Multimicroelectrode Investigation of Monkey Striate Cortex: Spike Train Correlations in the Infragranular Layers

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SUMMARY AND CONCLUSIONS

1. In the infragranular layers of the striate cortex of three monkeys, we studied tangential neuronal interactions by analyzing cross-correlograms calculated from spike trains recorded with 30 closely spaced microelectrodes.

2. There are two major types of correlogram structures—"narrow" peaks a few milliseconds wide, sometimes accompanied by small lateral troughs, and "broad" peaks ~30-100 ms wide. Isolated troughs are rare. Both types of structures are superimposed in the same correlograms; they are not due to shared optical stimulation.

3. In layer VI, narrow peaks are largest in a short lateral range of ~220 μm, and they depend on ocularity. In layer V, the lateral range is greater, and the dependency on ocularity is weak.

4. In addition, narrow peaks are largest at distances of 160 μm if the angles of preferred orientation are similar. In layer VI, however, at tangential distances of 300-400 μm, peaks are smaller, and troughs are found more often, for neuron pairs with parallel orientations compared with those with orthogonal orientations. From the agreement of this finding with a cooperative theory, we conclude that orientation selectivity is shaped by collective interactions.

5. Broad peaks always depend on ocularity, and the associated lateral interaction range exceeds the maximum of 1 mm investigated. Their size sharply decreases with receptive-field distance.

6. Average mutual delays of spikes of neuron pairs, manifest as lateral displacements of broad peaks, are interdependent; the delay between neurons 1 and 3 is the sum of that of neurons 1 and 2 and of neurons 2 and 3. This feature permits to rank the neurons on a "delay scale."

7. We conclude from 5 and 6 above that broad peaks partly result from intraretinal interactions whose effects are transmitted to the cortex via slow and fast pathways.

8. Lateral troughs adjacent to narrow peaks provide evidence that neurons at the "slow" end of the delay scale inhibit those at the "fast" end, and to a lesser extent, nondirectional neurons inhibit directional ones.

INTRODUCTION

A task of brain research is to understand neuronal functions in terms of anatomical structures. Usually the correspondence between the classical branches of neuroanatomy and single-unit recording can only be established via average properties. However, a view of the individual relationships between activity and connectivity can be gained by multiple microelectrode recording; functional properties of several neurons can be determined, and the correlations between their spike trains yield insight into anatomical connections. The anatomical picture derived differs from the usual one in several respects (47). First, in addition to monoor disynaptic connections demonstrated by classical neuroanatomy the spike-train correlations can monitor influences of polysynaptic pathways. In networks with multiple connections it is not clear a priori whether the bulk of the interaction passes via a few strong direct synapses or via thousands of weaker polysynaptic pathways. Second, activity correlations can show how much activity is
transmitted via a given connection. Third, however, the disentangling of activity correlations stemming from different pathways may be equivocal (45), so that the nature of participating interactions, and causal relationships, cannot always easily be deduced, whereas neuroanatomical methods usually permit one to recognize at least the direction of signal transfer.

There have been several attempts to analyze the connectivity of the visual cortex by activity correlations (10, 37, 44, 57, 58, 62; for a review see Ref. 32). The general weakness of the correlations was a great obstacle. However, it is in agreement with conclusions drawn from arborization overlaps of cell processes and synapse counts (8, 18). Because weaker correlations can be detected if more spikes are accumulated, some researchers (49, 56, 57, 60) have tried to overcome the difficulty of recording for several hours by stimulating iontophoretically one of the two neurons. However, the asymmetric pharmacological stimulation facilitates the detection of only some of the interaction pathways so that general conclusions must be drawn cautiously.

In the present experiments we have investigated intracortical correlations in area 17 with the intention to relate them to functional properties. We have used a large number of electrodes, since first, the number of neuron pairs grows approximately as the square of the number of electrodes, and second, a rigid array provides very stable recording conditions. The planar arrangement of the microelectrode tips permits a layerwise investigation of the cortex, and the array area is in the order of one hypercolumn size (28) within which the main interactions are expected to take place. We first present the results from cortical layers V and VI; in the present article we report on spike-train correlations (i.e., on properties of neuron pairs) and their relations to further parameters. In a subsequent article spatial distributions of properties of neurons and relationships between different response properties are treated.

**METHODS**

**Electrodes**

Each of the 30 microelectrodes consisted of platinum-iridium wire 5-μm thick coated with quartz glass with an overall diameter of 30 μm, manufactured by Battelle Institute, Frankfurt, West Germany (21). The ends of 50-mm pieces of such wire were ground with 3-μm-grained diamond paste to the shape of sharpened pencils (Fig. 1A). Resistances at 1,000 Hz were ~2 MΩ. Shapes and resistances were very similar for all electrodes. The elec-

**FIG. 1.** Multiple microelectrode. A: close view of one electrode; B: 5 x 6 array with an interelectrode separation of 160 μm.
trodes were held in parallel positions by three identical parallel metal grids (object holders 300 mesh for electron microscopes) so that a rectangular 5 × 6 array was formed with interelectrode distances of 160 μm (34; Fig. 1B). The tips lay in a plane perpendicular to the electrode wires. They were fixed in this position by pitch. The opposite ends of the electrodes were deinsulated in a drop of molten sodium carbonate, and they were connected to stumps of thicker wire by silver paint. Several experiments can be done with the same device without visually or electrically detectable deterioration of single electrodes. Tissue destruction is minimal, since the sum of the 30-electrode cross sections amounts to only 2.8% of the array area.

Animal preparation

Each monkey (vervet monkey, cercopithecus aethiops) was initially anesthetized by intramuscular injection of ketamine hydrochloride (10 mg/kg) and during surgery by a 3:1 mixture of N₂O and O₂ supplemented by halothane (Fluothane). After tracheal and venous cannulation, the animal was paralyzed with gallamine triethiodide (Flaxedil) (6 mg/kg·h⁻¹) supplemented by 0.1 mg/kg·h⁻¹ N,N'-diallylnortoxiferinium dichloride (Alloferin, Roche Laboratories, Nutley, NJ) and nourished by levulose (0.1 g·kg⁻¹·h⁻¹). Artificial pupils 1-mm wide were used. The two directions of gaze were brought to approximately the same point by a prism.

Optical stimulation

Stimuli were projected on a background of 1 cd/m². They were provided by a projector (36) supplemented by several motor-driven devices controlled by a Hivotronic quartz clock timer (Hi-Med Instruments, Reading, Berkshire, UK). Moving bars (luminance 100 cd/m²) measured 180 × 7 min of visual angle, and they moved through 180 min of arc in 1,800 ms with the aid of a mirror galvanometer. Between movements there was a 400- or 1,000-ms pause; in the longer pause the projection was rotated by 22.5° by a dove prism. Thus a series of bar movements in 16 equally spaced directions was generated. The series lasted 40 s.

