Neural Interaction in Cat Primary Auditory Cortex. Dependence on Recording Depth, Electrode Separation, and Age

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SUMMARY AND CONCLUSIONS

1. Neural activity was recorded with two independent electrodes separated by 0.5–2 mm, aligned in parallel, and advanced perpendicular to the surface of the cat auditory cortex. For smaller separations a solid-state multielectrode array with interelectrode distances of 125 μm was used. The difference in recording depths for the two independently movable electrodes was never more than 100 μm; the electrode contacts of the multielectrode array were at the same depth. Thus the correlation studies dominantly explored horizontal interactions.

2. Out of 995 neuron pairs recorded, 478 represented pairs of single units, whereas the other pairs were contaminated with 5–10% misclassified spikes. Only the single-unit pairs were further analyzed. Of those pairs, 338 showed a clear correlation peak, and in 329 of these the average peak heights were exceeding the Z > 4 significance level (P < 0.0001). Two hundred fifty-two of the significant correlograms (53% of total) could be attributed to common input; the remaining (16% of total) were indicative of unilateral excitation. For the 181 single-electrode pairs the percentage of unilateral excitation pairs (42%) was about the same as the percentage of common input pairs (38%). For the 297 dual-electrode pairs all but one of the 184 significant correlations were indicative of common input. The correlograms indicative of inhibition were found.

3. The correlograms with clear peaks were classified into three types: narrow (n = 40), mixed (n = 77), and broad (n = 221). Narrow and mixed types were with two exceptions found only for single-electrode pairs; broad types were found for single- and dual-electrode pairs. Narrow-type correlograms were in majority of the unilateral excitation type. Correlograms were calculated both for 1-msec binwidth (50-msec lead/lag time) and for 10-msec binwidth (500-msec lead/lag time). The correlograms were characterized by four parameters; the half width of the central peak, the peak correlation coefficient, the association index, and for unilateral excitation cases also by the effectiveness.

4. Across all three correlogram types the half width of the correlation peaks was significantly smaller for single-electrode pairs (mean, 27 ms) than for dual-electrode pairs (mean, 42 ms). For broad-type correlograms only, the mean half widths were not significantly different between single- and dual-electrode pairs.

5. The correlation coefficients (1-msec bin correlograms) were significantly larger for single-electrode pairs (mean, 0.038) than for dual-electrode pairs (mean, 0.011). The same was found for the 10-msec binwidth correlograms.

6. The association index was not significantly different for single- and dual-electrode pairs. In combination with the significant difference in correlation coefficients, this suggests that firings of single-electrode pairs are better synchronized than that the number of associated spikes remains the same.

7. For the 77 unilateral excitation pairs a presynaptic spike produced on average 0.4 postsynaptic spikes, with 61 values <0.5 and only 16 above that value. The values >0.5 were consistently found in cases where the postsynaptic neuron was bursting.

8. The parameters of the cross correlogram were studied as a function of recording depth below the dura surface, as a function of electrode separation in characteristic frequency (CF) difference in octaves above the lower CF of the pair, and as a function of age. The correlation coefficient for single-electrode pairs, in both the unilateral excitation and common input cases, decreased with recording depth. In contrast, for dual-electrode pairs, only the association index decreased with depth.

9. There was no change in the value of the correlation coefficient, ρ, nor in the percentage of significant correlations with CF difference in octaves (range, from 0 to 1.75). The mean ρ for common input single-electrode pairs (broad type only, CF difference always 0) was equal to 0.021 ± 0.019 (mean ± SD) and was significantly higher than for dual-electrode pairs with zero CF difference (0.01 ± 0.012).

10. The correlation coefficients for single-electrode pairs were significantly larger for single-electrode pairs (mean, 0.11) than for dual-electrode pairs (mean, 0.038) than for single-electrode pairs (mean, 0.011). The same was found for the 10-msec binwidth correlograms.

11. During the middle of the second postnatal week, and continuing up to 50 postnatal days, the correlation coefficients for unilateral excitation cases were quite high. The mean value was 0.27 (with individual values up to 0.4) and thereafter decreased steadily with age. In fact, correlation coefficient values >0.3 were not observed in kittens of age 90 days and up. For dual-electrode pairs both the correlation coefficient and the association index increased with age. This could be explained by an increase in the amount of uncorrelated spontaneous activity in both units as a result of an increase in the number of synaptic contacts. These observations also suggest that once a cortical synapse is formed it is essentially mature a very short time thereafter, the decrease in correlation coefficients being only the result from the added “noise” from the newly formed synaptic connections.

INTRODUCTION

The neocortex is considered by some as a highly interconnected neural network that largely works on its own output (Braitenberg 1978). It has been estimated that a mere 0.01–0.1% of the connections to a cortical pyramidal cell originate from the thalamus, i.e., convey sensory information; all the other connections are with cortical cells dominantly (~99%) from the same hemisphere. Even in layer IV the thalamic input contributes no more than 20% of all excitatory synapses (Douglas and Martin 1990). The terminal arborization of a single thalamic nerve fiber, however, covers an area several millimeters in diameter, and it is estimated that each thalamic afferent contacts thousands of cortical neurons. Specifically, for the auditory system this comprises the tonotopically organized projection from the ventral division of the medial geniculate body (MGBv) and the diffuse projection from the non tonotopically organized medial division of the MGB (MGBm). The horizon-
tal spread of thalamic arborizations ensures that many neurons in a particular layer receive simultaneous activation from a single source (Douglas and Martin 1990). It is therefore not surprising that 60–90% of cell pairs in sensory and motor cortex show correlated firing behavior, dominantly of the common input type (reviewed in Eggermont 1990 and Fetz et al. 1991). On the basis of the number of presynaptic, thalamic spikes that are correlated with a single post-synaptic, neocortical spike (Levick et al. 1977), Fetz et al. (1991) suggested that common input pairs in neocortex reflect a modest to good synchrony between the activity of 2–10 unobserved cells (presumably from the thalamus) that give rise to a spike in one of the observed cortical cells that is synchronized with a spike in the other cortical cell from which it was recorded. Morphological evidence also suggests that a single thalamic afferent provides 1–10 synapses to a single postsynaptic neuron (Douglas and Martin 1990).

