in the extracellular space and as these are the local causes of the field potentials they constitute the physiologically relevant information about cortical activation contained in the field potentials (Mitzdorf, 1985; Nicholson & Freeman, 1975; Pitts, 1952).

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It was concluded previously that the electrically evoked sinks and sources in the cat visual cortex are mainly due to grouped excitatory synaptic activities and that the sinks indicate the laminar locations and temporal successions of the most prominent synaptic relay stations. The spatio-temporal patterns of the electrically evoked CSD distributions indicated that the primary afferent activity is relayed within cortex along three different pathways. The sequence of activity in each pathway could be followed over three synaptic relays (Mitzdorf & Singer, 1978).

Electrical stimulation, however, is a rather crude, unnatural type of activation. Therefore, more natural visual stimuli have been applied in the present study. The results identify the cortical evoked potential generators as reflections of one general activation routine which includes stimulus-specific as well as abstract, central features of information processing. They thus shed light on a different aspect of cortical information processing than single-unit receptive fields.

METHODS

Eleven acute experiments were performed on adult cats. For surgery the animals were anaesthetized first with ketamine hydrochloride (30 mg/kg, i.m.) and then with pentobarbital (i.v.). Ear canals and wounds were infiltrated with the local anaesthetic Xylocain and the animals were mounted in a stereotaxic head holder. During recording they were paralyzed with hexcarbacholin bromide (.25 mg/kg/h, i.v.) and artificially ventilated. Anaesthesia was maintained with nitrous oxide (75% N_2O, 25% O_2) and pentobarbital (usually 1.5 mg/kg/h, i.v.; Hammond, 1978). Electrocorticogram and heart rate were continuously monitored. Body temperature and end-tidal CO_2 concentration of the expired air were maintained at 38°C and 3–4%, respectively. A glucose-Ringer-water solution was continuously infused through an orally inserted gastric catheter. In several cases the state of excitability of the CNS was changed during a recording session by intravenous injection of picrotoxin (.1 to 2.0 mg/kg) or by additional injection of pentobarbital (10 to 30 mg/kg).

The eyes were protected by contact lenses with artificial pupils 2 mm in diameter. Refraction was corrected with additional lenses. Atropine for pupil dilatation and neosynephrine for retraction of the nictinating membranes were applied every few hours. Isotonic saline was steadily dripped on the corneas to prevent drying. The retinal landmarks were projected onto a tangent screen either with a fundus camera or with an ophthalmoscope.

In all experiments bipolar electrodes for electrical stimulation were inserted stereotactically into the optic radiation (OR: A 6.5 ± 2.0, H 15.0, L 9.5) just above the lateral geniculate nucleus (LGN) and into the mesencephalic reticular formation (MRF: A 3.5, H 8.3, L 3.0). In several experiments stimulating electrodes were also placed in the optic chiasm (OX: A 14.5, H 4.5, L ± 2.0), in the thalamic nuclei ventralis medialis/submedius (VM/SM: A 10.5, H 9.5, L 2.0) and centralis medialis (CM: A 7.0, H 11.5, L 2.0). The stimulus pulses ranged from 20 to 40 mA in amplitude and were of 50 μs duration. MRF, VM/SM, and CM were usually activated by trains of 5 stimuli at 15 ms intervals.

For visual stimulation, high-luminance stroboscopic flashes, a few μs in duration were generated with a gas discharge tube. Ganzfeld luminance changes, grating appearance, disappearance, and reversal (usually square-wave gratings), and movements of gratings and bars were generated on a Hewlett Packard 1304A display. The display was usually placed 30 cm in front of the cat; its maximal luminance was about

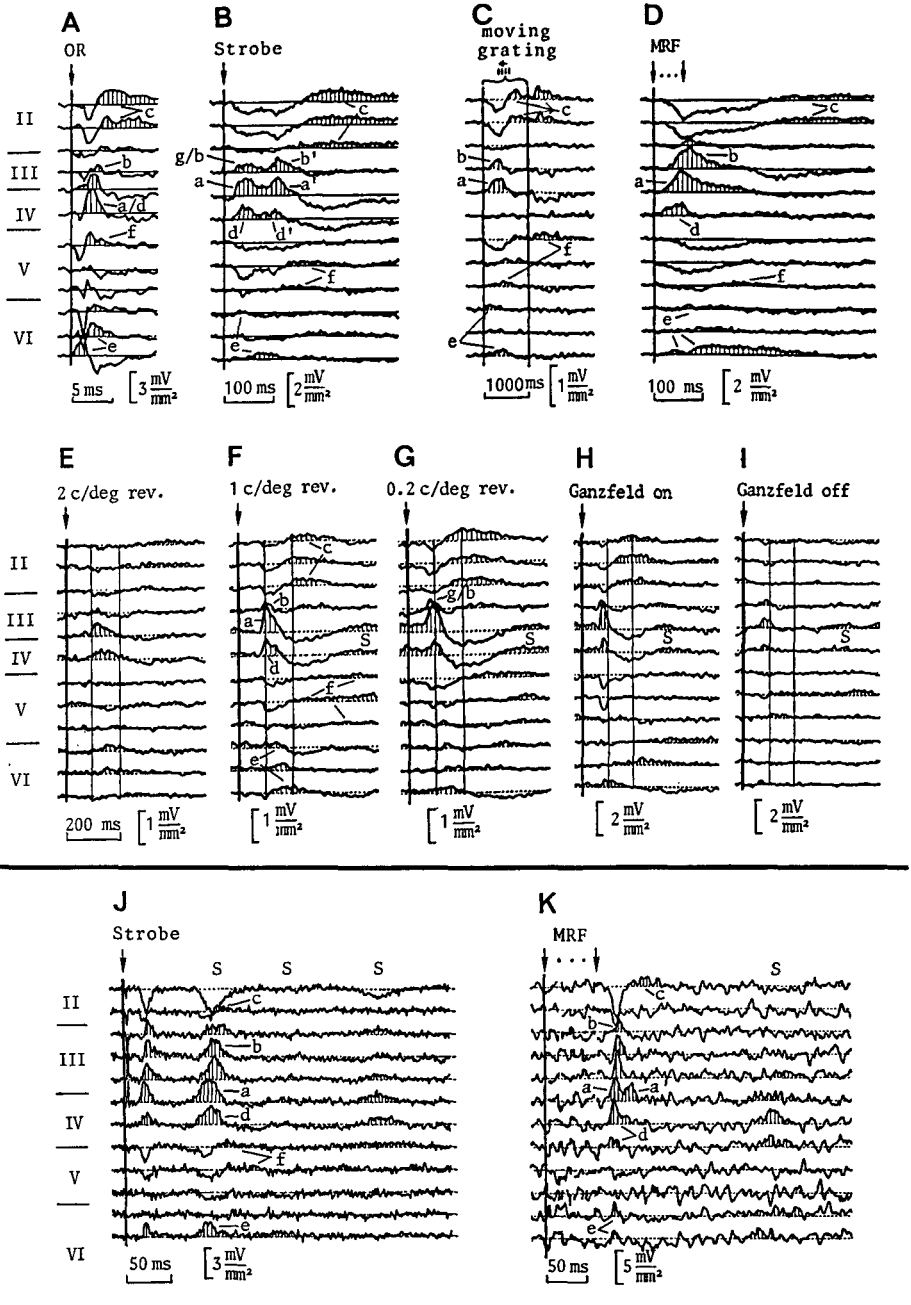
8 cd/m². (The two luminance levels of all gratings and Ganzfeld -on and -off stimuli, used for the activations shown in the figures, were the same, about 3 and 8 cd/m².) The background illumination of the room was in the range of .5 to 10 lux. The spatial frequencies and orientations of the gratings, velocities, contrasts, and interstimulus times were varied. Both monocular and binocular stimulation was applied and stimuli were either presented in the whole visual field, restricted to the receptive field region, or to the periphery.

For the simultaneous recording of evoked potentials in different cortical depths either 12 or 16 glass micropipettes were glued together so as to form a multielectrode with the tips approximately in one axis. In order to achieve this arrangement the shafts of the pipettes were bent in a microforge about 5 mm above their tips. Care was taken that no electrode tip was hidden within the array of shafts. The 12-fold multielectrodes had an equidistant tip spacing of 200 μm, the 16-fold multielectrodes a spacing of 150 μm or 170 μm (error $\pm$ 10%). The individual pipettes had tip diameters of 5 μm and were filled with isotonic saline, or 1.5 M NaCl, or 3 M NaCl. The resistances of the pipettes ranged from 1 to 3 MOhm. The signals were fed into a 16-fold pre- and main amplifier (input resistance 10^{12} Ohm, band pass .2 Hz–5 kHz) and then, by multiplexing, into a PDP11-computer. For simultaneous recording of 16 channels the maximal possible temporal resolution of the computer was .84 ms per channel, and the softwareprogram was limited to 360 points per channel. Usually 50 to 200 individual responses were averaged and then stored.

The experimental procedure was as follows: First a single pipette was used for single-unit recordings to find the receptive-field location of a cortical region. After penetration for about 3 mm the pipette was then retracted stepwise and potentials, evoked by stimulation of the OR (and OX) were recorded. From the resultant CSD it was judged whether all cortical laminae had been crossed by this track (see Mitzdorf & Singer, 1978). Then the multibarrel electrode was inserted at the same location. After it had properly penetrated (judged from recorded field potentials and CSDs) the cortex around it was covered with silicone paste. Then the various types of visual and electrical stimuli were applied and the corresponding field potentials recorded. Altogether 2300 averaged potential profiles were collected along 14 tracks in area 17, and 860 averaged potential profiles were collected along 8 tracks in area 18. In half the cases the cortical tissue investigated was dissected after the experiment and fixed in 5% formalin. Later, the recording tracks in these regions were reconstructed from Nissl-stained serial sections.