A large field of static visual noise (mean grain size ~3 min of arc, field diameter 4°, ~50% white noise of 100 cd/m²) performed a translatory (shifting) movement on a circular path of 120 min of arc diameter, so that at each instant the velocity vectors of all points were identical. One series consisted of an initial pause of 3,000 ms and two complete revolutions lasting 7,650 ms each. This stimulus was included in two of the experiments only.

A succession of gray, green, and red large-field lights, obtained by color foils and appearing about equally bright (20 cd/m²), were each presented for 2,000 ms, separated by 2,000 ms of darkness. All stimulus series were repeated ~20 times for each eye separately. However, in two of the experiments, the color flashes were only delivered binoc-
FIG. 2. Peristimulus time histograms for bars moving sequentially in 16 directions (right eye stimulation), arranged in the order of the electrode array. The series of 16 movements was repeated 20 times. Peak frequencies are given below each histogram. Stimuli and time course are sketched at top left. The slit, 7-min-of-arc wide, moved at 100 min of arc/s. No neuronal activity was detectable at EI (top right) and poor recording conditions were found at B5. The lower array shows recordings under the same conditions 0.50 h later. The similarity of all histograms demonstrates the recording stability.

ularly. A set of repetitions of a given stimulus series took ~8–15 min. Since the net recording time available for each of four or five layers was ~1 or 1.5 h, further stimuli (series of small shapes for stimulus reidentification experiments, series of small binocular disparities, bars moving with different velocities) were applied, and the resulting spike trains were included in the present correla-
tion analysis. However, here we do not refer to the corresponding neuronal responses.

**Spike recording**

Signals from the multielectrode were amplified by 30 conventional channels each provided with a hand-adjustable trigger level and a polarity reverser. Trigger levels were set under oscilloscope inspection while the orientation series of moving bars was running, or the large red field was switched on and off. Spike quality was assessed and segregated into three groups, namely quality 1 if there was a single well-isolated spike (this was the case for up to 50% of all electrodes), quality 2 for a spike with an uncertain mostly minor admixture of another spike (usually ~80% of all electrodes showed quality 1 or 2; see also “cross-correlations” in METHODS), and quality 3 for an unsolvable mixture of clearly responsive activity. If in the latter case no spike could be detected in ~1 min devoted to an electrode, the trigger level was set above the noise level so that nothing visible was triggered. Often these records later showed triggered events that we never saw but that must have been spikes, because we found very regular response properties at extremely low spike rates (often from inhibitory receptive fields). Before a stimulus series was started, the spike qualities were checked anew and mostly they were similar over the entire time span recorded from a layer. Because it was impossible to ascertain directly for each neuron that the spike remained unchanged, our assumption of recording from essentially the same neurons rests on the similarity of the quality records. Recording stability is demonstrated in Fig. 2 where poststimulus time histograms to moving bars had been accumulated for a second time ~15 min after the end of the first recording. The great stability, due to the tissue adhesion of the electrode array, is an additional benefit of multiple electrode recording.

A general remark is necessary here on the question of whether we record from a single neuron or not. It is clear for everybody participating in experiments such as the ones described here that we cannot be as certain about the quality of the recording of each electrode as if we had only one electrode. The principle of the present experiments is rather to make sure that most recordings are essentially from one neuron each and then to use all recordings. So far no evidence turned up that the lack of absolute certitude invalidated all our findings. Even in studies where a tight control is possible (e.g., Ref. 58) results are founded on the assumption that nearby neurons have similar properties. We feel that the advantages of recording from many pairs of neurons greatly outweigh the residual uncertainly about the spike isolation.

At the outset of our experiments we were very much preoccupied by the possibility of cross-talk between the electrodes artificially raising the probability of detecting simultaneous spikes at neighboring electrodes. However, cross-talk differs in an important respect from two neurons tending to fire synchronously. In the former case, each time a large spike is emitted at one electrode, the oscilloscope base line of the neighboring electrode should be slightly deflected by about the same amount, whereas two neurons tending to fire synchronously nevertheless emit the majority of their spikes asynchronously. To examine this situation, we have selected cases where a large spike was recorded at one electrode and only small signals were present at a neighboring electrode. The oscilloscope trace of the latter electrode was triggered by the large spike. The largest systematic deflections we occasionally saw were <10 μV. We always set the trigger level >30 μV, so that in the case of imperfect recordings we rather missed spikes but did not record with two electrodes from the same neuron.

Each triggered neuronal event produced a short rectangular pulse whose time of occurrence of the rising flank was stored in digital form on a disk of an Interdata M70 computer. The time resolution, limited by the computer, was 1 ms. One experiment produced 5–10 megabytes of data. Most of the off-line data evaluation was done on a VAX 11/730 computer (Digital Equipment, Marlboro, MA).

**Receptive-field localization**

It was not possible to explore the response properties of the neurons manually. For each neuron separately, the receptive-field positions were deduced from the responses to the moving-bar series by a back-projection technique done off line by the computer. To illustrate this, one may imagine for each electrode a photographic paper with a bar moving on it, with all spatial and temporal dimensions being identical to the stimulus used. However, the bar is only illuminated briefly when a spike is elicited. The paper will become blackened as shown in Fig. 3. A response latency around 60 ms had to be subtracted. For a given recording the same value was used for all electrodes. It was chosen such that the dark spots became sharpest for most electrodes. Although in principle a different latency might have to be subtracted for each individual neuron, the operation was generally unambiguous and not critical, since a latency increment of 20 ms only corresponded to a spatial displacement of 7 min of arc. For the same reason, the risk of mislocating a strongly direction selective neuron was a minor one. The main source of positional uncertainty was a different one. Strongly orientation-selective neurons sometimes responded well only to one or two of the stimulus angles offered, so that the position could be determined...
in one direction far better than in the orthogonal one. Therefore, for each determination of a distance between two receptive-field centers, an error was calculated as follows. By inspection of each dark spot, the uncertainty of the center position was determined in an optimal direction and in the orthogonal direction to the former, where it was largest in the case of strongly oriented neurons. Thereby, an elongated area of equal likelihood of the true center position was defined. In the case of two neurons, 1 and 2, two such areas could occupy arbitrary relative positions. Of course, the distance between the centers of the dark spots was taken as the receptive-field distance. The error of distance was composed of two partial values, namely the range of distances connecting the midpoint of area 1 to all points in area 2, and the range for the converse case. The widths of these two ranges were squared, and one-third of the square root of the sum was used as the error of receptive-field distance. For small fields the midpoint determination was accurate to 1 or 2 min of arc.

The method of back projection was also used to determine receptive-field sizes. However, the measurement of very small diameters was limited by the bar width that was 7 min of arc. In layer IVc most dark spots had about that diameter, but the fields were certainly much smaller.

**Eye dominance**

The eye dominance of each neuron was scaled between 0 (complete left-eye dominance) and 100 (complete right-eye dominance), with 50 signifying equal coupling to the eyes. The ranking was obtained by a magnitude comparison of responses to colored lights and to moving bars delivered successively to the two eyes. The scaling was based on maximum response rates, with the spontaneous rate being subtracted. It must be borne in mind, however, that a fully automatic scaling is not always possible because often the responses in the two eyes differ qualitatively (e.g., in one eye there may be strong responses to few orientations but in the other eye weaker responses to a greater number...
of orientations). In such cases an ad hoc scaling cannot be avoided.