In addition to the numerically modest number of synapses formed by thalamic afferents, there are extensive excitatory connections between cortical cells both radially within columns and tangentially within laminae. Topical injections of horseradish peroxidase and phaseolus vulgaris leukoagglutinin L in layers I–III of the primary auditory cortex suggest that most of the tangential labeling of axon collaterals of the pyramidal cells proceeds in a dorsoventral direction, i.e., within isofrequency sheets. However, additional patches occur over 1 mm anterior or posterior of the injection site and would therefore not lie in the same isofrequency band as the injection. The labeling appeared discrete with patches separated by ~1 mm over an up to 8-mm range dominantly in layers I–III but also in layer V. Injections in layer IV produce axon collateral spread in layer I over a distance of up to 4 mm (Reale et al. 1983; Wallace et al. 1991). This dense interconnection suggests a anisotropic connectivity that is strongest in the isofrequency sheets but not limited to it. Braitenberg and Schüz (1991) concluded on statistical and geometric grounds that the probability that two cortical neurons, with the axonal tree of one neuron overlapping the dendritic tree of the other neuron, make no synaptic contacts was ~0.9 and the probability of making just one contact was ~0.1. Probabilities for making more than one contact were negligibly small; thus in the system of pyramidal cell to pyramidal cell connections the influence of one neuron onto another's is very weak. Transcolumnar interaction was suggested to be at least an order of magnitude weaker than the intracolumnar interaction (reviewed in Fetz et al. 1991).

The strength of the correlation between cortical neurons, either as a result of thalamic common input or resulting from intracortical connections, is only modest. In Abeles' (1982) data the average peak correlation coefficient was only 0.06. A literature survey suggested (Abeles 1988) that even the strongest synapses did not exceed the peak strength of 0.25 postsynaptic spikes per presynaptic spike. This suggests that only a very small fraction of the firings of two cells is synchronized because of either a common input or a direct unilateral excitation and that the vast majority of the firings is due to asynchronous activation from a large number of other cells. Thus, despite the extensive horizontal connectivity, the cortex appears to be acting as a set of neurons that mostly produces uncorrelated firings and only occasionally seem to synchronize (Abeles 1982, 1988).

Neural interaction studies in auditory cortex comprised those by Dickson and Gerstein (1974), Abeles (1982), Frostig et al. (1983), and Espinosa and Gerstein (1988). The Gerstein group and Frostig et al. did focus on stimulus dependence of neural interaction and left the suggestion that the strength of a cross correlation may function as a code for stimulus-induced changes, a code that may provide better discrimination than the firing rate of the individual units of the neuron pair. The monograph by Abeles (1982) in addition stressed the statistical nature of the cortex with its weak interactions but with occasional signs of strong serial synchronization within a "synfire chain" of neurons. Thus, for practical, information-processing purposes, one could consider the cortical cells as independent.

Besides the low correlation strengths, an additional problem for studying neural interaction in the neocortex is formed by its low spontaneous activity, therefore stimulation is often used to increase the firing rate. A drawback of estimating neural correlations under sensory stimulus conditions is that, for removal of the correlation due to stimulus locking, one has to assume a linear superposition of spontaneously occurring spikes and stimulus-induced ones (Eggermont et al. 1983). Only if this assumption is justified will the subtraction of the so-called shift predictor (Perkel et al. 1967) result in a true estimate of the neural correlation (Melssen and Epping 1987). It is thus possible that stimulus-dependent correlations could be artifacts from violation of the superposition principle.

Various measures for the strength of neural correlation have been used; I only mention the contribution and effectiveness measures (Levick et al. 1972), the correlation coefficient (Abeles 1982), the association index (Epping and Eggermont 1987), the visibility index (Aertsen and Gerstein 1983; Melssen and Epping 1987), and the detectability index (Aertsen and Gerstein 1985) also called the Z-score (Eggermont 1991a). They all have their merits, however, in the case where most of the interaction will be of the common input type, measures such as contribution and effectiveness are less useful because they assume a unidirectional interaction between the neurons.

Most of the reported neural interaction in visual, auditory, and somatosensory cortex indeed appeared to be of the common input type. The width of these correlation peaks was, however, quite varied: under glutamate-induced firings in single columns in visual cortex, common-input peaks were only a few milliseconds wide (Toyama and Tanaka 1984), whereas under stimulus conditions in auditory or visual cortex, widths up to 200 ms were reported for single-electrode pairs as well as pairs recorded from different cortical columns (Dickson and Gerstein 1974; Hata et al. 1991; Kruger and Aiple 1988; Michalski et al. 1983).

This report will be on cross-correlations for cell pairs recorded under spontaneous conditions with single and dual electrodes separated by up to two octaves in characteristic frequency (CF) and at about the same depth below the dura surface. This recording setup allowed the exploration of the horizontal connectivity in a direction both perpendicular to and within the isofrequency slabs. First results on the development of neural interaction with age will also be reported.
METHODS

Animal preparation

Cats were premeditated with 0.25 ml/kg body wt of a mixture of 0.1 ml acepromazine (0.25 mg/ml) and 0.9 ml of atropine sulfate (0.5 mg/ml) subcutaneously. After ∼0.5 h they received an intramuscular injection of 25 mg/kg of ketamine (100 mg/ml) and an intraperitoneal injection of 20 mg/kg of pentobarbital sodium (65 mg/ml). The head was shaved, an incision was made in the skin overlying the skull, lidocaine hydrochloride (Durocain, 20 mg/ml) was injected subcutaneously and rubbed in gently, then the skin flap was removed and the skull cleared from overlying muscle tissue. Three small holes were drilled over the frontal cortex, and fine jeweller’s screws were inserted to serve as an anchor for a large screw that was cemented upside down on the skull with dental acrylic. The cement was allowed to harden for 15 min, and then a 8-mm-diam hole was trephined over the right temporal lobe. If needed, the hole was enlarged with small bone rongeurs to expose the anterior and posterior ectosylvian sulci, thereby assuring that the primary auditory cortex (Aitkin 1990) placed above the animal’s head, which was in the center. The sound-treated room was made anechoic for frequencies >625 Hz by covering walls and ceiling with acoustic wedges (Sonex 3°) and by covering exposed parts of the vibration isolation frame (TMC microg). The head was secured in position with the single screw. Additional acepromazine/atropine mixture was administered every 2 h, and light anesthesia was maintained with intramuscular injections of 2-5 mg·kg⁻¹·h⁻¹ of ketamine. The wound margins were infused every 2 h with Durocain, and also every 2 h new paraffin oil was added if needed. The temperature of the cat was maintained at 38°C with a thermostatically controlled blanket (Harvard Medical Systems). At the end of the experiment, the animals were killed with an overdose of pentobarbital sodium.

Acoustic stimulus presentation

Stimuli were presented from a set of nine speakers (Realistic Minimus-3.5) placed in a semicircle with a radius of 55 cm around the cat’s head, which was in the center. The sound-treated room was made anechoic for frequencies >625 Hz by covering walls and ceiling with acoustic wedges (Sonex 3°) and by covering exposed parts of the vibration isolation frame, equipment, and floor with wedge material as well. Calibration and monitoring of the sound field was done with the use of a B&K (type 4134) microphone placed above the animal’s head and facing the loudspeaker. The intensity rate contours, characteristic frequency, and tuning curve of the individual neurons were determined with tone pips presented once per second. The tone-pip stimulus ensemble consisted of 5 identical sequences of 81 tone bursts covering 5 octaves (tone separation, 1/16 of an octave) from 625 Hz to 20 kHz presented in pseudorandom frequency order at a fixed intensity level. The individual tone bursts had a gamma-shape envelope and an effective duration of 50 ms (Eggermont 1989, 1991b). Thus a complete stimulus ensemble had a duration of 405 s and was presented at various intensity levels. All stimuli were computer generated (Micro Vax II, Data Translation DT2751 12-bit D/A boards, WaveCk Brickwall low-pass filter, HP 8494 programmable attenuators, and Symetrix A-320 power amplifier). The spontaneous recordings were made for 900-s durations.