The relation between the different laminae of the visual cortex and the poles of the multielectrode was determined primarily from OR- and OX- evoked CSDs, recorded several times during the course of data acquisition. For the present application this physiological assessment (see Mitzdorf & Singer, 1978) is more precise than a histological localization by dye spots, because it takes account of eventual displacements of the cortical tissue during the recording session. It was further confirmed by comparison with the depth distributions of the CSD profiles recorded with a single pipette at higher spatial and temporal resolution and the histological reconstructions of the recording tracks.

The extracellular CSD distributions were calculated by the one-dimensional CSD method (e.g., Mitzdorf, 1985; Nicholson & Freeman, 1975; Pitts, 1952). Resistivity of the extracellular space was assumed constant (e.g., Freygang & Landau, 1955; Mitzdorf 1980) and the second spatial derivative of the field potentials was approximated by numerical differentiation (Mitzdorf & Singer, 1977, 1978):


A
OR
B
Strobe
C
moving grating
D
MRF
II
III
IV
V
VI
5 ms
100 ms
1000ms
E
2 c/deg rev.
F
1 c/deg rev.
G
0.2 c/deg rev.
H
Ganzfeld on
I
Ganzfeld off
200 ms
J
Strobe
S
K
MRF
50 ms

$$\mathrm{CSD}(z) \propto \frac{\partial^2 V(z)}{\partial z^2} \approx \frac{V(z+n\cdot\Delta z)-2V(z)+V(z-n\cdot\Delta z)}{(n\cdot\Delta z)^2}$$

where $V(z)$ is the extracellular potential in the cortical depth z ,and Δz is the distance between adjacent tips of the multielectrode, i.e., between adjacent potential recording depths. (In the figures the CSD calibrations are given in mV/mm^2 which correspond to about .5 mA/cm^3.)

RESULTS

The following description of the main properties of the evoked-potential generators is based on many close inspections of over 3000 CSD profiles. Therefore, the data selected for the figures cannot be taken as proofs of the statements, but simply as representative of the main observations. (As a help for the reader, many of the response components described in the text, have been marked with letters in the figures.)

The recording with multielectrodes (see Methods) has the disadvantage that the spatial resolution of the resulting CSD profiles is rather low. Therefore fine details of the spatial distributions of the CSDs may have been missed. On the other hand, the phenomena encountered in the present study appeared to be so complex that their main properties could only be assessed because the multielectrodes permitted the recording of many series of responses to different stimuli within short time intervals.

1. *Basic Pattern of Cortical Activation*

When comparing the CSDs, evoked by the various different types of stimuli, the most conspicuous observation was their qualitative similarity (see Figure 1). The main sink components of this basic pattern have been named a to f. Commonly the earliest sinks occur in the input layers IV (sink a/d) and VI (sink e). The sink in layer IV often has a slightly shorter onset latency in the upper part (sink a) than in the lower part of this layer (sink d). In most cases, with a small delay in onset, a sink as coherent as sink a

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FIGURE 1 Current source-density distributions in area 17 (A-I; intertip spacing of the multielectrode and distance in cortical depth between adjacent CSD traces $\Delta z = 150\mu m$, differentiation grid $n\cdot\Delta z = 300\mu m$, receptive field within central 3°) and area 18 (J, K; $\Delta z = 150\mu m$, $n\cdot\Delta z = 300\mu m$, receptive field 19° eccentric). The stimuli were A) electrical stimulation of the optic radiation, B and J) strobe flash, C) movement of a .5 cycle/deg grating at a velocity of 5°/s for 1000 ms, D and K) electrical activation of the mesencephalic reticular formation (a 60 ms train of 5 pulses), E) reversal of a 2 cycle/deg grating, F) reversal of a 1 cycle/deg grating, G) reversal of a .2 cycle/deg grating, H) abrupt Ganzfeld-luminance increase, I) abrupt Ganzfeld-luminance decrease.

In this and the following figures the laminar subdivisions are indicated to the left of the CSDs. The times of abrupt stimuli are indicated by arrows and the durations of movements by brackets above the CSDs. For ease of judging latencies, vertical bars are drawn at the times of stimulation, and in several profiles also at certain poststimulus times. In each CSD trace upward deflections (hatched) represent current sinks (reflecting excitatory synaptic activities) and downward deflections represent current sources. Many of the sinks have been marked by letters (referring to the text); secondary responses are marked by S. Note the qualitative similarities of the different responses, and their different time and amplitude scales (for details see Results Section 1). Series E to H further demonstrates the gradual differences in responses to stimuli with many versus few contours (for details see Results Section 2A).

is evoked in layer III (sink b). These early sinks may then be followed by more dissipated sinks in layers II (sink c) and V (sink f). Sinks a/d and b may also be followed by similar sinks (named a', d', and b'), either before or after the onset of sink c (evident in Figures 1B, 4C, 5A, B, D; responses to strobe flashes recorded in the area-centralis region of area 17 always had these additional components – see Figure 1B). The concomitant sources are located predominantly above the sinks a and b, above and below the sinks d, e, and f, and below sink c. In some cases sink e could be further differentiated into an early component e1 with the concomitant source mainly above and a later component e2 with sources above and below. The CSDs in area 18 consist of the same types of components as the CSDs in area 17.

Commonly, the specific activations (primary responses) were followed by one or several further activations (secondary responses). Weak secondary responses consisted of the components a/d and e, eventually also b; strong secondary responses consisted of all components a to f (see e.g., Figure 1F–K). In several series of recordings so-called wavelets (e.g., Cowey, 1964; Laufer & Verzeano, 1967) were evoked (see e.g., Figure 6A). These high-frequency oscillations were in the range of 20 to 80 Hz and were superimposed on responses to large, abrupt luminance changes. The CSDs of these wavelets had components alternatingly in the middle and deepest layers and in layers II and V, thus indicating the same basic pattern of activation as the other non-repetitive responses.

Two specific points deserve mentioning: First, in the visually evoked CSDs the latency difference between sinks a/d and b is often so small that these two sinks cannot be distinguished any more by this criterion (see e.g., Figures 1B, G–I). (As suggested by other findings – see Section 2B – a further short-latency component g may contribute significantly to the sink in layer III in these cases.) Second, in many CSDs where sink b is rather large, the sink in lower layer IV is no longer present – most likely because it is cancelled by a source (see e.g., Figures 1C, 5B and C).

In summary, all different cortical activations, including the primary responses to electrical or visual stimulation, the responses to stimulation of nonspecific midbrain or thalamic regions (MRF, VM/SM, CM), the delayed secondary responses, and the high-frequency oscillations, generate CSD distributions which are qualitatively very similar. Irrespective of the type of stimulus, either the full pattern (including the early sinks a/d, b, and e, and the late sinks c and f) is evoked, or only the first part with the sinks in the input layers and perhaps sink b is apparent. Often, also, sinks a/d and b occur twice in close succession. A schematic diagram of the basic pattern of sinks is shown in Figure 7A.

Quantitatively the CSDs differ in their amplitudes and time courses (latencies and durations) by factors of up to 20 and to 200, respectively (note the different time and amplitude scales in Figure 1). The stronger the stimulus (e.g., electrical stimulation of the primary afferents versus visual stimulation; Strobe flash versus Ganzfeld on, off and grating on, off, reversal; high versus low contrast of a grating stimulus) the faster the activation pattern runs off, and the larger its amplitudes.

By combining the amplitudes and durations of the CSDs, a rough estimate of the effectiveness of the various types of stimuli in activating the cortex has been made. Comparison of the total sink currents, i.e., the time integrals over the sinks, revealed that electrical stimulation and all the abrupt visual stimuli are about equally effective, but moving bars or gratings are about five times more effective in activating area 17. With respect to area 18, electrical stimulation is two to three times more effective than all the visual stimuli.

2. *Stimulus-Specific Properties*

Although the most conspicuous observation was the qualitative similarity of the responses to different stimuli, close inspection of series of responses – recorded under otherwise constant conditions – did reveal some minor stimulus-specific modulations of the basic activation pattern. These are described in the following three sections.

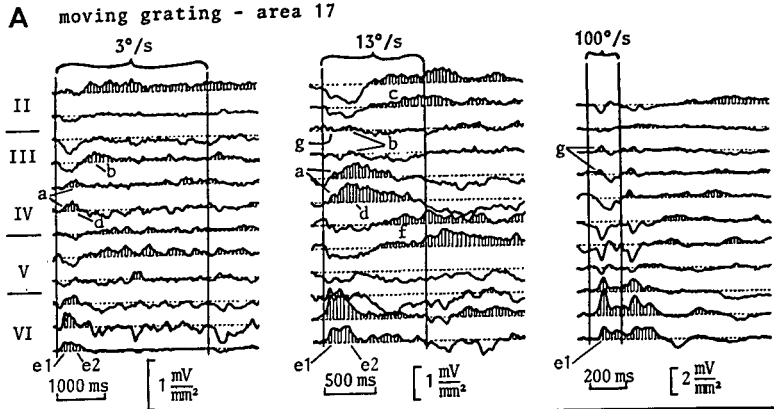
A) *Contour Versus Contrast of Abrupt Stimuli*

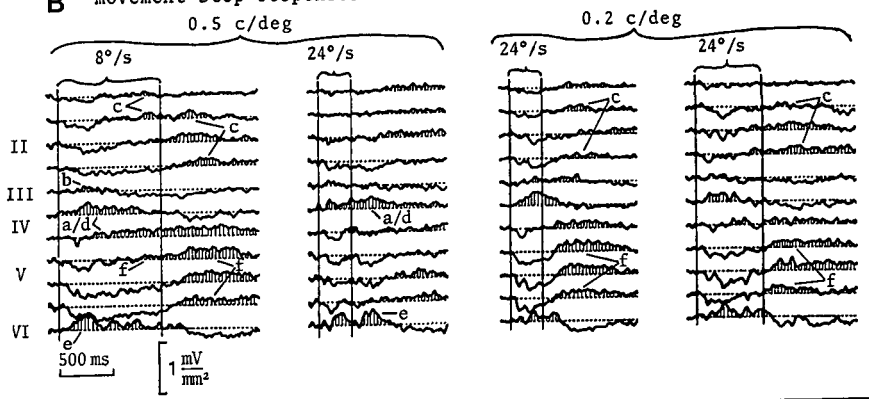
Two complementary characteristics of visual stimuli are their content of contrast or change of luminance and their content of contour or outline or structuredness (Jeffreys, 1977; Kulikowski, 1978). The differential influences of these two characteristics on the basic activation pattern were revealed by comparing the responses to Ganzfeld-on and -off stimuli (pure luminance changes) and the responses to the appearance, disappearance, and reversal of gratings of various spatial frequencies (contours and local luminance changes, but constant average luminance). (For examples see Figure 1E–I and Figure 5B).