**Spike-train correlations**

**PROCEDURE.** We first describe the procedure leading to a spike-train cross-correlogram (47; here briefly termed correlogram). Out of a given pair of neurons, one is selected to be the reference neuron. A correlogram with a binwidth of 1 ms contains in its central bin the total number of synchronous spikes of the two neurons. In the nth bin to the right all cases are counted where a spike of the reference neuron is followed n milliseconds later by a spike of the partner neuron. Similarly, the left-side bins contain the cases where a spike of the reference neuron is preceded by a spike of the partner neuron. If the reference and partner neurons are interchanged, the correlogram is mirror reflected. Note that in general each partner spike is counted several times, because it is a successor (with different delays) of several reference spikes. We have accumulated correlograms with binwidths of 1 and 11 ms.

In principle, correlograms with a finer resolution than 1 ms would be desirable in some cases, but this was not feasible due to limitations of the computer equipment then available. The overall effect on fine temporal structures being presented by 1-ms correlograms is essentially a smearing out so that, e.g., an isolated sharp peak in a high-resolution correlogram displaced by 0.3 ms from the center would show up in our correlograms as a larger count in the central 1-ms bin and a smaller count in the adjacent bin. Thus an asymmetric flank of a central peak can indicate the preferential occurrence of a small delay between spikes from two neurons.

Since the spontaneous activity of many cortical neurons is low or even zero, correlations cannot be observed without stimulation. However, two neurons not being interconnected will show correlated firing if they both respond to the same stimulus. This "external correlation" usually forms a fraction of the observed total correlation. This fraction can be split off if the stimulus is repeated after a sufficiently long time t because the correlogram will then show a peak around the zero point and another far laterally at t, so far away that no truly neural interactions are expected to interfere. In our experiments, t ranged between 13 and 50 s, depending on the particular stimuli used, and it was always the duration of the entire stimulus series so that only responses to identical stimuli were interrelated. The lateral peak at t represents the isolated external correlation termed shift predictor (47). If a stimulus is repeated several times, many shift predictors are obtained from different pairings of repetitions. We have always calculated all of them and used their average, which is then much smoother than the correlogram. The excess of the correlation over the shift predictor can be considered to represent the isolated neural correlation under the assumption that both types of correlation superimpose linearly. Accepting that assumption, we have subtracted the shift predictor from the raw correlogram.

**PEAK ANALYSIS.** Conclusions about neuronal interactions are drawn from the shapes of the central parts of correlograms. Because there is no general algorithm to define structures such as peaks or troughs, we first inspected thousands of correlograms to determine the most frequently encountered shapes. These were various structures, mostly peaks a few milliseconds wide ("narrow peaks") but also troughs sometimes asymmetrically associated with peaks. These structures were superimposed on much broader peaks — 60-ms wide ("broad peaks"). The parameters of narrow structures so far were determined by eye. A smooth interpolation curve connecting the weakly undulated left and right lateral parts of the correlograms (binwidth 1 ms) was used as a base line. As the most relevant narrow structures seen were only 1- to 3-ms wide, we defined a limit of width of 7 ms for narrow peaks and troughs, and the lateral displacements of their approximate centers of gravity were limited to 4 ms. We only measured either a peak (its height, area, and lateral displacement) or a trough, whichever was more prominent, although in some cases significant characteristics of the central structures were lost (but see "asymmetric averaging" described below). It was not necessary to use the shift predictor as a base line, because it never showed structures in the millisecond domain, and besides its vertical displacement, owing to correlations on slower time scales, would have to be dealt with.

Broad peaks are much more stereotyped than narrow structures so that their parameters could reliably be measured by a computer program. Correlograms with binwidths of 11 ms were used, and the shift predictor was subtracted). The next step...
was to smooth the net correlogram five times (a smoothing step is to replace each bin content by half its previous value plus one-fourth of each of the neighboring previous bin contents). Then the largest bin content was sought in the central eleven bins. Around the abscissa of that bin, a new range of eleven bin contents was considered. The center of gravity of the positive bin contents was then taken as the “peak area.” The area of the peak was determined five times (a smoothing step is to replace each bin content by the average of the contents of the central eleven bins). Then the largest value within the same range, taking a correlogram smoothed only once, was taken as the “peak height.” The center of gravity of the positive bin contents used above was defined as the “lateral displacement of the peak. A number of limits in the procedure defined the cases of failure of peak detection.

It must be born in mind that the narrow peaks are in general superimposed on the broad peaks but the overall effect of narrow peak parameters on those of the broad ones is negligible due to the comparatively small size of the former. Thus the same correlogram might have, e.g., a narrow peak displaced by 0.5 ms to the right and a broad peak displaced by 7 ms to the left.

**NORMALIZATION.** Among other things, correlograms are calculated to determine and to compare neuronal coupling strengths. To compare narrow correlogram structures for neurons with differing spike rates, we and others (42) have normalized them by the square roots of the total spike counts that are equivalent to a normalization by the average spike rates. For narrow peaks, where few spikes are counted twice, this measure gives an approximation for the fraction of each cell’s spikes contributing to the peak. Thus, if, e.g., two neurons emitted 5,000 and 20,000 spikes in a given time span and the measured correlogram peak area comprised 70 spike pair counts, then the peak size would be 0.007.

The areas of the narrow correlogram peaks, when no normalization was applied, tended to be proportional to the square root of the two spike counts, but a large scatter was also present. The above normalization eliminated this trend, so that an additional justification for its application was thereby provided.

However, the areas of the broad peaks after this normalization still showed a systematic increase with spike count. Therefore we used a different normalization. Peak areas were divided by the product of the total spike counts. Since data from recordings with different total durations were compared, they were converted to a standard duration of 6,000 s by multiplying peak areas and total spike counts by the factor 6,000 s/(actual duration), before normalizing in the described way.

The use of the product normalization makes the results noncomparable to the cases of the normalized narrow peaks. However, we have multiplied the normalized areas of the broad peaks by 10,000, which is the approximate order of magnitude by which the two normalizations differ.

**CORRELOGRAM AVERAGING.** In some cases, when the general nature of the relations between spike-train correlations and other variables were to be elucidated, the total ranges of these variables were subdivided into sections of appropriate widths, and all available correlograms within each section were averaged after individual normalization. Each correlogram between two neurons is mirror reflected if reference and partner neurons are interchanged. If the central structures were asymmetric, the result of averaging would then depend on the choice of the reference neuron in each pair. Of course, if relationships were sought between neurons with different properties, e.g., between direction-selective and nonelective ones, then we systematically chose the former ones as the reference neurons and the latter as partner neurons. By this constraint the ambiguity was abolished and averaging revealed whether there was a systematic asymmetry related to the selectivity in question. However, if none of the two neurons was privileged, e.g., when distance dependencies were sought, we applied “asymmetric averaging.” We used the one of the two mirror versions that had more counts in the 3-ms bins adjacent to and to the right of the central bin. In this way, annihilations of higher and lower lateral structures could be avoided, but also artificial structures could be created from noisy but structureless individual correlograms. Therefore a control operation performed in the same way in far lateral bins monitored how much asymmetry would be generated by chance (see legend of Fig. 12). This procedure is particularly important if a statement on the absence of correlation is required. All operations so far described were paralleled by corresponding ones for the shift predictor.