Recording and spike separation procedure

Two tungsten microelectrodes (Micro Probe) with impedances between 1.5 and 2.5 MΩ were independently advanced perpendicular to the primary auditory cortex surface with the use of remotely controlled motorized hydraulic microdrives (Trent-Wells Mark III). Tip separation of the microelectrodes at the surface was within 0.5–2 mm. In selected animals we also used a five-pronged solid-state multielectrode with horizontal electrode tip separations of 125 μm (Kipke et al. 1991). The electrode signals were amplified with the use of extracellular preamplifiers (Dagan 2400) and filtered to remove evoked field potentials between 200 Hz (Kentu VBF8, high-pass, 24 dB/oct) and 3 kHz (6 dB/oct, Dagan roll-off). The signals were sampled through 12-bit A/D converters (Data Translant, DT 2752) into a PDP 11/53 microcomputer, together with a timing signal from two Schmitt triggers. In general, the recorded signal on each electrode contained activity of more than one neural unit. The PDP was programmed to separate these multiunit spike trains into single-unit spike trains with the use of a maximum variance algorithm (Salganicoff et al. 1988). We added a feature that allowed us to save the waveforms both of the learning set and those during the actual experiment so that we could examine in retrospect the quality of the separation, only data with <5% misclassifications were included in the following analysis. In addition, an inclusion distance (in standard deviations) from the center of each cluster could be selected (usually 2 SD was chosen); spikes outside these areas were classified as class 0 and not stored. The spikes from the separation classes, each assumed to represent a particular neuron, were coded for display. The unit code plus the time of the spike occurrence were sent to the MicroVax II, which presented on a Vectrix graphics processor an on-line color-coded multiunit dot display organized per frequency or in case of spontaneous activity as a function of recording time.

Data analysis

Neural interaction was estimated from the cross correlogram, also called cross-coincidence histogram. The cross correlogram, \( R_{AB}(kΔ) \), is defined as the number of spikes from neuron \( A \) in bin \( kΔ \) given a spike of neuron \( B \) in bin \( 0 \). \( Δ \) is the bin size and \( k = 0, \ldots, K - 1 \). We will use the symbol \( r \) to indicate the lag time, \( r = kΔ \). The expectancy of the cross correlogram under the assumption of independence of the two spike trains is given by

\[
E = N_A N_B / T = N_A N_B / N
\]

with \( T \) the duration of the recording, \( N = T / Δ \) is the number of bins in the record, and \( N_A \) and \( N_B \) are the numbers of spikes of the \( A \), respectively, \( B \) train. The standard deviation for the cross correlogram under the assumption of independence and the additional assumption of Poisson distributed numbers of coincidences per bin is given by the square root of the expected value, \( SD = E^{1/2} \).

A cross correlogram is defined here as significant when we can find at least one bin value that is larger than the expected value plus 4 SD; for large background-bin counts \( E > 9 \) (Wiegner and Wierzbitcka 1987), this would correspond with \( P < 0.0001 \). A more continuous classification can be obtained by transforming the cross correlogram into a Z-score, according to

\[
Z_{AB}(0) = [R_{AB}(r) - E]/(E)^{1/2}
\]

with the peak strength of the cross correlation at lag \( 0 \) can also be
quantified by the correlation coefficient (Abeces 1982) which is defined as

\[ \rho(\tau_0) = \frac{[R_{AB}(\tau_0) - E]}{\sqrt{\left( N_A - \frac{N_A^2}{T} \right) \Delta \left( N_B - \frac{N_B^2}{T} \right) \Delta}} \]  

(3)

and for mean firing rates <5/s can be approximated with <5% error by

\[ \rho(\tau_0) \approx \frac{[R_{AB}(\tau_0) - E]}{(N_A N_B)^{1/2}} \]  

(4)

For this latter approximation, there is a simple linear relationship between \( \rho(\tau_0) \) and \( Z_{AB}(\tau_0) \), where \( \tau_0 \) is the lag for the peak bin

\[ \rho(\tau_0) = (\Delta/T)^{1/2} Z_{AB}(\tau_0) \]  

(5)

In our particular situation where \( T \approx 900 \) s and \( \Delta \) is either 1 or 10 ms, a \( Z_{AB}(\tau_0) \) of 4, indicative of a significant cross correlogram, would correspond to \( \rho \) values of 0.004 and 0.013.

The standard deviation of the correlation coefficient has been given by Shao and Chen (1987), and rewriting it in terms of \( E' \) and \( N - T/\Delta \), while neglecting terms of the order of \( 1/N^2 \) and higher, leads to

\[ \text{SD}(\rho) = \left[ \frac{1}{N} \left( 1 - \frac{E'}{N} \right)^{1/2} \right] \]  

(6)

which for low firing rates and long recording times such as in the present study will be close to \((1/N)^{1/2}\). In our case for correlograms based on 10-ms bins, the value for the SD will thus be

\[ \text{SD}(\rho(10)) = 0.003 \]

and for 1-ms bin correlogram

\[ \text{SD}(\rho(1)) = 0.001 \]

These values indeed amount to one-quarter of the value of the correlation coefficients we considered significantly different from zero.

A drawback of the use of the peak-correlation coefficient or the peak Z-score for determining the significance of an interaction is that only the largest bin count is considered. This, as we will see in RESULTS, can give rise to spurious positive correlations even with Z-scores >4. Measures that take into account the number of spikes in the entire correlation peak are the effectiveness (the average number of correlated postsynaptic spikes per presynaptic spike) and the contribution (the number of presynaptic spikes on average required to produce 1 postsynaptic spike) (Levick et al. 1972), but these measures require a distinction between presynaptic and postsynaptic spike. In cases of common input, which constitutes the vast majority of cortical interactions, a symmetrical measure such as the association index (Epping and Eggermont 1987; Voigt and Young 1990) is more appropriate. The association index, \( A \), is defined as the area under the correlation peak above the expected value (in number of spikes times duration) divided by the expected value under independence: \( A = \text{Area above E-level}/E \). A value of zero indicates two independent spike trains, a negative value would be found in case of inhibition (Voigt and Young 1990), and values above zero for excitation or common excitatory input (Epping and Eggermont 1987). If the peak would only be one bin wide, which can always be accommodated for, A would be identical to the visibility index. The significance of A is difficult to estimate because adjacent bins in the cross correlogram cannot be considered as independent.