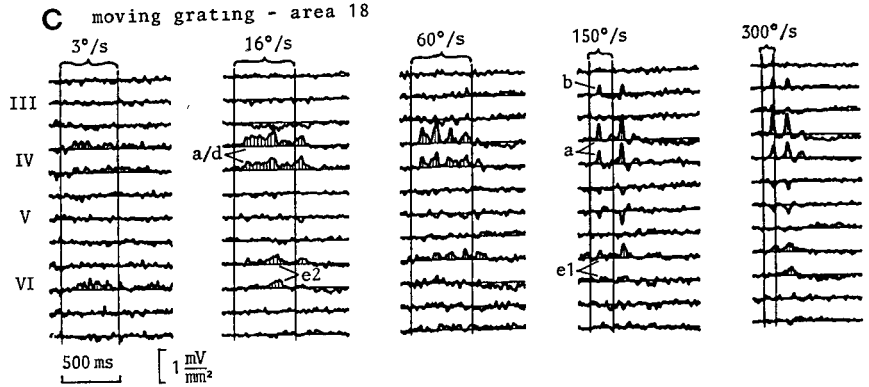
Increasing the contour content of a stimulus, for example by increasing the spatial frequency of a reversing grating, rather consistently led to the following changes in the response: The latencies of the early sinks a/d and e increased, but at different rates. Whereas the two sinks had equal latencies (or sometimes sink e even preceded sink a/d) in responses to reversals of low-spatial-frequency gratings, sink e was delayed by up to 50 ms more than sink a/d in responses to reversals of high-spatial-frequency gratings. With increasing spatial frequencies these sinks became less coherent and smaller in amplitude. The currents flowing into both these sinks in layers IV and VI came mainly from above in the responses to stimuli containing few or no contours; they were drawn more from below in the responses to contour-rich stimuli. These differential properties indicate a predominance of sinks a (and g – see below) and e1 in responses to stimuli with few contours and a predominance of sinks d and e2 in the responses to contour-rich stimuli. Furthermore, there was a tendency for the sequence of activation to be followed through in the supragranular layers more completely (to upper layer III and to layer II) in the responses to stimuli with few or no contours. Finally, response series in which sinks a' and/or b' were discernible, revealed that the time interval between components a, b and a', b' decreased systematically with decreasing contour-content of the stimulus (see e.g., Figure 5B; components b' marked by arrows).

The low-frequency limit of responses to stimuli with decreasing contours was the Ganzfeld-on response. The Ganzfeld-off response, on the other hand, was more variable: In several series it was more similar to the responses to contour-rich stimuli; in other series it was similar to the Ganzfeld-on response, but usually with a much smaller sink e.

Slow changes of luminance (ramp stimuli) also evoked shallow sinks in the input layers (or even the full activation pattern). Their onset latency increased with decreasing ramp slope. Mostly, the sinks in the input layers, after having decreased, increased again and continued until the ramp stimulus was terminated. The termination of the ramp increase or decrease also evoked a response, indicating that even the transition from a steady increase or decrease to constant luminance (i.e., a slope change is a relevant stimulus. All these phenomena were seen in area 18 as well as in area 17. (The onset latencies were shorter in area 18 by about 10%.)


A moving grating - area 17
3°/s
13°/s
100°/s
II
III
IV
V
VI
a
b
c
d
e1
e2
f
g
1000 ms
500 ms
200 ms
1 mV/mm²
2 mV/mm²


B movement-stop responses - area 17
0.5 c/deg
0.2 c/deg
8°/s
24°/s
24°/s
24°/s
II
III
IV
V
VI
a/d
b
c
e
f
500 ms
1 mV/mm²


C moving grating - area 18
3°/s
16°/s
60°/s
150°/s
300°/s
III
IV
V
VI
a
a/d
b
e1
e2
500 ms
1 mV/mm²

B) *Movement of Patterns*

In the responses to moving-pattern stimuli systematic influences of the velocity and the spatial frequency of the grating could be identified. These stimulus conditions were some of the rare cases where the two areas 17 and 18 clearly reacted differently in several respects. (For examples see Figure 2A and C.)

The most prominent feature of a moving-grating stimulus is *the onset of movement.* It initiates the basic pattern of activation. With increasing velocity (and to same extent also with decreasing spatial frequency) of the grating, the latency to onset of the early sinks is reduced, and the successive components follow more closely. With low-velocity movements, in both areas, the tonic (sustained) sink components in the input layers (d and e2) dominate; with intermediate-velocity movements the more phasic components (a and e1) become more dominant. With high-velocity movements (above about 50°/s) in area 17 sinks a and d are much reduced; sink e1 becomes predominant together with an additional early sink, labelled g, at the border of laminae IV and III. Like sink e1, sink g is rather coherent and draws its current exclusively from above. In area 18, in contrast to area 17, sink a becomes steadily larger in amplitude, whereas sink e1 stays about the same with higher-velocity movements.

During the movement of the grating the sustained sinks d and e2, in area 17, often showed amplitude modulations at the frequencies at which the individual bars of the gratings moved over the receptive field. Such modulations were apparent in the velocity range of about 5–20°/s. In area 18 the first part of the activation procedure is modulated differently: With increasing velocity (also in the range of 5–20°/s) sinks a/d and e become steadily more phasic with a rhythmicity of about 10 Hz. At velocities higher than about 60°/s the first of the rhythmically evoked sinks a becomes even larger, the first sink e1 stays about the same, and the successive sinks in both input layers become smaller. (Similarities between the 10 Hz rhythmicity and repetitive secondary responses suggest a kinship between the two phenomena – compare the CSDs of Figures 2C and 1J; more specifically, moving gratings appear to enhance secondary responses in area 18.)

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FIGURE 2 CSD responses to moving gratings.

A) Responses in area 17 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m, receptive field within central 3°) to slow, intermediate, and fast movement of a .2 cycle/deg grating. Note the gradual decrease of the tonic components and the gradual increase of the transient components from left to right (for details see Results Section 2B).

B) Responses in area 17 ($\Delta z = 170\mu$m, $n \cdot \Delta z = 340\mu$m, receptive field within central 3°) to slow and fast movement of a .15 cycle/deg grating and fast movement of short and long duration of a .2 cycle/deg grating. Note that the response to movement stop in the second of the four CSDs starts with sinks in layers IV and VI, whereas the responses to movement stop of the remaining three CSDs consist of sinks in layers II and V only. The second-CSD stimulus differs from the first-CSD stimulus by its higher velocity and from the third-CSD stimulus by its higher spatial frequency. The right pair of CSDs demonstrates that sinks c and f are in fact due to movement stop, since their latency is coupled to the movement stop, not to the movement onset (for details see Results Section 2B).

C) Responses in area 18 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m) to slow, intermediate, and fast movements of a .2 cycle/deg grating. Note that the responses during the movements are more phasic the higher the velocity is, and that a large response is evoked also by the stop of high-velocity movements (for details see Results Section 2B).

The cessation of movement is another prominent feature of this type of stimulus. In area 17 it initiates sinks c and f when the preceding movement of the grating was of low or intermediate velocity. When the transition to the late part of the activation sequence had occurred already during the movement then the amplitudes of these sinks increased even more due to the movement stop (see e.g., Figure 1C). If the grating was moved at higher velocities, however, the movement stop evoked the entire activation sequence. The transition between these two types of responses to movement stop depends on the velocity as well as the spatial frequency of the grating (4°/s for 1 cycle/deg gratings, 20°/s for .5 cycle/deg gratings, 30–100°/s for .2 cycle/deg gratings). (Figure 2B shows examples.)

In area 18 the cessation of movement does not evoke any response at all after movements at low or intermediate velocities. (The peaks apparent after movement stop in the left three CSDs of Figure 2C have too short latencies to be attributable to the movement stops.) Gratings moved at very high velocities, on the other hand, do evoke a response to movement stop. This response is rather similar in shape and latency to the corresponding response to movement onset (see the two CSDs to the right in Figure 2C. Actually, the rightmost CSD in Figure 2C is an exceptional result, because usually a clear movement-stop response was apparent only when the preceding grating movement had lasted for more than 200 ms. The exception here may be due to the temporal coincidence of the virtual movement-stop response with a secondary response.).

C) *Retinotopically Corresponding and Noncorresponding Activations*

The most perplexing observation of the present study was that also retinotopically noncorresponding stimuli evoked the basic pattern of activation. This phenomenon of significant nonretinotopic activations disagrees most strikingly with the common present hypothesis concerning information precessing in primary visual cortex. Close inspection of responses to retinotopic and nonretinotopic activations revealed some consistent details of this phenomenon.

When a single bar or edge was moved over a large area of the visual field, the most prominent activation occurred at about the time when the stimulus crossed the receptive-field region of the cortical recording site (for examples see Figure 3; receptive fields marked by crosses above the CSDs). Components a/d and b of this activation started rather precisely at the time when the bar moved over the receptive-field center; i.e., their onset latencies are consistent with strict retinotopic activation. Sink e usually started earlier, indicating that its receptive field is larger. In some CSDs weak components c and f preceding the retinotopic activation, were discernible (see e.g., left CSD in Figure 3A), indicating even larger receptive fields of these components. But, in addition to these more or less retinotopic activations, also the onset of movement, when the bar or edge was far away from the receptive-field region, commonly evoked the activation pattern, although weaker (in Figure 3 the early components of these responses are marked by asterisks).