In certain other cases, we first determined normalized peak areas in individual curves, and these values were averaged for all cases falling into each section (as explained above). Graphic displays showing such averages are accompanied by vertical bars whose half length indicates the average error of the mean.

**Recording-site reconstruction**

The corner electrodes of the matrix were marked at regular intervals so that the penetration depths could be observed under the dissecting microscope. Recordings were taken at four or five depths proceeding from top to bottom. At the end of an experiment, currents of 2 μA were passed for 4 s through selected electrodes. The animal was then killed by an overdose of pentobarbital sodium (Nembutal), and the relevant brain part was
sectioned and Nissl-stained. The tracks were reconstructed in three dimensions, the angles of the tracks against the planes of the sections were determined from the successions of track pieces in each section. The fact that there were several tracks at known distances greatly facilitated the reconstruction, since otherwise many tracks would not have been detected. The true cortical vertical was determined from the main direction of large blood vessels in the same way as the track directions, and both angles were then put into relation.

RESULTS

The present report is essentially based on results from three monkeys. In two animals (animals 7 and 8) we recorded from the upper parts of layer VI and in one animal (animal 6), the electrode tips lay in a slightly oblique plane spanning essentially the entire thickness of layer V, with the leftmost row of six electrodes (A row, closest to the 17/18 border) being at the deepest level. Recordings taken at sites located above the ones considered here will be treated later.

A nonaveraged section of the digitized recordings of 4 s duration is shown in Fig. 4. It is clear that no reliable correlations can be determined from most neuron pairs if such short sections are examined. Therefore, in order to maximize the sensitivity for small correlation effects we accumulated correlograms across the entire 1.5 h of recording time in a

FIG. 4. Digitized spike trains of responses to moving bars. Section of spike trains whose histograms are shown in Fig. 2. Black bars (bottom) indicate examples of approximately synchronized spikes.
layer so that the spike trains usually contained the responses to over a hundred different stimuli, each having been applied \( \sim 20 \) times.

In about one-half of all correlograms, structures a few milliseconds wide can be recognized. Most of them are central peaks frequently having asymmetric flanks (Fig. 5A). The shift predictor (dashed curve) shows how the neurons would correlate if they were not neurally interconnected but if all responses to the stimuli, and the synchronizing effect of the stimulation, remained the same.

In Fig. 5B the correlograms of electrode \( D4 \) with all remaining electrodes are shown. Here the abscissae are compressed. Each bin is 11 ms wide. Now a broad peak stands out clearly in all correlograms. The curve \( D4/D5 \) represents the same, but compressed, correlogram as the one shown in Fig. 5A, where the central part of the broad peak can be recognized as a slight asymmetric elevation spanning the entire section depicted.

A few synchronous spikes contributing to broad peaks can be recognized by eye in Fig. 4 above the short black bars at the bottom. For clarity, the black bars point to examples in which more than just a pair of neurons was approximatively synchronized. At present it is not known whether such higher correlations are a general phenomenon. It can also be seen that such synchronizations may be temporally well separated from visual responses.

Figure 5B reveals that in some cases the shift predictor has a significant structure in the compressed correlograms. However, we never observed any pair of neurons in the visual cortex in which even a sharply timed stimulus such as a flash or a jerk produced a shift-predictor peak less than \( -50 \) ms wide. In some pairs of neurons the wide-bin correlograms show further lateral peaks at \( -100 \) ms from the center (Fig. 5D), and a tendency for cyclic bursting can be recognized in the autocorrelograms (not shown). Figure 5C shows the same correlogram as Fig. 5D but with 1 ms resolution. The regularities related to cyclic bursting will be treated elsewhere.

The weakness of the correlations represented by the narrow peaks may be appreciated by the examples of Fig. 5, A and C. If we take, as a base line, the smooth continuation of the underlying broad peak through the middle section, the peak area of the excess correlation corresponds to 240 and 85 spike pairs, respectively, observed in \( \sim 1.5 \) h while moving bars crossed the receptive fields \( \sim 1,000 \) times, and further stimuli occurred still more often. Although most of these spike pairs appear when the spike rates are highest, it is clear that an excess spike pair appears far less often than in each response. Considering the total numbers of spikes given in the figure legend it may also be noted that in the examples shown the correlated spike pairs occurred for roughly 1% of all spikes. Judged by our pool of data, in monkey visual cortex such a correlation is already a relatively large one.

Broad peaks are observed in many more correlograms, and if compared with the narrow peaks they stand out more clearly against the noise level. If one picks out in Fig. 5B the pair \( D4/D5 \), it can be deduced from the number of counts contained in the maximally filled bin given below the curve that its broad peak contains \( \sim 6,000 \) counts. From the total spike counts given for Fig. 5A it follows that every third and 15th spike, respectively, is a member of a (loosely) synchronized pair. For neurons with lower spike rates it may be only 1%. The percentages give an upper limit because each spike may be a member of several spike pairs all contributing to the same broad peak.

All of \( \sim 1,200 \) correlograms (each in 2 versions with 1- and 11-ms binwidths) from the infragranular layers of three monkeys were first hand analyzed after subtraction of the shift predictor, and we measured an area and a lateral displacement of a peak or a trough (whichever was more prominent) deviating from the surrounding level. The lateral peaks \( \sim 100 \) ms distant from the origin so far were ignored. It was only after having recognized some regular relationships between correlogram structures and other parameters that we began to apply the peak measuring computer program to the broad peaks. The results reported are based on the latter procedure.