RESULTS

The data reported here are from recordings of spontaneous activity from 312 neurons (856 pairs) from all layers of the primary auditory cortex in 9 adult cats and from 79 neurons (139 pairs) recorded in 7 kittens 9–60 days of age. Of these 995 pairs, slightly more than one-half (517) pairs were not further analyzed because one or both of the “units” in the pair had to be considered as “multiunit,” i.e., contained >5% misclassifications. The remaining 478 pairs (401 adult and 77 kitten pairs) comprising 181 single-electrode pairs and 297 dual-electrode pairs form the basis for this report. An overview of the percentage of occurrence of correlations is shown in Table 1.

For both young and adult groups, the percentage of significant pair correlations based solely on the \( Z_{AB} > 4 \) criterion, was \( \approx 87\% \). Yet visual inspection of these correlograms failed in many cases to show a clear peak. This was mostly the case for pairs with low numbers of coincidences and even lower expected values in which case the \( Z \)-scores became artificially high. Visual inspection of the correlograms resulted in 338/478 (71%) correlations with a clear peak, and only 9 of those failed to reach the significance criterion of \( Z_{AB} > 4 \). Thus 329 correlograms showed statistically significant and clearly visible peaks. For pairs in which both units had >100 spikes in 900 s (389 cases), the percentage of significant correlations was close to 90% (i.e., 349 significant correlations). This suggests that the \( Z_{AB} > 4 \) criterion combined with a minimum spike-count criterion of 100 is comparable with visual scoring. In the following analysis the significance of correlograms is based on the more conservative combined visual scoring and the statistical significance criterion.

A nearly perfect linear relationship with the predicted slopes (according to Eq. 5) was found between correlation coefficients and Z-scores; for the 1-ms binwidth correlograms the slope was 0.001, and for the 10 ms binwidth correlograms we obtained 0.003; the squared correlation coefficients for these relationships were, respectively, 1 and 0.999. So significance criteria can be based on both \( Z \) or \( \rho \).

The cross correlograms were classified into three main categories: 1) narrow: correlograms with a sharp peak mostly located a few milliseconds away from zero lag and having a width <5 ms; 2) broad: those correlograms with a broad peak (width, >5 ms) straddling zero lag time; and 3) mixed: correlograms with a broad peak and superimposed narrow peak. The narrow and mixed category were with two exceptions found for pairs recorded on a single electrode; the broad category was found for pairs recorded on single as well as dual electrodes. The two cases showing the

<table>
<thead>
<tr>
<th>Total number of pair correlograms</th>
<th>Total number of single-unit pairs</th>
<th>Total number of dual-electrode pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>995</td>
<td>478</td>
<td>589</td>
</tr>
<tr>
<td>Number of single-unit pairs</td>
<td>406</td>
<td>181</td>
</tr>
<tr>
<td>Number of dual-electrode pairs</td>
<td>589</td>
<td>297</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentages.
narrow or mixed type correlograms for dual-electrode pairs were obtained for an electrode separation of only 125 μm. The cross correlograms were classified into 40 (12%) narrow, 221 (65%) broad, and 77 (23%) mixed types.

The majority of the significant correlograms (252/329, which is 53% of the total number of pair correlations) was indicative for common input.

**Individual data**

Examples of cross correlograms with different half width and for two different time bases (50-ms lag/lead time with 1-ms bins, and 500-ms lead/lag time with 10 ms bins) are shown in Fig. 1. Figure 1A shows a narrow correlogram, most likely indicative of a unilateral excitation, for a single-electrode neuron pair (CF = 2.5 kHz) recorded in a 47-day-old kitten at ~1,100 μm below the dura surface. A 1-ms dead time around zero is observed, and the cross-correlation peak is displaced 2 ms from zero lag time with a peak-correlation coefficient of 0.125. In the 500-ms time-base correlogram (ρ = 0.235) a faint background oscillation is noted. The significance levels for excitation (expected value plus 4 SD) are drawn in. Figure 1B shows a mixed correlogram for a single-electrode pair (CF = 20 kHz), recorded in a 104-day-old cat at 1,900 μm below the dura, consisting of a narrow peak on a relatively broad pedestal (ρ = 0.039). The long time-base correlogram (ρ = 0.123) shows suppression regions around 50 ms lag time that exceeded the significance level for inhibition or suppression. In this case the suppression could be attributed to the autocorrelation properties of the two units. Figure 1C shows one of the few examples of a mixed correlogram for a dual-electrode pair (CFs 7.0 and 11.9 kHz), recorded in a 92-day-old cat at a depth corresponding to layer II, with a narrow central peak around zero lag time superimposed on a rather broad pedestal (ρ = 0.052). In the long time-base correlogram (ρ = 0.32), evidence for an oscillatory process, reflecting the oscillatory autocorrelograms of the two units, can be seen. The suppression regions are significant at the 0.0001 level but completely attributable to the single-unit autocorrelograms. Figure 1D shows a broad correlogram (half width, 29 μs; ρ = 0.014) obtained for a dual-electrode pair (CFs both 20 kHz or slightly higher), recorded at a depth of 440 μm in a 1-year-old cat, with the peak around zero and evidence for a 10 Hz oscillation in the long time base correlogram (ρ = 0.099). Figure 1, E and F, both representing dual-electrode pairs (CFs in both cases close to 20 kHz), shows examples of asymmetric cross correlograms. In Fig. 1E the asymmetric suppression is significant at the 0.0001 level. The asymmetries could completely be explained by the long-tailed autocorrelograms for the B unit. In Fig. 1F the B unit was weakly oscillatory and had burstlike properties.

In all these cases the frequency response areas were identical (single-electrode pairs and some dual-electrode pairs) or showed overlap at higher tone-pip intensities (in case of dual-electrode pairs). For example, the pair shown in Fig. 1C was recorded on electrodes separated by ~1 mm (CFs, respectively, 7 and 11.9 kHz), and the response areas overlapped as shown in Fig. 2. This figure shows side by side dot displays for 100 ms after the 50-ms tone-pip onset and for stimulus frequencies from 625 Hz to 20 kHz (log scale, 5 decades) for intensities of 75 (Fig. 2A) to 25 dB p.e. SPL (Fig. 2F) in 10-dB steps. The threshold for unit A, left column, was most likely ~45 dB. The threshold for unit B was much better defined and estimated at 20 dB SPL. The CF was also better defined for unit B (CF, 11.9 kHz) than for unit A (CF, ~7 kHz). The response latencies (including 1.5-ms acoustic delay) at high intensities were comparable at ~12–14 ms. Postactivation suppression was more pronounced for the A unit.

**Group results**

The peak positions in the cross correlograms were in 182/338 (54%) of the cases situated at 0 and in 90 cases (27%) either at ±2 ms. The remaining correlograms had peaks at delays between 2 and 10 ms.