Such nonretinotopic activations were even more obvious when larger areas of the noncorresponding visual field were stimulated (for examples see Figures 4 and 5D). Responses to abrupt visual stimuli were usually not much smaller when the receptive-field region was spared by the stimulus. Consistently, however, the onset latencies of components a, a' and b, b' were increased; components a' and b' usually increased in amplitude, while components a and b became smaller. Component e usually did not shift as much in onset latency as components a, a', b, b', but its later part became more

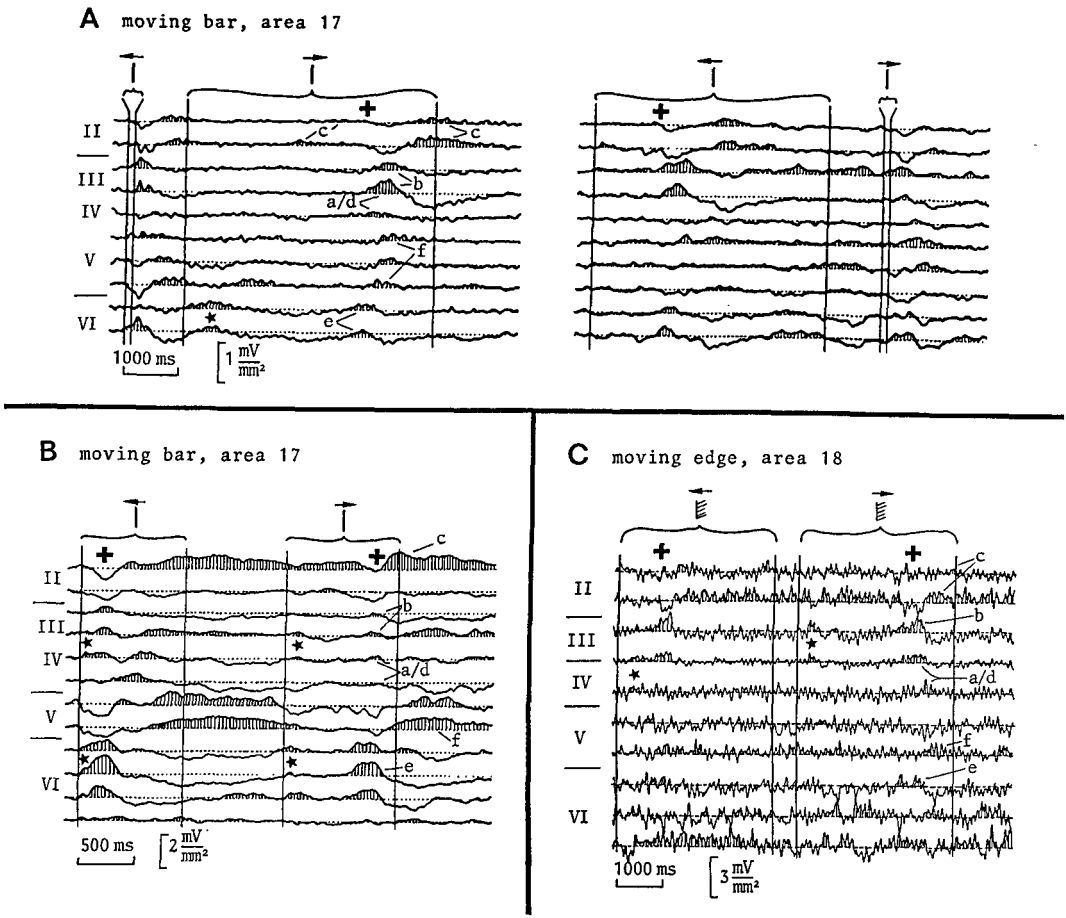


FIGURE 3 CSD responses to a moving bar or edge.
A) Responses in area 17 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m, receptive field 3° eccentric) to fast movement (100°/s) of a bar to the left followed by slow movement (2°/s) to the right (left CSD), and to the same stimulus, except that the velocities were interchanged (right CSD).
B) Responses in area 17 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m, receptive field within central 3°) to the back and fro movement (20°/s) of a bar.
C) Responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m, receptive field 12° eccentric) to the back and fro movement (16°/s) of an edge.
The times when the bar or edge crossed the receptive field of the recording region are indicated by crosses above the CSDs. Note the retinotopically corresponding activations and the responses to the onsets of movement, marked by asterisks (for details see Results Section 2C).

dominant, as well. Obviously, the response to whole-field stimulation is not the linear summation of the responses to stimulation of subregions (see Figure 4A).

Responses to moving gratings which spared the receptive-field region were usually more phasic than the corresponding responses to stimulation in the receptive-field region. They were the larger, the higher the velocity of movement. Detailed comparisons suggest that components a, d, b, and e2 are predominantly retinotopically evoked, that component e1 is predominantly due to nonretinotopic (far peripheral)

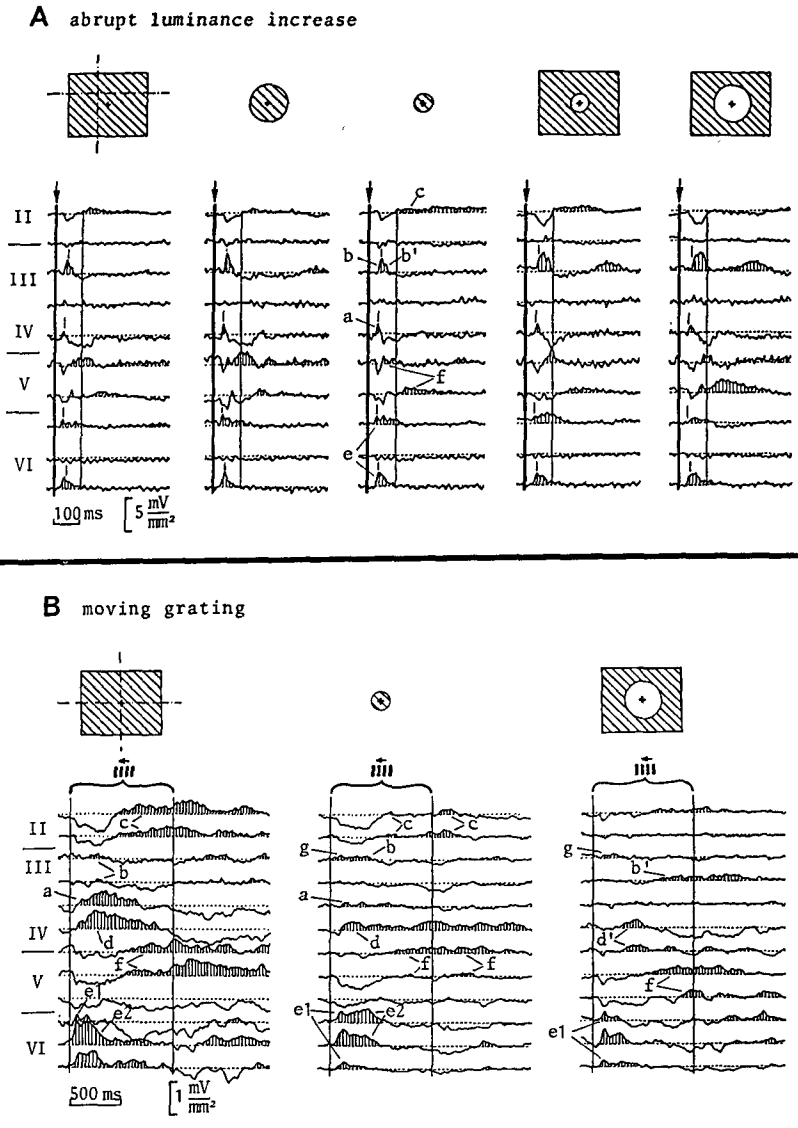


FIGURE 4 CSD responses to retinotopically corresponding and noncorresponding stimuli: The areas of stimulation are indicated by hatching in the insets. The stimulus display subtended $40 \times 50°$ and was centered on the receptive field (marked by a cross). The small circles had a diameter of 12°, the large circles had a diameter of 24°.

A) Responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu m$, receptive field 10° eccentric) to an abrupt Ganzfeld-luminance increase. Note that the response to whole-field stimulation is not a linear summation of the responses to stimulation of subregions. Note also that the onset latencies of the responses are gradually more delayed the more that the region around the receptive field is spared by the stimulus (for comparison the peak latencies of the retinotopically evoked components a, b, and e of the middle CSD response are indicated by vertical bars in *all* CSD responses - for details see Results Section 2C).

B) Responses in area 17 ($\Delta z = 150\mu m$, $n \cdot \Delta z = 300\mu m$, receptive field within central 3°) to movement (13°/s) of a .2 cycle/deg grating (taken from the same series of recordings as the examples of Figure 2A). Note the predominance of components a, d, and e2 in the response to stimulation of the central 12°, and the slight predominance of component e1 in the response to peripheral stimulation (for details see Results Section 2C).

stimulation, and that component g is evoked about equally well by retinotopic and nonretinotopic activations. Late sinks in layers IV and III in responses to nonretinotopic activations presumably represent delayed components a', d', and b'. The movement-stop response to slow movements in area 17, which consists only of components c and f (see Results Section 2B), originates mainly from retinotopic activation, but it is larger, the larger the stimulus region.

D) *Ocular Dominance and Orientation Specificity*

In several series of recordings the same stimulus was presented to either eye alone and to both eyes. Comparison of the responses revealed that a strong predominance of one eye never occurred. The size of the binocular response was always larger than either monocular response but smaller than their sum. Variation of the orientation of abruptly changing gratings (reversal, on, or off) never revealed any significant orientation preference. Slight superiorities of specific orientations were observed in several of the responses to moving gratings or bars.