There seems to be a dichotomy of narrow and broad peaks (Fig. 5). Most narrow peaks were \( \sim 4 \) ms wide, and most broad peaks were \( \sim 100 \) ms wide. Therefore we chose 7 and 176 ms as upper limits for the widths of the nar-
FIG. 5. Examples of spike-train cross-correlograms showing narrow (A and C) and broad (B and D) peaks, for neurons in layer VI. The vertical bars designate counts per bin. The dashed lines are the shift predictors, i.e. the correlation components induced by shared stimulation. A: resolution of 1 ms/bin, neurons D4 (14,400 spikes) and D5 (89,700 spikes) from monkey 7. B: correlograms of electrode D4 with all other electrodes; monkey 7, resolution 11 ms/bin. The curve below D4 is the same, but compressed, correlogram as in A. Numbers below each curve are maximum amplitude [counts per bin (left)]; maximum amplitude divided by the binwidth of 0.011 s and the total number of spikes of the reference neuron D4 in Hz (middle); and same as middle but counts of D4 replaced by those of the individual partner neuron (right). If the curves were all printed so that the lateral levels of the shift predictors, instead of the maximum amplitudes, were at the same height, then the picture would not differ very much for most electrodes, and the visible peak areas would then appear as normalized by the product of the total spike counts, which is the basis of comparison used throughout here. C: resolution of 1 ms/bin, neurons C6 (22,500 spikes) and D6 (39,000 spikes) from monkey 8. D: same correlogram as in C, resolution 11 ms/bin.
row and broad peaks, respectively. It was rare that the tip of a broader peak than the limit was cut off and measured\(^2\)). In the following, the areas and lateral displacements of the narrow and broad peaks are put into relation to physiological and anatomical parameters. As mentioned in METHODS, narrow peaks were normalized by the geometric mean of the two pertinent spike counts. Broad peaks, however, were found on the average to be proportional to the product of the total spike counts (Fig. 6), and therefore, the product was used for normalization. There is no further justification for doing so than that a large part of the total variation is removed.

It has been pointed out (2) that in spike-train correlograms peaks are more often encountered than troughs. We confirm the observation that in the present experiment the overall ratio of occurrence of narrow peaks and isolated troughs is 12:1, and only a few unconvincing broad troughs have been seen. Small asymmetric depressions accompanying narrow central peaks, however, are more common. A section is devoted to them.

**Dependence on electrode distance**

Inspection of raw correlograms printed in an array arrangement immediately reveals that narrow peaks are largest, and most frequently encountered, at the shortest lateral distances, whereas many correlograms are nearly flat in the millisecond range if the neurons are separated by more than 0.5 mm. In contrast, no decrease of broad peak areas with interelectrode distance is apparent when figures such as Fig. 5B are inspected.

Because eye dominance is more likely to be similar in neurons separated by short distances, a cursory inspection of correlograms gives the impression that most narrow peaks occur between neurons of like eye dominance. For broad peaks the clearest picture with respect to eye dominance is found in layer IVc where the loci of the neuron pairs having the largest peaks retrace the ocular dominance stripes (33).

In Fig. 7, the results for layer VI are shown in more detail. Figure 7A shows for layer VI that indeed narrow-peak interactions are strongest for distances of less than ~220 μm and for pairs of neurons with similar eye dominance [eye dominance ranges from 0 (left) to 100 (right)]. Although there is a much

\[ \log(\text{product of spike rates}) \]  
\[ \text{relative units} \]

![Fig. 5. (continued)](image)

**FIG. 5.** (continued)
FIG. 7. Dependence of areas of correlogram peaks (N, narrow; B, broad) on tangential-cortical distance and on eye dominance in layer VI. "Relative" refers to the different normalizations described in the methods for narrow and broad peaks. Error bars in this and all other figures are ±1 SD. A: data for narrow peaks from monkeys 7 and 8. The first abscissa value is taken at the shortest distance of 160 μm, whereas the remaining values are averages of distance ranges whose limits are indicated. B: examples of pairs of neurons where pronounced shared-input peaks are observed at larger intracortical distances (E5/A2, 800 μm; E5/C1, 670 μm). The polar plots of responses to oriented bars show dissimilar preferred angles. Monkey 7, layer VI, spike counts: E5, A2, C1; 5,100, 7,700, 4,400 spikes, respectively; eye dominance: 93, 85, 41, respectively. Dashed curve, shift predictor; scale bars, 20 spikes. C: data for broad correlogram peaks from monkeys 7 and 8.

smaller number of cases where neuron pairs separated by 160 μm are dominated by different eyes, it is clear that it is not the smaller number but the opposite eye dominance itself that is related to the weak interactions at shorter distances. At larger distances, there is a suggestion that narrow-peak interactions remain still somewhat stronger for similar eye dominance. At least we can say that there is no pronounced reversal of eye-dominance dependency with increasing distance.

The individual data shown as averages in Fig. 7 have a large scatter that partly results from dependencies on other variables (see below) but partly appears irregular. Neuron E5
in layer VI of monkey 7 is an example for which, besides pronounced narrow correlogram peaks at the shortest range of 160 µm, the correlograms with neurons C1 and A2, distant by 670 and 800 µm, respectively, show 1-ms-wide large central peaks (Fig. 7B). Other neurons in between do not show such peaks with E5. Except for similar values on the delay scale (see below), the neurons have no properties precisely in common with E5, in particular the well-defined angles of preferred orientation strongly differ.

In layer VI the areas of the broad correlation peaks show only a weak decrease with distance but a clearcut decrease with increasing eye-dominance difference (Fig. 7C). Thus a given neuron may interact in the broad-peak range nearly as strongly with a distant (1 mm) as with a nearby neuron, provided the eye dominance is similar.

In layer V the recording plane is tilted. The situation is best illustrated by the orientation-tuning curves (Fig. 8A). For each electrode, the magnitudes of the responses to the moving bar are plotted as a function of the bar-movement direction. (Actually, the sum of 2 such figures, obtained from stimulation of either eye, is depicted). The arrangement corresponds to the visuotopic representation of the electrodes, i.e., the general direction from the cortical locations of electrodes A6 to E1 corresponds to an upward and rightward progression in the visual field. Orientation-tuning sharpness clearly increases from right to left, and we know from the histological reconstruction that this is paralleled by increasing recording depth within layer V.

If we take the left three columns of electrodes (A, B, and C, corresponding to lower layer V) separately from the right two columns (D and E, corresponding to upper layer V), the data show a much smaller dependency of narrow-peak magnitude on eye dominance compared with layer VI, and owing to the reduced number of neuron pairs available the dependency is at the limit of sta-
tistical significance. As in layer VI it is only seen at the shortest interelectrode distance (not shown). The decrease with distance is clearly more shallow in layer V. Half the 160-μm value is reached only at ~400 μm. In the narrow-peak domain the two parts of layer V do not differ significantly, but there is a greater difference to the layer VI data; many more peaks occupy only the central 1-ms bin in layer V than in layer VI, but the overall peak areas are comparable.

The main difference between upper and lower layer V is that in the former the broad peaks are, on the average, three times higher than in the latter. This is immediately apparent on inspection of the raw data. However, the eye dominance and distance dependencies are, except for that factor, very similar, so that both halves have been lumped together in Fig. 8B. As in layer VI, there is only a weak decrease of peak magnitude with distance, and the dependency on eye dominance is pronounced.

The relationship between the eye-dominance values of two neurons is not entirely described by taking the difference between these values; it might be that two balanced binocular neurons correlate in a different way compared with, say, two left monocular neurons. Therefore, the relations described were also examined with respect to the product of the eye dominance deviations from 50. This product is small or zero whenever at least one neuron is symmetrically binocular, and large positive and negative values are obtained for pairs of monocular neurons. The relationships seen largely corresponded to those reported above, so that our apprehension was without object.