Frequency distributions for half width of the cross correlograms for single (□) and dual (□ II) electrodes in adult cats are shown in Fig. 3. It is clear that narrow-peaked correlograms (or mixed when the pedestal is lower than half height) dominantly occur for single-electrode pairs. The half width of the cross correlogram was significantly smaller (P < 0.05) for single electrodes (mean, 27 ms) than for dual electrodes (mean, 42 ms). In case of broad correlograms only, the difference in half width was not significantly different between single- and dual-electrode pairs. In case that only single-electrode pairs were considered, no significant difference was found between the half width for the mixed (mean, 26 ms) and broad (mean, 27 ms) category.

The distribution of correlation coefficient values for all the significant 1- and 10-ms bin correlograms is shown in Fig. 4, A and B. The vast majority of correlation coefficient values for the 1-ms bin cases was <0.07, and the highest value observed was 0.4. The correlation coefficients for the 10-ms bin correlograms were generally larger than for the 1-ms bin correlograms. The correlation coefficients, ρ, for 50- and 500-ms correlograms were significantly larger for single-electrode pairs (means, 0.038 and 0.111) than for dual electrode pairs (means, 0.011 and 0.049). For the group of broad correlograms this difference was significant as well. Figure 5A shows the curvilinear relationship between the logarithms of both correlation coefficients. In 77/329 of the cases with significant correlation peaks (16% of single-unit pair correlations), we saw evidence for unidirectional excitation (Fig. 1A shows an example). For the unidirectional excitation cases the mean ρ(1) was equal to 0.08, and the mean ρ(10) was equal to 0.18, and a linear relationship between the logarithms of the two correlation coefficients was found (Fig. 5B).

The effectiveness measure for these unilateral excitation cases was between 0.018 and 2.8 with a mean value of 0.403 (SD = 0.463), and the distribution is shown in Fig. 6. The vast majority of values (56/77) was <0.5. The values <0.5 were consistently found in cases where the postsynaptic neuron was bursting.

Figure 7 shows the distribution of A values for single (□) and dual (□ II) electrodes, which in some way resembles that for the half widths (cf. Fig. 3); one notices that the modes of the distribution are 1 and 8 ms. The mean association index, A, for broad-peaked correlograms was larger for single electrodes (mean, 31.9 s; SD = 39.6) than for dual electrodes (mean, 21.0 s; SD = 60.1), however, this difference
FIG. 1. Examples of cross correlograms on a short time base (1-ms bins) and a long time base (10-ms bins). In the left and right top corners of each graph, the peak count and the correlation coefficient are shown. The upper and lower 4 SD boundaries are drawn in. A: example of a narrow-type correlogram for a single-electrode pair indicative of unilateral excitation; the correlation coefficients were, respectively, 0.125 and 0.235 for the short and long bin correlogram. B: example of a mixed-type correlogram for a single-electrode pair. Correlation coefficients were, respectively, 0.039 and 0.0123. C: example of a mixed-type correlogram for a dual-electrode pair with correlation coefficients of 0.052 and 0.32. D: example of a broad-type correlogram from a dual-electrode pair; correlation coefficient 0.014 and 0.099, respectively. E: example of an asymmetric, broad-type correlogram for a dual-electrode pair. Correlation coefficients 0.16 and 0.1. F: another example of an asymmetric, broad-type correlogram for a dual-electrode pair with correlation coefficients of 0.011 and 0.092.

was not statistically significant. For single-electrode pairs recorded in adult cats, the association index was significantly different for the three correlogram categories ($F_{2,121} = 14.47, P = 0.0001$), with the mean value for the narrow correlograms (1.5 s) smaller than for the broad correlograms (mean, 30.2 s) but not significantly smaller than for the mixed category (mean, 6.5 s). Such a significant difference could not be demonstrated for the young animals ($F_{2,26} = 1.52, P = 0.24$) most likely because of the smaller group size.

The log of the association index (based on the 10-ms binwidth correlograms) was negatively correlated with the log of the correlation coefficient for the 10-ms binwidth correlograms ($P = 0.0018$). This suggest that the broadening of the correlogram usually occurs at the expense of the peak value.
Fig. 2. Series of single-unit dot displays for the unit pair shown in Fig. 1C. As a result of spontaneous activity, this is a better illustration of the tuning properties than a tuning curve.

Adult data showed a dependence on recording depth (in \( \mu \text{m} \) below the dura surface; we considered only data from those cats where a complete recording profile, with recordings roughly at every 100 \( \mu \text{m} \), through the entire thickness of the cortex was made) with respect to the parameters of the correlograms. For single electrodes, half width and association index were not significantly dependent on depth, whereas the correlation coefficient decreased significantly with depth \( (P = 0.0005) \) as shown in Fig. 8A. This was found for the unilateral excitation cases and the common input cases separately as well as combined. For dual electrodes the association index decreased with depth \( (P = 0.0012) \) as shown in Fig. 8B but the half width and the correlation coefficient were not significantly dependent on depth. In two individual cats a slightly different behavior was noted: dual-electrode pairs showed a nearly constant \( \rho \) and \( A \) for the 650- to 1,600-\( \mu \text{m} \) region, and \( \rho \) increased both toward the surface and toward deeper layers. The association index, however, behaved in a reciprocal way to \( \rho \): \( A \) was maximum in the range of 650-1,600 \( \mu \text{m} \) and decreased both toward the surface and toward depths of 2,300 \( \mu \text{m} \). In the two other cats the behavior was more in line with the average behavior.

The dependence on CF of the correlogram parameters was explored: the logarithm of the half width increased with the logarithm of the CF \( (P = 0.045) \), whereas the logarithm of the correlation coefficient decreased with the logarithm of the CF \( (P = 0.0001) \). Because of the range of CF values in this study, mostly in the 2 to 20-kHz range, the logarithm of CF can be considered roughly proportional to the distance of the recording site from the rostral border of the primary auditory cortex (Merzenich et al. 1975). Although there was a dependence of the correlation coefficient with cortical location, surprisingly no dependence of the correlation coefficient on the CF difference in octaves was found. This is clear from a plot of the logarithm of the correlation coefficient for dual-electrode pairs as a function of the CF difference in octaves; the values for single-electrode pairs are drawn in for reference (Fig. 9). Note that the various symbols in this figure reflect the number of overlapping data points, which is equal to the number of radii on the star symbols. Comparing the \( \rho \) values for single-electrode pairs and dual-electrode pairs with a zero CF difference showed...
no further decrease with electrode separation. The incidence of significant correlations did not change significantly with increasing CF separation. Deleting units with CF values assigned close to 20 kHz (highest frequency tested), and which therefore may not have been as accurate, did not change this picture.