3. *Nonspecific Influences on the CSDs*

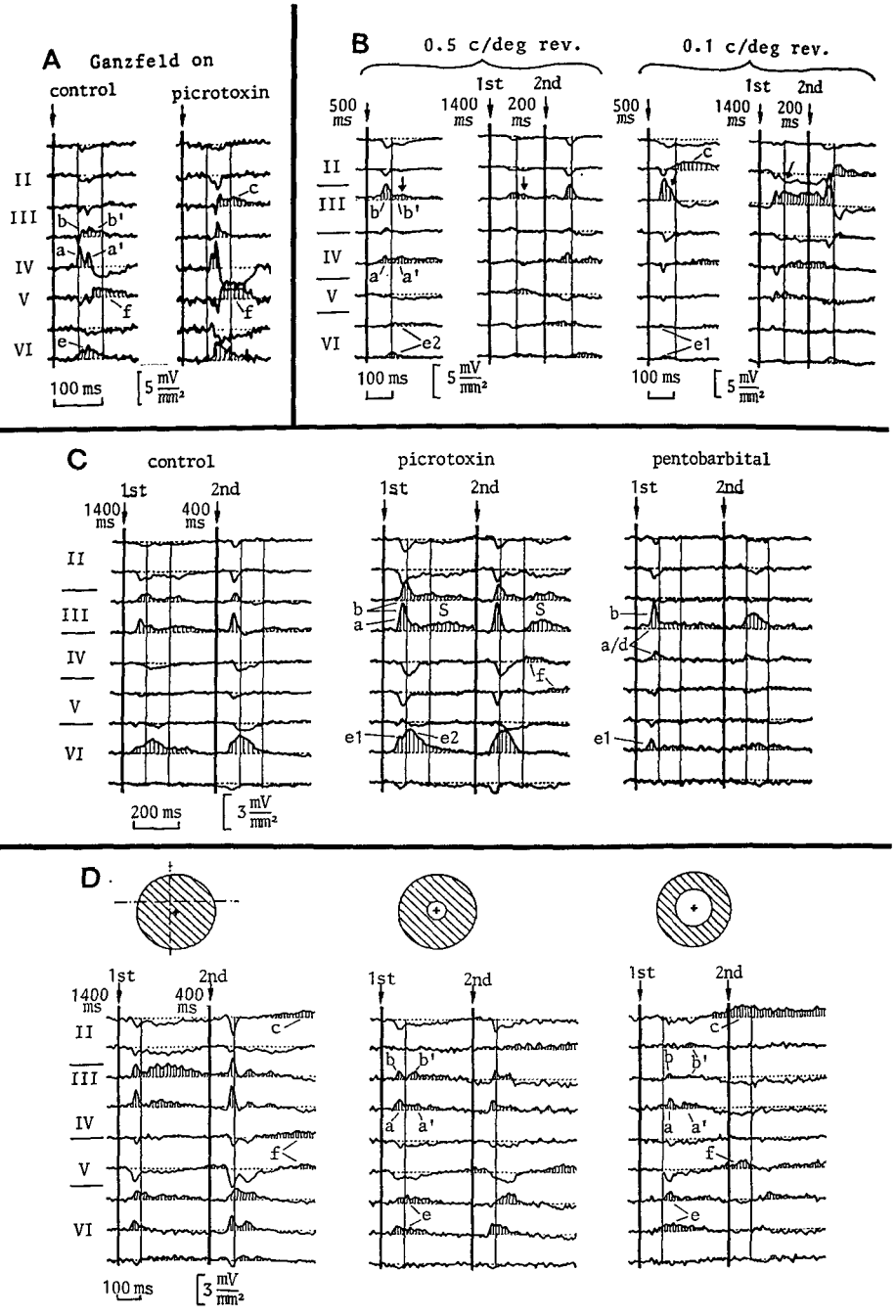
A major problem when trying to correlate response properties with stimulus properties was the large influence of nonspecific factors. One of them, the general state of excitability of the CNS, is rather trivial (although not well controllable in experiments with anaesthetized animals). Another factor which was found greatly to influence the evoked response was the ongoing cortical activity (spontaneous or evoked by a preceding stimulus).

A) *General State of Excitability*

During states of low excitability the cortical responses were of small amplitude and consisted predominantly only of sinks in the input layers. Repetitive "after-discharges" in the alpha-frequency range (e.g., Fuster & Docter, 1962; Torres & Warner, 1962) were also rather common. During states of high excitability, the late components c and f were usually rather large, and also the secondary responses were enhanced. Examples of the results from experimental manipulation of the general state of excitability are shown in Figure 5A and C.

B) *Interactions of Successive Responses*

Temporal interactions between responses were investigated by varying the interstimulus times. When two identical abrupt visual stimuli were presented in close succession, usually the second response was larger and more coherent; often, only the second response included the late sinks c and f. This "facilitation" phenomenon was also obvious with Ganzfeld-on and, though less pronounced, with Ganzfeld-off responses. Often sink a/d was facilitated more than sink e. This facilitatory type of interaction between two responses was strongest when the stimuli were separated by about 200 to 300 ms; it also occurred at smaller interstimulus times and, gradually becoming weaker, up to intervals of about 600 ms. (Examples of responses to double stimuli are shown in Figures 5B, C, D and 6C; the interstimulus times are indicated to the left of the arrows above the CSDs.)


A Ganzfeld on
control
picrotoxin
II
III
IV
V
VI
100 ms
5 mV/mm²
B
0.5 c/deg rev.
0.1 c/deg rev.
1st
2nd
500 ms
1400 ms
200 ms
e1
e2
C
control
picrotoxin
pentobarbital
400 ms
200 ms
3 mV/mm²
S
D

Usually, during states of very high general excitability this facilitation effect was weak; during states of very low excitability the second response was even smaller than the first response (see e.g., Figure 5C). Furthermore, when only small subregions of the visual field (retinotopically corresponding or noncorresponding) were stimulated, then the facilitation of the second response was usually weaker; or the first response, including the late components c and f, was even larger (see Figure 5D).

Paradoxically, the onset latencies of the early sinks were prolonged in most of the facilitated responses. This latency increase was usually about 30 ms; but increases up to 70 ms were also observed. On the average, it was larger for Ganzfeld-on than for Ganzfeld-off responses and for sink a/d than for sink e. Similar increases in onset latency, concomitant with response enlargement were also observed after the application of picrotoxin (see e.g., Figure 5A). (The contrary effect was observed for weak responses, recorded during states of low excitability. These are usually delayed and very dissipated in time. Whenever the second of such weak responses was facilitated, then its latency was concomitantly decreased.)

In most cases where the second response was facilitated a rather tonic sink (usually of a secondary response to the first stimulus) was present in layer IV or III or both. Furthermore, if successive recordings of responses to identical double stimuli differed in the degree of facilitation, then the larger second response was associated with a larger coincident secondary response in layers IV/III. Also, stimuli applied during spontaneously occurring sinks in layers IV/III yielded facilitated responses. On the contrary, responses were depressed when they coincided with a sink in layer II. Obviously, the facilitations as well as the depressions were more than just linear summations of the coincident components of the two overlapping responses.

Trains of several stimuli with intervals of about 100 to 500 ms usually induced duplex rhythms with facilitated (i.e., large and delayed) second, fourth, sixth, . . . responses and smaller first, third, fifth, . . . responses. When the interstimulus time was

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←

FIGURE 5 A) CSD responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m) to an abrupt Ganzfeld-luminance increase, before (left CSD) and after the application of picrotoxin (right CSD). Note the amplitude increases of the components, especially components c and f, as well as the increase in onset latency (for details see Results Section 3A).

B) CSD responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m, receptive field 10° eccentric) to reversal of a .5 cycle/deg grating (left half) and a .1 cycle/deg grating (right half). Note the dependence of the response on the preceding interstimulus time (indicated to the left of the stimulus arrows above the CSDs). Note especially the facilitations of the right most responses in both series (for details see Results Sections 3B and 2A).

C) CSD responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m, receptive field 12° eccentric) to appearance (1st stimulus) and disappearance (2nd stimulus) of a .1 cycle/deg grating at constant average luminance before and after the application of picrotoxin and, 20 min later, of pentobarbital. Note the increase in sink amplitudes following injection of picrotoxin and the reverse effect of pentobarbital. Note also the facilitation (control) and depression (pentobarbital) of the second response (for details see Results Section 3).

D) CSD responses in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m, receptive field 12° eccentric) to appearance (1st stimulus) and disappearance (2nd stimulus) of a .1 cycle/deg grating at constant average luminance, presented in a large area (72° in diameter, left CSD), sparing a region of 22° in diameter around the receptive field (middle CSD), and sparing a region of 44° in diameter around the receptive field (right CSD). Note that facilitation of the second response (including components c and f) occurs only in the left CSD, whereas in the right CSD the first response already includes components c and f and the second response is depressed. Note also the gradual increase in onset latency of the responses and the increase in amplitude of component a' the more that the region around the receptive field is spared by the stimulus (for details see Results Sections 3B and 2C).