It is difficult to ascertain that peaks with intermediate widths constitute a separate class, but it is clear from inspection of the data that they are rare. One hint that they do not occur randomly is that striking examples are observed in layer VI only, and they appear mostly at the shortest distance of 160 μm and again at ~500 μm (Fig. 9A).

The cases where a trough was the most prominent structure in a correlogram were scarce. Depressions several tens of milliseconds wide were too ill defined to be analyzed systematically, but some regularities could be seen for narrow troughs. Most of them were laterally displaced. In layer V only 4 out of 435 correlograms showed slight depressions; the corresponding interneuronal distances ranged between 600 and 900 μm. In layer VI a greater number was detected. Some examples are shown in Fig. 9B. The distribution of their occurrence, peaking at ~500 μm, is depicted in Fig. 9C.

**Dependence on receptive-field distance**

Receptive-field positions were determined from moving-bar responses as described in METHODS. As an example, Fig. 10, A and B, shows plots of the receptive fields, drawn into the same part of the left- and right-eye visual field, for six adjacent electrodes in layer VI of *monkey 8*. For the example shown we know from layer IVc directly above (unpublished observations) that the cortical magnification factor is 7.5 and 10 min of arc/cortical millimeter for vertical and horizontal directions, respectively, in the visual field, or 1.2 and 1.6 min of arc, respectively, between neighboring electrodes. In contrast, actual distances of up to 20 min of arc can be seen to occur even between well-localized fields of neurons recorded at neighboring electrodes and larger fields whose limits are not easily delineated (e.g., C5 in Fig. 10B) may have a still larger positional offset. Thus, in the infragranular layers, the scatter of receptive-field positions is so pronounced that the comparatively small retinotopic progression cannot easily be detected within our recording area.

Only excitatory receptive fields were considered, and their distances were only determined for neurons dominated by the same eye, i.e., the neurons had to have eye dominance values either both <50 (left eye) or both >50 (right eye). This eliminates about one-half of all pairs of neurons. In addition, if the estimated distance error (see METHODS) exceeded the visual angle corresponding to one cortical millimeter the quality of the distance information for a given pair was considered to be so low that these pairs were taken separately. In *monkeys 7 and 8* the limiting angle was 9 min of arc, and in *monkey 6* it was 11 min of arc. Because the magnification factors were different for vertical and horizontal directions, their averages have been used.

The ranges of receptive-field distances with small errors were from 0–47 and 0–37 min of arc, respectively, for *monkeys 7 and 8* (layer
Fig. 9. Correlograms with more rarely encountered shapes. Dashed lines, shift predictors. A: example of a peak with an intermediate width. Layer VI of monkey 7; B3, 16,700 spikes; D6, 120,900 spikes. B: examples of correlograms where a narrow trough was the most prominent central structure. From top to bottom: monkey 6 (layer V) electrodes D1/C5 (3,830/4,460 spikes); 6 (V), E1/C5 (5,070/4,460); 7 (VI), E3/A6 (10,520/28,460); 8 (VI), C2/E4 (9,670/95,860); 7 (VI), E2/D5 (3,750/89,760); 8 (VI), A2/E5 (88,400/180,770). Most troughs were offset from the center. Conclusions on the shape and the lateral extension of the troughs must be drawn cautiously because the signal-to-noise ratio is very low. Scale bar, 0.002 (geometric mean normalization). The bottom correlogram in reality is ~2 times as high as it has been drawn. C: distance dependence of the frequency of occurrence of narrow troughs being the most prominent correlogram structure. The frequency was measured relative to the total number of neuron pairs having distance values in each of the abscissa ranges. Layer VI, monkeys 7 and 8. The total number of troughs was 49.

VI), and in monkey 6 it was 10 and 22 min of arc for the lower and upper layer V, respectively. In Fig. 11A it can be seen that the areas of broad correlation peaks decrease considerably with increasing receptive-field distance. It is clear that this dependency explains much more of the variation of the data than the decrease with intracortical distance. The figure has to be compared with the top (solid) curve in Fig. 7C (similar eye dominance), which shows only a weak average slope.

If pairs of neurons with a larger distance error are considered, the decrease with receptive-field distance is less pronounced (Fig. 11B). Inspection of individual cases shows that there are, e.g., pairs of neurons both having very extended, largely overlapping excitatory regions in their receptive fields, but the midpoints are quite distant from each other, and the distance value is fairly uncertain. If the idea is correct that a large broad peak results from a large receptive-field overlap, then it is not astonishing that in the example mentioned a strong interaction is observed. However, replacing distance by overlap throughout is much less successful in explaining the
FIG. 10. Receptive field plots for 6 adjacent electrodes in layer VI, monkey 8; left eye (A), right eye (B). The 4 lateral black pixels in each frame designate the same loci in the visual fields of each eye. As determined in layer IVc directly above, the regular retinoptic progression from one electrode to the next corresponds to <1 pixel. The actual position differences greatly exceed that value. In B, electrodes E4 and C3, only the bar movements contributing excitatory response have been selected to contribute to the plot. E5 is nearly unresponsive in the right eye.

variation of the broad peaks because it is not clear how to normalize overlap by receptive-field sizes if these greatly differ.

In the lower layer V the curve corresponding to Fig. 11A consists only of one point because all neuron pairs with well-defined receptive-field distances had the field midpoints very close to each other. In the upper layer V (Fig. 11C) a curve through two points can just be drawn, again a strong decrease is the most probable interpretation.

The narrow peaks of the correlograms, reflecting more direct intracortical connections and shared input from bifurcating fibers, depend on receptive-field distance as well, as shown by the averaged correlograms of Fig. 12. If the receptive fields are separated by <7 min of arc, there is a much larger central peak than in the remaining cases. In layer V, the obliqueness of the recording plane, necessitating a subdivision of the data, made it impossible to get a correspondingly clear picture.

Broad peaks are often accompanied by further lateral maxima (Fig. 5D). This phenomenon is visible in all monkeys but it is particularly pronounced in monkey 8. In contrast to the central peak, the magnitudes of lateral correlogram deflections rather tend to increase slightly with receptive-field distance. More detailed analyses of pertinent phenomena will be treated elsewhere.
Asymmetries of broad correlogram peaks, delay scale

The broad correlogram peaks frequently are offset from the center by up to \( \sim 25 \) ms in either direction. Figure 13A shows the example of electrode C6 in layer VI of monkey 7 correlating with the electrodes of the D column. The curves represent the correlograms after subtraction of the shift predictor. For the same recording, in Fig. 13B, the distribution of all offsets is depicted in a double matrix arrangement. Each small rectangle represents the correlogram of one electrode taken as a reference electrode and all the others taken as partner electrodes. The filled and empty circles indicate the correlograms having a rightward- and leftward-shifted peak, respectively. The dot indicates the position of the reference electrode. The cross marks electrode EI from which no useful activity was obtained in this recording. No symbol is printed for centered or absent peaks.