The age dependence was explored separately for narrow- and broad-peaked cross correlograms, and the findings are summarized in Table 2. For narrow cross correlograms, all obtained for single-electrode pairs, the correlation coefficient decreased with age (regression analysis, \( P \) values, respectively, 0.012 and 0.0042 for the 1- and 10-ms bin correlograms). Figure 10A shows the age dependence of \( \rho(10) \); a clear difference in \( \rho \) values between the young age group (<60 days) and the adult group can be seen. In contrast for broad correlograms from dual-electrode pairs, both correlation coefficients as well as the association index increased with age (\( P \) values, respectively, 0.0003, 0.0002, and...
FIG. 9. Dependence of the correlation coefficient on the difference in characteristic frequency in octaves for dual-electrode pairs. For comparison the values of the correlation coefficient for single-electrode, broad-type correlograms are drawn in as well. The various symbols in this figure reflect the number of overlapping data points that is equal to the number of radii on the star symbols.

0.0008). Figure 10B shows that the nonzero slope for the regression of $\rho(10)$ on age is largely due to correlation coefficients in the range of 0.15–0.45 for the oldest cat. The percentage of unilateral excitation pairs was larger for young animals than for adult ones, whereas for the proportion of common input pairs the reverse was true. Parameters for broad correlograms recorded on single electrodes did not show any age dependence.

\[ y = -0.001x + 265; r^2 = 0.214 \]

\[ y = 2.13E-4x + 0.031; r^2 = 0.074 \]

FIG. 10. Age dependence for the correlation coefficient for narrow-type, single-electrode pair, correlograms (A) and for broad type, dual electrode pair, correlograms (B).

### Table 2. Age differences in the occurrence of cross correlations

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Adult</th>
<th>Young</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of single-unit pairs</td>
<td>478</td>
<td>401</td>
<td>77</td>
</tr>
<tr>
<td>Number of pairs with visually clear peaks</td>
<td>338 (69)</td>
<td>282 (70)</td>
<td>56 (73)</td>
</tr>
<tr>
<td>Number of single-electrode pairs ($Z &gt; 4$)</td>
<td>145 (30)</td>
<td>111 (29)</td>
<td>28 (36)</td>
</tr>
<tr>
<td>Number of dual-electrode pairs ($Z &gt; 4$)</td>
<td>184 (38)</td>
<td>157 (39)</td>
<td>27 (35)</td>
</tr>
<tr>
<td>Number of unilateral excitation pairs</td>
<td>77 (16)</td>
<td>60 (15)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>Number of common-input pairs</td>
<td>261 (55)</td>
<td>222 (55)</td>
<td>39 (51)</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentages.

### Discussion

**Recordings are exclusively from pyramidal cells**

The dominant interaction feature of the cortex is that of pyramidal cell to pyramidal cell connection. On the basis of the assumption that the synapses between cells are entirely made by chance and that the cortex consists of 85% pyramidal cells and 15% stellate cells, Braitenberg and Schüz (1991) computed the probabilities of synaptic connections between various cell types. From pyramidal cell to pyramidal cell, one expects $\sim 72\% (0.85^2)$ of the total amount of synapses to be present as excitatory synapses on dendritic spines. The pyramidal cell to stellate cell interaction is mediated by excitatory synapses onto the dendritic shafts (13% of total). The stellate cell to pyramidal cell connections are through inhibitory synapses on pyramidal cell bodies (13% of total), and finally the interaction from stellate cell to stellate cell as inhibitory synapses on dendritic shafts is represented by only 2% of the total amount of synapses. It is thus likely that the excitatory connections between pyramidal cells will form the morphological substrate for the majority of the observed neural pair interactions.

Recordings with relatively large (1.5–2.5 MΩ) tungsten microelectrodes are most likely from the larger, pyramidal cells in the cortex and missing the smaller stellate and basket cells. The spikes in the present study invariably were of "regular spike" appearance (McCormick et al. 1985), adding weight to the assumption that all recordings were indeed from pyramidal cells. The bias for large cell recordings combined with the prevalence of synapses with and between pyramidal cells makes this very likely indeed. It is therefore understandable that no unilateral inhibitory interactions, presumably involving smooth stellate and basket cells, were obtained in this study.

**Spike separation procedure**

The single-electrode recordings always consisted of spikes from more than one unit. Using spike separators to sort out the single-unit spike trains from a multunit record has the inherent weakness that superimposed spikes are sorted in a separate class; such spikes are thus effectively removed from the single unit spike trains and thus from the analysis. It is generally possible to decompose these compound spikes if one is sure about the waveforms of the contributing single-unit spikes, however, this is a very elaborate procedure that also requires storage of all spike waveforms. The result of not performing that decomposition is that, within ±1 spike duration, there will be no coincidences in
the correlogram. After subtraction of the expected value of the correlogram, this will show up in the cross correlogram as a trough. Only those troughs that extend well beyond this ±1.5 ms spike duration and were of sufficient size could be considered as indicative of a negative correlation. We have not seen any evidence in our material for such unilateral inhibitions. Because of the limited extension of the inhibitory connections in cortex, the large majority of these negative correlations will be on a single electrode. The “dead” time of the spike separator could thus result in serious underestimation of the incidence of direct inhibitory interactions. Interactions of the reciprocal input type that would feature a relatively wide trough around the origin of the correlogram may still be detected, however, were not seen either in this study.

Another factor that could influence the cross-correlation results is misclassification of spikes. If there are random misclassifications and only a fraction of the spikes is misclassified (say < 5%), the effect is marginal (as simulations have shown; unpublished observations). Our off line quality check procedure allowed 5% misclassified spikes per class to be acceptable. Classes with more than this number of misclassifications were not further considered; this eliminated about one-half of the potential number of pair correlations in our study. More serious problems could occur when spikes in a burst showed a decrease in amplitude, and the smaller ones tended to be classified as another neuron. We have not found any evidence for this in our data.

The effect of dead time on the pair correlations is clear from Fig. I A, where a narrow peak is found 2 ms to the left of the central bin. The unilateral nature of the peak suggested a direct excitatory connection between the units. The dead time of ~1.5 ms precludes the estimate of the synaptic delay between the two units and also eliminates any definitive statements about the shape of the cross-correlation peak. As a consequence the estimates of the correlation coefficients may be lower than they really are because spikes occurring during the spike sorter’s dead time may have failed to contribute to the correlation peak.

Significance of cross correlations

Various measures to judge the significance of the cross correlograms have been used. Statistical criteria, based on Poisson distributed counts per bin, are usually only valid for high background bin counts (Wiegner and Wierzbicka 1987). Not all our recordings fulfilled that criterion. Therefore we opted for a combined visual and statistical criterion. Visual inspection allowed us to select only those correlograms with a clear peak. On this selection of correlograms, the criterion of peak amplitude larger than the expected value plus 4 SD was used. Other criteria could have been used; such as random shuffling of pairs, with the proviso that they consisted of nonsimultaneous recordings, and computation of the expected range of peak values for this set of independent pairs. One can then use criteria for say the 0.1% false-positive level in the randomized material and use that to set the significance level for the simultaneously recorded pairs (Eggermont 1991a). For our data the correlation coefficients values were linearly related to the Z-score. A derivation of an estimate for the SD of the correlation coefficient led to the establishment of a significance level for correlation coefficients that corresponded very closely with significance levels based on Z-scores. Thus, for purposes of significance of correlograms, either parameter could be used.