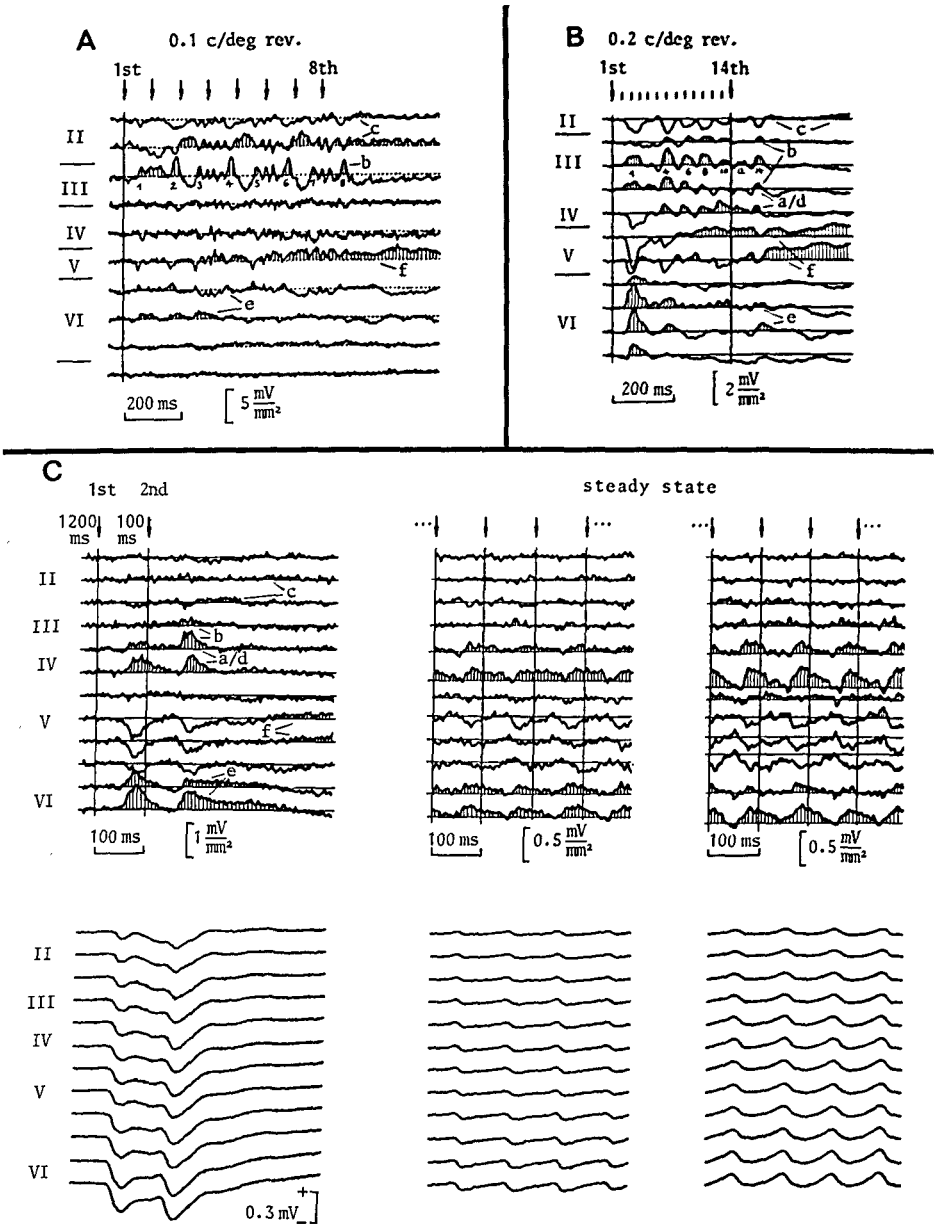

FIGURE 6 A) CSD response in area 18 ($\Delta z = n \cdot \Delta z = 200\mu$m, receptive field 10° eccentric) to 8 reversals of a .1 cycle/deg grating at intervals of 100 ms. Note the duplex rhythm of the responses, the large components c and f at the end, and the high-frequency wavelets in the third, fifth, and seventh responses (for details see Results Section 3B).
B) CSD response in area 18 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m, receptive field within central 3°) evoked by 14 reversals of an .2 cycle/deg grating at intervals of 30 ms. Note the gap between the 1st and the 4th response, the duplex rhythm thereafter, and the large sinks c and f at the end. Note also that sink e is modulated by every stimulus (for details see Results Section 3B). (By ignoring the modulations in layers IV/III, the CSD may also be viewed as *one* slow activation pattern.)
C) CSD responses in area 17 ($\Delta z = 150\mu$m, $n \cdot \Delta z = 300\mu$m, receptive field within central 3°) evoked by double reversals of a .5 cycle/deg grating with a 100 ms interval, preceded by a pause of 1200 ms (left CSD), and evoked by a long train of repetitive reversals at 100 ms intervals (middle and right CSD). Below the CSDs the field potentials are also shown. (The baselines of the steady-state CSDs are arbitrary, because no prestimulus values are available in this situation. The chosen levels are justified, however, by extrapolation from steady-state data with longer interstimulus intervals and by analogy to data from limited train stimuli.) Note that the rightmost CSD and potential profile are more harmonic and larger in amplitude than the middle profiles, but still much smaller than the responses to double reversal (for details see Results Section 3B).

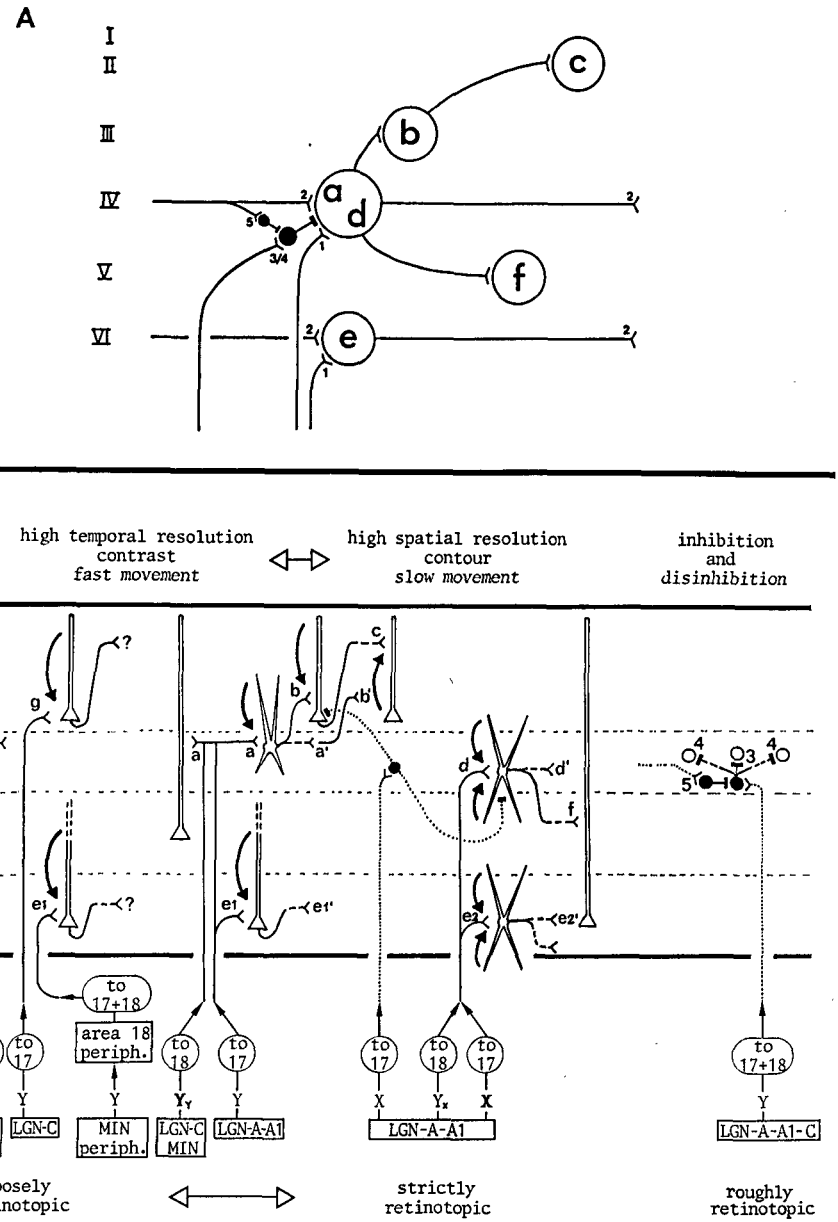

FIGURE 7 A) Schematic diagram of the basic pattern of synaptic activations in cortex as suggested by the intracortical CSDs. It consists of early components a, d, and e in the input layers IV and VI, an intermediate component b in layer III, and late components c and f in layers II and V. The early components a, d, and e are activated by specific and nonspecific afferents (1) and by intrinsic short- and long-distance connections (2). Intracortical inhibition is mediated by afferents (3/4) and is reduced by intrinsic connections (5) via interneurons (filled circles) and acts predominantly on the early components of the cortical activation process.

B) Summary diagram of intracortical circuits and different types of primary afferents in areas 17 and 18, as suggested by the electrically and visually evoked CSDs (see Discussion Sections 1 and 2). Characteristic features of stimuli which dominate activation of circuits are indicated above, retinotopic correspondence of activation is indicated below. Axons mediating intracortical inhibition are dotted (see Discussion Sections 2 and 4). Interrupted axons indicate that long-distance connections are involved. The curved arrows indicate the direction of current flow in the extracellular space, caused by the excitatory synaptic activities of the various relays.

reduced to 50 or 30 ms then a more complex response pattern arose with some type of rearrangement after the first response and then delayed responses to every other stimulus only; in some cases layer VI activity was still modulated by every stimulus. The last response was usually more prominent than the preceding ones, especially its components c and f. When the repetition frequency was increased further then only the onset and the offset of the stimulus train led to responses. (For examples see Figure 6A, B.)

When the stimuli were presented in the steady-state condition of continual presentation for several minutes, no duplex rhythm was apparent; but responses averaged during the later part of the presentation were larger in amplitude and "more harmonic" in shape than the responses averaged during the first few minutes of presentation. However, in all cases the steady-state responses were much smaller than the responses to single or double stimuli. (An example is shown in Figure 6C.)

DISCUSSION

The present investigation of CSD profiles in the cat primary visual cortex has revealed that the responses to different types of stimuli are all qualitatively very similar. A consistent relation between the strength of the stimuli and the strength and speed of activation was observed. Furthermore, systematic temporal and spatial interactions between the response to an external stimulus and the ongoing activity in the cortex could be identified. The specific information, contained in the visual stimuli, including their location in the visual field, were found to be reflected only in modulations of the uniform basic pattern of activation. Correlations as well as discrepancies of these results with other physiological and anatomical findings will be discussed in this section. The main conclusions which will be drawn about the neuronal causes of the evoked-potential generators are schematically summarized in Figure 7B.