It is obvious that the distribution of the symbols is not random. In Fig. 13B, the fact...
that, for electrode C4, the correlated spikes at nearly all other electrodes occur earlier (O) than the C4 spikes, must essentially be a property of C4 alone. We may consider this neuron as a slow one because a fraction of its spikes is preferentially delayed with respect to the occurrence of a spike on any other electrode. Correspondingly, B3 would be a fast neuron. To obtain a ranking of all neurons, each neuron in turn was taken as a reference, and the lateral peak displacements with all other neurons were averaged. This amounts grossly to counting the excess of filled over empty symbols in each small matrix of the figure, but, in addition, the more quantitative averaging specifies the ranking in terms of milliseconds. The idea is that the rank difference of two neurons equals the correlogram peak displacement actually observed. In layer VI the agreement is quite good. In Fig. 13C the actual peak displacements are drawn as a function of the values predicted from the average delay scale. A narrow cloud with a 45° slope would indicate a perfect match.

Thus the 435 values of correlogram peak displacements can be reduced to only 30 values on a delay scale whose differences describe the original data. This is not trivial, and cannot be achieved with random peak displacements. For the individual neuron pairs the finding signifies that if neuron 2 is delayed with respect to neuron 1, and neuron 3 in turn is delayed with respect to neuron 2, then neuron 3 will be found to be delayed with respect to neuron 1, and the delay will be the sum of the former two. This is not generally true for arbitrary correlating spike trains but is a special property of the spike trains observed here. It is helpful to imagine that the neurons receive input with different delays from a single unknown source.

In layer V more pairs than in layer VI had mutually conflicting shifts, so that there was a somewhat reduced agreement between actual shifts and values from the average scale, and the cloud corresponding to Fig. 13C was slightly less stretched.

Two observations relate narrow-peak correlations to the delay scale. First, the narrow peaks, and in particular, the contents of the central correlogram bin in layer V as well as in layer VI, are about twice as big if their positions on the scale differ by no more than 3 ms compared with the cases with differences of >10 ms. Second, the spatial spread of narrow-peak interactions depends on the position on the delay scale of the neurons involved. The decrease with distance is about...
FIG. 13. Asymmetries of broad correlogram peaks in layer VI of monkey 7. A: examples of net correlations, after subtraction of the shift predictor, of electrode C6 (36,800 spikes) paired with electrodes D1 to D6 (from top to bottom: 5,900, 44,100, 6,600, 10,400, 89,700, 120,900 spikes, respectively). Vertical bars indicate counts per bin which is 11-ms wide. B: distribution of asymmetries. The neurons, taken as references, are represented by a 5×6 array of hatched rectangles labeled by a letter and a number. Within each rectangle, the partner neurons are represented by a 5×6 array of dots, and the reference neuron itself is a small black dot. White/black dots designate partner neurons firing preferentially before/after the reference neurons. There is no symbol for centered or absent peaks, and crosses designate unsatisfactory recordings. The cases of A are marked by a frame. C: comparison of position differences on the delay scale with actual correlogram peak displacements. If the range of observed displacements was the same, but the individual values were mutually conflicting (e.g., neuron 1 later than neuron 2, and neuron 2 later than neuron 3 but neuron 1 earlier than neuron 3) the cloud of symbols would have the same horizontal extent, but there would be no corresponding vertical elevation.
similar in relative terms for fast-fast, fast-slow, and slow-slow pairs (the scale was subdivided in 2 halves only), but the size of all correlations (geometric-mean normalized) is the largest for fast-fast pairs, so that these interactions are often detectable across the entire range of recording distances, whereas those of slow-slow pairs mostly vanish at distances of \(\sim 0.5\) mm.

In a subsequent publication the rankings of the neurons on the delay scale will be compared with further neuronal properties.

**Dependence on the angle of preferred orientation**

The simplest idea of the wiring of an orientation-specific neuron would be that the neuron in question is influenced by hierarchically lower neurons having laterally located receptive fields. The influence would have to be excitatory (inhibitory), if the receptive fields are located under the optimally (non-optimally) oriented bar stimulus. Analyzing cross-correlations we saw no significant effect of this type in the infragranular layers. However, in layer VI we found another kind of interaction involving orientation angles (monkey 8, Fig. 14). At intracortical distances \(< 250\) \(\mu\)m the narrow correlogram peaks are largest \((P < 2.5\% \text{ that they are equal})\), if the preferred orientation angles are similar but at \(\sim 300-400\) \(\mu\)m the situation is reversed; neuron pairs with similar angles are much more weakly correlated than those with dissimilar angles \((P < 0.25\% \text{ that they are equally correlated})\). At still larger distances, the dependency on orientation angles vanishes. The difference at the right end of the scale is not significant. The results from layer VI of both monkeys 7 and 8 are remarkably similar in all

![FIG. 14. Dependence of narrow correlogram structures on the difference of preferred orientation angles and on distances in layer VI. The range of differences was subdivided into a parallel (0–45°) and an orthogonal group (45–90°) and marked by corresponding symbols. Neurons ranking below 15 on the tuning-sharpness scale (0–100) were discarded. A: Averaged narrow-peak areas from monkey 8. For distances below \(\sim 250\) \(\mu\)m, neuron pairs with parallel preferred angles (A) correlate more strongly, but at 300–400 \(\mu\)m, orthogonally oriented neurons (I) are more likely to correlate. B: Distance dependence of the occurrence of narrow troughs being the most prominent correlogram structures. The frequency was measured relative to the total number of neuron pairs having distance values in each of the abscissa and angular ranges. Layer VI, monkeys 7 and 8. The total number of troughs was 46. At larger distances, troughs are most frequent for pairs with parallel preferred orientations.](http://jn.physiology.org/)

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respects, except that in *monkey* 7 the correlation peaks for parallel and orthogonal orientations at distances of 160 μm differ more strongly than in *monkey* 8. In contrast, in layer V there was only a moderate excess of correlation for parallel preferred orientations at 160 μm and no significant difference at larger distances.

The broad correlogram peaks showed only a slightly stronger coupling for neurons with similar preferred angles, separated by no more than the minimal electrode distance of 160 μm.

The result of Fig. 14A is again apparent when narrow correlogram troughs are related to differences of preferred orientation angles (Fig. 14B, both monkeys). In the range >250 μm there is a great excess of occurrences of troughs for parallel over orthogonal angles (P < 0.25% that there is no excess). The two cases where troughs were seen at distances <250 μm yield no significant relation. We have preferred to count the troughs, rather than to rely on the measurements of their dimensions because the latter are too ill defined in many cases.