Our findings of 53% of common input correlograms and 16% of unilateral excitation correlograms and the absence of signs of direct inhibitory interactions or reciprocal input in our spontaneous recordings differ somewhat from findings in other reports on interaction in auditory cortex. Abeles (1982) found 45% flat correlograms, 28% common input, 12.5% excitation, 8% inhibition, and 2% with bilateral troughs. Dickson and Gerstein (1974) found 50% common input and 5% functional interaction, a fraction of which was inhibitory in nature. In Frostig ct al.’s (1983) single-electrode pair data, 66% of the pairs showed common input, 8% reciprocal input, and 12% direct excitation, whereas there was no sign of direct inhibitory interactions. All these results were obtained in unanesthetized animals. Thus, compared with these studies, we observed about the same percentage of common input pairs and unilateral excitation, however, considerably less reciprocal input and unilateral inhibition pairs. As we have discussed before, this may have been due to the use of tungsten electrodes.

A common input peak can arise both from shared excitatory input but also from shared inhibitory input. The latter condition is expected to occur much less frequently. Again, if we assume that we record exclusively from pyramidal cells, where 85% of the synapses on pyramidal cells are excitatory and 15% are inhibitory, the likelihood of common excitatory input would be a factor 7 higher than that of common inhibitory input. The duration of an excitatory postsynaptic potential (EPSP) in mature cat cortex is of the order of 10 ms, whereas that of an inhibitory postsynaptic potential (IPSP) is generally > 50 ms (Ribauipierre et al. 1972), and their rise times vary accordingly. Because the primary effect of a common input correlogram is, under certain model assumptions, formed by the convolution of their postsynaptic potentials, one would expect that those correlogram peaks with larger half widths were the result of common inhibitory inputs. The presence of bursting, which also may increase the central peak width, makes this conclusion not universally valid. So for practical purposes we have no unambiguous way to distinguish common inhibitory input from common excitatory input from the width or size of the cross-correlation peak.

The incidence of positive and negative correlations in our material is thus largely comparable with that in other reports concerned with the auditory cortex. The range of values of the correlation coefficient agrees well with those of Abeles (1982), although in our material several higher values are found, mostly for unilateral excitation cases. The width of the central peak in the cross correlogram was within the range of values reported for both auditory and visual cortex.

Effects of anesthesia

The correlation properties of neurons in the cerebral cortex are dependent on the attentive or sleep state of the ani-
mal (Noda and Adey 1970, 1973; Burns and Webb 1979); during slow-wave sleep or anesthesia, high correlations in the firing rate of simultaneous recorded neurons are obtained, whereas during arousal, wakefulness, or REM sleep, neurons discharged quite independently. This led Burns and Webb (1979) to state that “it is not unreasonable that when the brain is processing information, neighboring cortical neurons are very unlikely to be found doing the same thing at the same time.” Comparing the values of the correlation coefficient values from our study with those from Abeles (1982, 1988), which were obtained in awake animals, suggests that the light ketamine anesthesia that was employed in the present study did not result in major differences. The mean correlation coefficients in this study for single electrode pairs were, respectively, 0.038 and 0.111 for our 1- and 10-ms bin correlograms as compared with Abeles’ value of 0.06 for 5-ms bin correlograms. On the basis of change in binwidth alone, one would expect for our data a correlation coefficient of 0.08 for 5-ms correlograms, which is quite comparable with Abeles’ value. The incidence of significant correlations, however, was considerably higher in our study than in Abeles’ (1982, 1988) studies in behaving animals and slightly higher than in Dickson and Geister’s (1974) report on correlations in awake, paralyzed animals. So it cannot be excluded that the light anesthesia used in the present study is favorable for inducing correlative behavior between neighboring and distant units. This could have been caused by an anesthesia-related decrease in uncorrelated, background activity on both neurons relative to the awake condition. The increased background activity in awake animals will reduce the value of the correlation coefficients and in some cases could make them statistically insignificant.

**What does the value of a correlation coefficient imply for cortical processing?**

Correlation coefficients only quantify peak values, i.e., the fraction of nearly perfectly synchronized spikes in the output spike train that were correlated with spikes in the input train. This measure differed for different binwidths in the correlogram, and we have computed correlation coefficients for both 1-ms bin and for 10-ms bin correlograms. The range of values for the 1-ms bin correlograms rarely exceeded 0.07 with the largest value of 0.4. This suggested that, although statistically significant [if \( p(1) \) exceeds 0.004], the correlations between cortical, presumably pyramidal, cells at the same depth below the dura surface are extremely weak. Rarely more than 10% of the spikes in the B spike train could be accounted for by spikes in the A train. These values were different for single- versus dual-electrode pairs, even if only the broad category of correlograms was considered, because single-electrode pairs invariably showed larger correlation coefficient values. This suggests that the functional interaction between cells belonging to the same cortical column is stronger than that of cells in different columns. Thus the weight of a single neuron in cortical processing seems to be minimal, and the fact that single (visual) cortical neurons appear unable to signal unambiguously the presence of a particular stimulus or stimulus feature (Douglas and Martin 1990) appears to corroborate this.

A measure that takes into account the number of spikes in the entire correlation peak is the association index. In contrast to the correlation coefficient, the association index was not significantly different for single-electrode versus dual-electrode pairs. This suggests that the smaller correlation coefficients found for dual-electrode pairs are generally the result of the broadening of the cross-correlation peak, whereas the number of associated spikes in the peak did not change. Thus the difference between single- and dual-electrode pair interactions is largely a matter of synchronization. Because the half widths are considerable the difference is unlikely to be caused by differences in axonal conduction time or the interposition of a few synapses in the common input pathway. A more likely cause is a differing number of inputs from uncorrelated neurons on dual-electrode pairs.

The effectiveness of presynaptic spikes for unilateral excitation cases was \( \sim 0.4 \), suggesting that the effect of a presynaptic spike on the postsynaptic spike train is quite pronounced in these cases. This value is \( \sim 3.5 \) times as high as that of the correlation coefficient (0.12 ± 0.09) in the same group, suggesting that even in these narrow and mixed type correlograms short, 3- to 4-spike postsynaptic bursts are quite frequent. The effectiveness for this group was linearly related \( (y = 1.419x + 0.116, r^2 = 0.305, P = 0.0016) \) to the correlation coefficient for the 1-ms bin correlograms.