1. *The Neuronal Causes of the Basic Activation Pattern*

Since all the different visually and electrically evoked CSDs are qualitatively very similar (Results Section 1) it is most likely that they are all caused by the same types of neuronal activities. According to the preceding study of electrically evoked CSDs, these are excitatory synaptic ensemble activities (Mitzdorf & Singer, 1978). Two facts corroborate this attribution by analogy. First, the changes in visually evoked CSDs brought about by the action of drugs which interfere with the effectiveness of excitatory or inhibitory synaptic transmission (see Results Section 3A) agree best with the notion that inhibitory synaptic activations do not make any significant, direct contributions to the CSDs. Second, contributions from action potentials to CSDs are even less likely if the activations are temporally more dissipated (Mitzdorf, 1985), as is the case for the visually and the nonspecifically evoked activities.

The similarities of all the differently evoked CSDs also indicate that the same intracortical relays and the same cell types are involved in all these activations. Thus, according to the preceding study (Mitzdorf & Singer, 1978), the activation components in layer IV represent monosynaptic activity (sinks a, d) and intracortically relayed disynaptic activity (sinks a', d'). In area 17 component a was attributable to *Y*-type activity and component d to *X*-type activity. From layer IV the *Y*-type activity is projected predominantly to layer III (components b and b') and then to layer II (component c). The *X*-type activity is projected predominantly to layer V (component f).

Layer VI receives monosynaptic *Y*-type activity (early part of component e) and *X*-type activity (later part of component e). In area 18 all components are presumably mediated by *Y*-type activity (see Figure 7B). (Neither in the preceding nor in the present study was any component definitely attributable to *W*-type activity – in agreement with other physiological studies: Ferster & Lindström, 1983: Martin & Whitteridge, 1984; Mulliken et al., 1984; Price, 1985.)

In the main, these interpretations are in good agreement with recent anatomical reconstructions of single-cell axons (Gilbert & Wiesel, 1983, 1985; Lund et al., 1979; Martin & Whitteridge, 1984). Two discrepancies are apparent, however: First, some *X*-type cells were found which project up to lower layer III. In the CSDs this *X*-type activation is probably concealed by the much stronger *Y*-type activation. Second, only one of these reports (Martin & Whitteridge, 1984) suggests significant polysynaptic *X*-type activation within layer V, whereas the CSDs suggest a predominance of *X*-type over *Y*-type activation in this layer. (However, only few axonal arborizations of spiny stellate cells from lower layer IV could so far be reconstructed.) The generality of the basic circuitry, indicated in Figure 7A, is corroborated by the fact that strong intracortical stimulation evokes the same sequence of events (unpublished observation) and by the finding that epileptogenic drugs are most effective if they are applied in layer IV, where all major intracortical pathways start (Ebersole & Chatt, 1984); furthermore, electrical stimulation of the MRF was found to increase deoxyglucose uptake in layers IV/III of primary sensory cortex (Gonzalez-Lima & Scheich, 1984).

The large temporal range of the basic activation pattern from a duration of about 10 ms after electrical stimulation of the primary afferents to a duration of several seconds in response to slowly moving gratings (see Results Section 1) poses a problem. The durations of the monosynaptic components a/d and e are in agreement with the corresponding scatter of afferent input, which is extremely low after electrical stimulation of the primary afferents, about a factor of 10 more dissipated in responses to abrupt visual stimuli; and a moving bar or grating causes retinal responses as long as the movement lasts. The large temporal range of the whole activation pattern may therefore imply either very long time spans for summation of synaptic inputs in the individual cells, or it implies that the transitions from one mass-action component to the next inhere massive compensations of sinks and sources from fast but temporally widely scattered activation sequences of different subgroups. The latter explanation is unlikely, however, because components c and f outlasted the afferent activation by much more than 10 ms in most responses. The alternative explanation needs further evaluation.

The estimate of the effectiveness of the various types of stimuli in activating cortex (Results Section 1) revealed that moving stimuli are more effective than electrical or abrupt visual stimuli in area 17 and electrical activation is more effective than all the visual stimuli in area 18. The superiority of moving stimuli for area 17 is comprehensible when one considers that the activation time of this type of stimulus is long (compared to abrupt stimuli), and that many cells in this area respond tonically. The slight superiority of Ganzfeld-on stimuli over abrupt grating stimuli in both areas (see Results Section 2A) may be astonishing, however, in view of the receptive-field properties of single cells (Hubel & Wiesel, 1962, 1965). But the present results do in fact, agree with single-unit results in this respect because the average values of all single-unit responses have to be considered for an adequate comparison: "Nonadequate" Ganzfeld stimuli evoke few responses in many of the cortical cells (e.g., Baumgartner et al., 1965; Fromm & Bond, 1967; Fuster, 1961; Glass, 1977) . Adequate stimuli, on

the other hand, evoke many action potentials, but only in a few cells (e.g., Rose & Blakemore, 1974). According to the data of the various single-unit studies, mentioned above, Ganzfeld-luminance changes are in fact more effective than adequate stimuli if the total numbers of evoked action potentials are compared.

2. *Anatomical and Physiologial Correlates of the Stimulus-Specific Modulations*

Only minor modulations of the primary activation pattern were observed when the specific features of the visual stimuli were varied (see Results Section 2). This basic uniformity of the primary evoked CSDs clearly contradicts a strict correlation between specific stimulus features and certain intracortical activation components. It rather indicates that every type of stimulus activates every type of relay and that the specific features of the stimulus are only reflected in minor differences in the relative strengths of these activations.

In area 17 the stimulus-specific modulations of the basic CSD pattern can largely be explained by differences in the relative strength of the *X*-type and the *Y*-type activations. The relative predominance of the *X*-type activations (components d and e2) by contour-rich stimuli agrees with the higher spatial resolution of the *X*-type cells; the relative predominance of the *Y*-type activations (components a, b, c, e1) by abrupt luminance changes or high-velocity movements agrees with the better temporal resolution of the *Y*-type cells (Lennie, 1980). Since the contour- versus contrast-specific modulations of the basic CSD pattern were found to be identical in areas 17 and 18, the *Y*-type afferents to area 18 are supposed to consist of a contour-preferring and a contrast-preferring subgroup, analogous to the *X*- and the *Y*-type subgroups of afferents to area 17 (indicated by Y_x and Y_y in Figure 7B). This conclusion agrees well with single-unit studies which revealed close similarity of receptive-field types and their laminar distributions in these two areas (e.g., Harvey, 1980), and with the finding by Frascella and Lehmkuhle (1984) that the *X*/*Y* dichotomy does *not* parallel the spatial/temporal-resolution dichotomy of cells in the LGN.

Since the afferents from A-laminae of the LGN terminate in layers IV and VI via collaterals (Ferster & LeVay, 1978; Gilbert & Wiesel, 1979; LeVay & Gilbert, 1976; Leventhal, 1979) they cannot be the only causes of the early sinks in these layers. Additional afferents must be postulated because the transient parts of these components may differ quantitatively, in onset latencies, and in temporal resolution properties (see Results Sections 2 and 3). The leading components in layers III/IV (very transient a and g) may be due to afferent activation via the C-laminae of the LGN or the MIN. These afferents are predominantly fast conducting, *Y*-type, and terminate exclusively at the border of layers IV and III in area 17 and in layer IV in area 18 (LeVay & Gilbert, 1976; Leventhal, 1979). The leading component e1 is not attributable to activation by primary afferents, since none of these terminate exclusively in layer VI. This component is evoked best by very fast movements, presented in the periphery of the visual field (see Results Sections 2B and C). Riva Sanseverino et al. (1979) found single units in area 18 which respond best to very fast movements, especially in the peripheral visual field; Wilson (1968) described a projection from the border region of areas 18 and 19 to area 17; and Kawamura (1973) found dense degenerating fibers of large caliber in layers V and VI of area 17 after lesioning areas 18 and 19. Therefore, the leading component e1 in layer VI is supposed to be activated via intracortical connections from regions of area 18 which represent the peripheral visual field. (Activations of single cells, excluding the inputs from the A-laminae of the LGN, have been investigated by Malpeli – 1983.)

During slow movements of gratings the individual bars of the gratings cause activations in the input layers IV and VI in area 17 (see Results Section 2B). In single-unit investigations this type of response has been found to be a characteristic property of simple cells (e.g., Movshon et al. 1978a, 1978b). Those are, in many respects, equivalent to *X*-type cells in area 17 (Lennie, 1980). Therefore, the CSD components modulated by the individual bars of a grating are, most likely, the *X*-type relays d and e2 of area 17. The fact that no corresponding modulations were apparent in the CSDs of area 18 is discrepant with single-unit results. This suggests that the rhythmic activation of secondary responses (probably involving mainly complex cells) predominates in the mass-action responses, so that minor stimulus-specific modulations of simple-cell activities are concealed.

A further CSD property which was apparent only in area 17 was the special movement-stop response which consisted of the components c and f (see Results Section 2B). This response is most likely mediated solely by *X*-type cells because it was not evoked in area 18, was more prominent in central than in peripheral regions of are 17, and was related to slow movements of the stimulus. Direct activation of this movement-stop response by primary afferents can be ruled out because the components are located in layers II and V. It may probably be caused by the release from inhibition of those cells which cause the activations c and f.

3. *The Violations of Retinotopy*

The present investigation revealed that nonretinotopic stimulations yield mass-action responses of similar size as retinotopic stimulations (see Results Section 2C). This is not an artifact caused by the inappropriate use of the one-dimensional CSD method. Although this method localizes the sinks and sources only in the vertical direction, the lateral extent of the activations, contributing to the CSDs, is rather small. This lateral catchment can be estimated from the onset latencies of components a and b in the retinotopic responses to the back and fro movement of a bar (see Results Section 2C): Taking the velocities of the moving bars and the cortical magnification factors (Bilge et al., 1967; Tusa et al., 1978, 1979) into account, a lateral inaccuracy due to the one-dimensional CSD method of about 1 mm results. (This rather precise incidental localization of the sinks and sources in the tangential direction is conceivable because the sink/source dipoles are predominantly oriented vertically; and potentials of dipoles fade out very rapidly in the perpendicular direction.) The systematic latency increases of responses to nonretinotopic abrupt stimuli are also inconsistent with large tangential far-field contributions.

Hence, although only the one-dimensional CSD method has been applied, the sinks and sources are localized well enough in the tangential direction to allow an experimental segregation of activations evoked by retinotopically corresponding and noncorresponding stimuli. (The same conclusion was reached by Ebersole and Kaplan, 1981, from simultaneous recordings, 2 to 3 mm apart, of cortical responses to punctate stimuli.) The catchment size of 1 mm may, however, partly be responsible for the negative results in search for orientation specificities and ocular dominances (Results Section 2D). (A more detailed investigation of this point is still needed to reveal the precise orientation-tuning curves of the individual CSD components.)

From the responses to moving gratings and bars it could be tentatively concluded that components a, b, d, and e2 are evoked in a rather retinotopic manner, whereas component g is evoked in a less strict retinotopic manner, and component e1 is caused

predominantly by nonretinotopic stimuli (Results Section 2C). (The latter two components g and e1 may be related to the periphery effect, a predominantly excitatory, fast, nonretinotopic activation found in retina and LGN – McIlwain, 1964; Fischer and Krüger, 1974.) The nonretinotopic components, evoked in layers IV/III by slow and intermediate grating movements and by the onset of movement of a bar, have long enough onset latencies for them to be mediated intracortically (i.e., components a'/d' and b'; see layer-IV synapses "2" in Figure 7A). Also the delays of the response components in layers IV/III to nonretinotopic abrupt stimuli are compatible with them being relayed intracortically (whereas the rather constant onset latency of component e1 is compatible with its nonretinotopic nature). The predominance of the second components (or later parts) of the activations in layers IV, III, and VI in these nonretinotopic responses further suggest that intracortically mediated activations at their terminal sites favour the a-a'-b' pathway (and the e-e' relay), whereas retinotopic afferent activations favour the direct pathway a-b to the supragranular layers. Finally, the nonlinearity of summation of responses to stimulation of subregions of the visual field may be explained by the action of lateral inhibition (indicated by synapse "4" in Figure 7A and to the right in Figure 7B). (The lack of topographic localization of visually evoked potentials has already been described by several authors – Cowey, 1964; Doty, 1958; Ebersole and Kaplan, 1981; Jeffreys, 1977; Srebro, 1985; Vaughan and Gross, 1969; and the nonlinear summation of contributions evoked from different regions of the visual field has also been previously observed – Campbell and Maffei, 1970.)

Anatomical features of neocortex agree well with the presumed tangential spread of activity in layers IV and VI: Many fibers run tangentially within the cortical areas, predominantly in the two bands of Baillarger, and terminate predominantly in or at the borders of the input layers (e.g., Fisken et al., 1975; Garey et al., 1968; Rockland & Lund, 1983). Furthermore, the majority of fibers activating the input layers are *not* primary afferents (Collonier & Rossignol, 1969; Davis & Sterling, 1979; Garey & Powell, 1971; Hornung & Garey, 1981; LeVay & Gilbert, 1976; Somogyi, 1978).

The classical results about the receptive fields of single cells (e.g., Hubel & Wiesel, 1962, 1965), however, are discrepant with the present result of major delocalized activation components in the visual cortex. This discrepancy may be resolved by considering the two basic differencies in the two methods: First, the CSD method lays hold of synaptic activities (supra- *and* subthreshold activations), whereas the properties of receptive fields are concluded from cell responses. Hence, the CSD method reveals one more step of the intracortical processing of afferent information that the investigation of action potentials. Second, the CSD method lays hold of mass actions. These mass actions are assessed whether they are concentrated on a small region of cortex or spread out over a wider area – presuming that they are orderly arranged with respect to cortical depth. The vigorous receptive-field-type firing of a single cell, on the contrary, reflects a very local activation (which may, however, occur in all cortical layers through which the cell extends its dendrites). The differences in receptive-field properties of cells at slightly different tangential locations indicate the focal character of this activation. (Its anatomical correlate is the microcolumn or module with a diameter of about 30 μm – e.g., Mountcastle, 1979; Szentágothai, 1979.) This tangentially sharply localized activation of single cells is, most likely, identical with the synaptic activations causing the localized components a, b, d, and e2 in the CSDs. This combination of the results from the two methods leads to the conclusion that the classical receptive-field responses are generated predominantly by excitatory monosynaptic activations in the input layers and by disynaptic activation in layer III (to-

gether with concomitant inhibitory activation which sharpens the receptive field even more – Sillito, 1975). In perfect agreement with this conclusion, Tanaka (1983) in a cross-correlation analysis of corresponding geniculate and cortical cells found only direct, monosynaptic relations.

The intracortically mediated, delocalized activation components of the CSDs presume the generation of action potentials on the preceding level of activation. This consequence is not discrepant with receptive-field responses if far-reaching axons are assumed to be involved and if the delocalized components are supposed to reflect only subthreshold activities (which may be largely the case for components c and f). Nonretinotopically evoked CSD components may, however, be followed by further activation components (components b, c, a', b', f follow nonretinotopically evoked components a and d – see above). These findings do imply visually evoked action potentials in retinotopically noncorresponding cells. But these cells are supposed to be widely scattered and to contribute only few action potentials each. Therefore these nonretinotopically evoked action potentials are likely to be ignored (or neglected as "spontaneous activities" of the cells) when the classical receptive-field properties are investigated. (The agreement of poststimulus-time histograms and evoked potentials, achieved by Fox and O'Brian, 1965, from large samples of responses, probably indicates the relation between synaptic mass actions and "spontaneous activity".) Actually, a few investigators have concentrated on such subtleties of visully evoked single-unit responses in cortex (for a review see Allman et al., 1985). Although the dominant effect of retinotopically noncorresponding stimuli was inhibitory, some long-range excitatory effects have in fact been revealed (Blakemore & Tobin, 1972; Jones, 1970; Maffei & Fiorentini, 1976).

4. *The Influence of the Internal State on Peripheral Activations*

Rather dramatic effects of conditioning stimuli (or coincidences with spontaneous activities) on evoked responses have been observed in the present study (see Results Section 3B). (Strong interactions between ongoing activity and evoked responses have also been demonstrated – and investigated in the frequency domain – by Başar, 1980.) The second response was facilitated and its latency to onset prolonged when it coincided with a sink in the middle layers. However, when it coincided with the late sink component c of the preceding response then it was depressed. Depression instead of facilitation of the second response was also observed when the animal had received a high dose of pentobarbital or when the visual stimulus was presented in a small region of the visual field only.

The depressory effects may have a rather simple explanation. The first afferent impulse not only leads to activation of the visual system, but concomitantly evokes inhibition (synapses "3" and "4" in Figures 7A and B). This inhibition is large if the activation was strong and is increased by pentobarbital. Therefore, after the injection of an additional dose of pentobarbital and after strong activations, which usually include the late component c, the second afferent impulse arrives at a strongly inhibited cortex (and LGN) and can only cause a small response. Since the evoked cortical inhibition is mediated disynaptically (e.g., Singer et al. 1975; Toyama et al., 1974) and has a slower time course than the evoked excitation it can be assumed to coincide approximately with the late excitatory activation c.

Probably more interesting is the phenomenon of facilitation, which commonly occurred when the CNS was in an intermediate state of excitability and when the first stimulus evoked a moderate response (mostly comprising components a' and b' and/or

a secondary response). An explanation could be found for the paradoxical latency increases of the facilitated CSDs (but not for the corresponding effect of picrotoxin): Delays of single-unit responses in the same range were found in the cat LGN if the stimulus was preceded (up to 600 ms) by a conditioning stimulus (e.g. Brooks & Huber, 1971, 1972; Singer & Phillips, 1974). But, in contrast to the cortical CSDs, the delayed responses in the LGN were reduced in strength. Hence, the delay of the facilitated CSDs most likely is due to the delayed arrival of the primary afferent impulse in cortex, whereas the facilitation itself should be due mainly to intracortical interactions. It is speculated that this facilitation is based on subtle disinhibitory interactions between distant cells or modules: A moderate stimulus may activate some cells or modules more effectively than others. These could inhibit their less effectively activated competitors (via the synaptic activations "4" in Figure 7) and thus reduce the lateral inhibition acting on themselves. Alternatively, intracortically mediated long-distance activations of layers IV/III might cause disinhibition beyond the region of classical lateral inhibition (synapse "5" in Figure 7). In both cases a second stimulus would then yield a larger response in these disinhibited modules.

The association of facilitation with sinks in layers IV/III (mostly secondary responses) as well as the subtle competitions between pathways a–b and a–a'–b' (and e–e') suggest that the evaluating phases of cortical processes are comprised in the activation components in layers IV/III and VI; whereas the late part of the activation pattern (components c and f) may reflect the termination phase of such processes. Previous correlations of secondary components of evoked potentials (similar to components a', b') with complex brain functions (Brazier et al., 1961; John, 1967; Libet et al., 1967; Sakhiulina & Merzhanova, 1966), as well as the susceptibility to deprivation of such components (Glass & Hall, 1982; Siegel et al., 1973; Snyder & Shapley, 1979) corroborate the relation of the first phase of the cortical activation pattern with information processing. The activation of the late part by the cessation of a slow movement in area 17, its predominance in the last response to a train of stimuli, as well as its coincidence with increased cortical inhibition agree with the above association of this phase of cortex activation with the closure of an evaluation.

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