**Depth effects on the horizontal interaction**

One could speculate that the decrease in \( p \) and \( A \) with depth is due to a decreasing common input with depth. The tonotopically organized input from the MGBv is most widespread in the middle layers, and this should cause increased correlations for single-unit pairs with identical CF, whereas the diffuse input from the MGBm is strongest in layers I and VI, and this should therefore increase the correlation for dual-electrode pairs with different CFs in these layers (Winer 1991). Intracortical connectivity is supposedly strongest in layers I–III (Wallace et al. 1991), which should give rise to increased correlations as well. Combining the thalamic and intracortical connectivity patterns suggests that those within the upper layers are somewhat more abundant than in the deeper layers, and hence one could then expect somewhat larger values for \( p \) and \( A \). This remains entirely at the level of speculation, however.

**Effects of CF difference on the cross correlation**

In our material about one-half (77/151) of single-electrode pairs showed unequivocal signs of unilateral excitation, whereas this was absent in the dual-electrode pairs. Dual-electrode pair correlation coefficients were only about a factor 2 smaller than those for single-electrode pairs. This is much less than the order of magnitude difference that was deduced by Fetz et al. (1991) from Ts’o et al.’s (1986) data for intracolumnar versus transcolumnar interaction in visual cortex. The drop from single-electrode pair mean value of 0.02 (for broad correlograms only) to 0.01 for dual-electrode pairs with the same CF suggested that, even within an isofrequency sheet, correlation decreases with distance. We
did not see any further decrease in the value of the correlation coefficients for CF differences up to 1.75 octaves, which roughly corresponds to 1.75-mm electrode separation (Merzenich et al. 1975). Hata et al. (1991) found a marked decrease in the proportion of cell pairs with correlated firings under stimulus conditions for horizontal electrode separations of 0.4-1 mm but did not quantify the strengths of the correlations. In contrast, our spontaneous data do not show a change in the incidence of correlations with separation in CF. It is commonly believed (e.g., Stryker 1989; White 1989) that corticocortical interactions are excitatory at very short range (within a column) and inhibitory up to 400-μm distance. Our data, although they cannot distinguish between common excitatory and common inhibitory input, obtained under spontaneous conditions seem to argue against such a short range of interaction. It remains possible, however, that under stimulus conditions the range of neural interaction is much more restricted than under spontaneous conditions because of the synchronization of lateral inhibition through tonotopically organized common input from the ventral division of the MGB. Narrow-type correlograms in visual cortex were restricted to distances of ~220 μm, and broad correlograms extended over distances >1 mm (Krüger and Aiple 1988; Michalski et al. 1983). This larger range for the broad correlograms could be related to the extension of axon collaterals of neurons in the vicinity and might involve both pyramidal and nonpyramidal cells. Axon collaterals extend over longer distances (up to 3-8 mm) horizontal to the dura surface (e.g., Ts'o et al. 1986 for supragranular layers in the visual cortex; Wallace et al. 1991 for the primary auditory cortex). Simultaneous activation of neurons within two distant columns will not only be mediated by direct connections between the pair of cells, but more likely also by common input to these cells from the divergent afferents from the medial division of the MGB. Common input from the nontopographically organized broadly tuned neurons from the MGBm (Winer 1984) or from pyramidal cell axon collaterals branching out of the isofrequency sheets (Wallace et al. 1991) can explain why neurons with rather different tuning curves show relatively strong common input under spontaneous conditions.

**Effect of age on the cross correlation**

The first synapses to be formed in neocortex are between layer I axons and the apical dendrites of layer V and VI pyramidal cells. At E55 the projections from both the ventral and medial division of the MGB are present, and the organization is very similar to those in mature cats, however, the pattern of connections linking cortical areas in postnatal kittens is very different from that in adult cats (Payne et al. 1988). The projections from thalamus to cortex in the cat form quite secure synapses at postnatal day 6 (Purpura et al. 1965), and together with those from one cortical area to another both achieve their mature form some 4-6 wk after birth. The shorter intrinsic connections also develop mainly after birth. The number of synapses in visual cortex increases sharply after the first postnatal week to ~6 wk after birth. At birth an average neuron forms only between 0.8 and 3% of the adult number of synapses (Payne et al. 1988). In visual cortex these synapses will be mainly of the corticocortical and local arboring collaterals type that make excitatory synapses; the thalamic and callosal projections do not seem to start (excitatory) synapse formation until after the end of the first postnatal week. During this first postnatal week inhibitory synapses are most likely completely absent, because no IPSPs can be elicited during that period (Miller 1988). Thus it was surprising that in the present study the correlation coefficients for narrow-type, single-electrode pair, correlograms during the middle of the second postnatal week were quite high. The mean value during this period was 0.27 (with individual values up to 0.4) and remained high up to postnatal day 50, thereafter the correlation coefficient decreased with age. In fact, correlation coefficient values >0.3 for narrow-type correlogram pairs were not observed in kittens age 90 days and up.

The reduction in the correlation coefficient with age may be entirely due to the increase in the number of background spikes, mainly as a consequence of the increase in firing rate with age (Faggermert 1991c). Leaving out the normalization, i.e., the division by \((N_aN_b)^{1/2}\), in the calculation of the correlation coefficient (Eq. 3) showed that the age dependence for the single-electrode, narrow correlogram, subgroup disappeared (P values now, respectively, 0.18 and 0.27). Considering only the dependence of the peak value of the correlogram without subtracting the expected value (which is also affected by the total number of spikes) basically corroborates this; there was no age dependence left (P values, respectively, 0.19 and 0.42). The increase in firing rate was therefore mainly due to the increase in uncorrelated firings, most likely the result of the increased connectivity between cortical cells. The average correlation coefficient decreased by about a factor 3-4 between 10 days and 70 days of age. This suggests about a factor 3-4 increase in the background activity, i.e., in the firing rates of both units, because the percentage of synchronized spikes is relatively small compared with the overall firing rates. Under the assumption of unchanging synaptic efficacy, i.e., the product of EPSP amplitude and decay time remains more or less constant with age; this can be accomplished by a three- to fourfold increase in the total number of synapses over that period. Evidence from electronmicroscopic studies suggests that in the rat cortex the density of dendritic spines increases about fourfold between the first postnatal week and the end of postnatal week four (reviewed in Miller 1988). In the cat that period may be slightly longer; up to 6 wk. Because the number of spines will be proportional to the number of synaptic contacts and thus to the number of inputs, this could explain the decrease in the value of the unilateral excitation correlation coefficients. This observation also suggests that, once a cortical synapse is formed, it is essentially mature a very short time thereafter, the decrease in correlation coefficients being only the result from the added "noise" from the newly formed synaptic connections.

G. Smith wrote the stimulus generation software, data acquisition software, and the data analysis software and provided valuable suggestions throughout the experiment. D. Anderson kindly provided us with a sample of solid state multielectrode arrays.
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