**Asymmetries of narrow correlogram peaks**

In a first step, the peak displacements, ranging between 0 and ±3 ms, abstracted from the raw correlograms, were compared with physiological parameters, but no clear relationships were found, with the exception of receptive-field distance (Fig. 12), where the decreasing content of the central bin makes the peaks appear relatively more asymmetric. This example taught us that large central bin contents might override significant asymmetries appearing small in comparison. Therefore, we focused our attention on the cases where the bin contents in the neighboring bins to both sides of the center clearly differed. Fig. 15A shows an example. The reference neuron A5 is highly direction selective, as shown by the polar diagram, and on the delay scale it is 11 ms faster than the partner neuron B4, which is only weakly direction selective. It is clear that the rightward asymmetry in the central bins of the correlogram is not responsible for the rightward displacement of the underlying broad peak depicted on a compressed abscissa in Fig. 15B. We wondered whether such a parallel relationship between the asymmetries of narrow and broad peaks was a general phenomenon. We have averaged all correlograms of neuron pairs where the reference neuron was placed at least 9 ms higher on the delay scale than the partner neuron. (Remember that for a given pair of neurons a large difference on the delay scale is equivalent to a large asymmetry of the broad correlogram peak.) Figure 15C shows for *monkey* 8 that indeed in the average there is a depression to the left and an excess to the right of the center bin, and this central structure is superimposed on a broad peak whose displacement to the right is the consequence of the delay scale selection. The picture is the average of 33 individual curves. If inspected by eye, in 13 of them no structures convincingly exceeding the noise level can be seen, and yet, in most of them there are less counts to the left than to the right of the center. In 16 curves the relationship can clearly be recognized individually, and only four curves show counterexamples. *Monkey* 7 yields a similar picture, with the only difference that the width of the trough to the left is somewhat wider, namely ~4 ms. The central structure in the curve of Fig. 15C signifies that a spike in a fast neuron is more likely to be followed within a millisecond, but less likely to be preceded, by a spike in a slow neuron, and a possible interpretation of this relationship is shown in the inset of Fig. 15C (see also DISCUSSION).

However, there are exceptions to the average case, involving only some pairs of neurons formed with either neuron D5 or neuron C2 of *monkey* 7. In these cases there are prominent asymmetric structures in the correlograms, but their polarity is reversed (Fig. 15D). Neuron C2 shows a small, sharply defined excitatory region with moderate orientation selectivity in the receptive-field plot, but in addition, there is a wide lateral zone on one side of the field center showing direction selectivity in one eye only, otherwise the center is surrounded by an inhibitory zone. The spike was large and well isolated. Neuron D5 is nonoriented and only weakly direction selective, which is unusual for a neuron in the fast half of the scale. Because the counterexamples of the two neurons were rare but clearcut, we have suspected that rather than segregating neurons into slow and fast ones one should consider nondirectional neurons versus directional ones because the examples...
FIG. 15. Asymmetries of narrow correlogram peaks in layer VI. The dashed lines are the shift predictors. A: example of a frequently encountered asymmetric central correlogram structure. Monkey 7, electrode A5 (reference) 152,000 spikes; B4, 13400 spikes. A5 is 11 ms closer to the fast end of the delay scale than B4. Scale bar, 100 spikes. Right: corresponding orientation polar plots. B: same correlogram, compressed abscissa. Scale bar, 1,000 spikes/11-ms bin. C: averaged correlogram for all 33 cases of monkey 8 where the reference neuron was located at least 9 ms further toward the fast end of the delay scale than the partner neuron. The pronounced slope is due to this selection. A narrow asymmetric structure with the same polarity is apparent in the center. Scale bar, 0.001 (normalization by the geometric mean of the total spike counts). The bottom part of the correlogram has been cut off; the zero level is ~6 scale bars below the shift predictor. Inset: suggested interpretation in terms of neuronal wiring. D: example from monkey 7 conflicting with C. Neuron C3 is 5.5 ms closer to the slow end of the delay scale than D5. Scale bar, 100 spikes. D5 (reference). 89,700 spikes; C3, 10,200 spikes. Compared with A, the polarity of the central structure qualitatively depends in the same way on direction selectivity but in the opposite way on the delay difference. E: averaged correlogram for all 93 cases of layer VI of monkey 8 where the reference neuron is at least 34 units more directional than the partner neuron (directionality index from 0 to 100). The similarity to C is due to the correlation between directionality and the delay scale. Scale bar, 0.001 (normalization by the geometric mean of the total spike counts). F: example of a correlogram with a peak exclusively occupying off-center bins. Monkey 8, D4, 28,900 spikes, A2, 87,500 spikes. Scale bar, 300 spikes.

of Fig. 15, A and D would then correspond to each other. However, there again, we found a number of exceptions. As a whole, the asymmetric central structure in Fig. 15C is somewhat less consistently predicted by the directionality difference than by the delay difference. In Fig. 15E, the narrow trough to the left of the middle is smaller than in Fig. 15C.

It is surprising that although most neuronal response characteristics in layer V (at least at the deeper level) could not be distinguished from those of layer VI, not the slightest evidence for an asymmetric central correlogram structure could be detected, neither for fast versus slow, nor for directional versus nondirectional neurons.

Among the asymmetric structures we had also expected to find peaks a few milliseconds wide located 1 or 2 ms off-center. These would be interpretable as mono- or disynaptic projections (9, 15, 56, 63). However, there were only 11 clear cases of this type among 870 correlograms of layer VI, and one out of 435 in layer V. (Dominant centered peaks
and asymmetric structures encompassing the central bin were much more common.) Figure 15F shows the most prominent example interpretable as D4 projecting to A2. Although D4 contributes only <1% of all spikes of A2, the temporal sequences of minor undulations in the response histograms of these two neurons are very similar in detail. Both neurons are located at the slow extremity of the delay scale, and A2 is exceptional in its direction-nonselective suppressive response to moving noise patterns.

If direction selectivity of a given neuron is to be explained on the basis of inhibitory connections, further neurons should have their receptive fields relatively displaced in the direction of the most responsive movement direction, and they should exert an inhibition delayed by at least 10 ms of milliseconds, since direction selectivity is easily apparent at stimulus velocities of 1 min of arc/10 ms, and the receptive-field displacements must certainly be >1 min of arc. Thus, at first sight, it seems that correlogram structures in the millisecond domain cannot explain direction selectivity. Rather, relations to broad correlogram peaks should be examined. We have subdivided the range of relevant angles (absolute value of the difference between the angle of preferred movement of the reference neuron and the relative displacement of the receptive fields, 0 to 180°) into three bins encompassing 60° each. The cases in the three bins signify that the receptive field of the partner neuron is relatively displaced in, orthogonal to, and against the direction of preferred movement of the reference neuron. We have examined whether the averaged correlograms in the three bins differed with respect to the depth of a lateral depression but neither this was the case, nor could we find analogous dependencies of narrow correlogram structures.

We have also taken into consideration the positions of the neurons in the tangential cortical plane, instead of the receptive-field positions. In fact, if there was no receptive-field scatter, and no eye dominance columns, then by virtue of cortical retinotopy the two types of position should be equivalent. With the aid of the retinotopy known from layer IV, the preferred directions of movement were projected into the cortical plane. We were surprised that now the narrow asymmetrical structure of Fig. 15C was indeed more pronounced in both monkeys when the inhibiting neuron was located in the cortical direction of preferred movement.

**DISCUSSION**

So far, theoretical reflections on spike train cross-correlograms (1, 2, 19, 20, 30, 31, 45–47) have been quite elaborate, but the analysis of actual recordings from networks with multiple connections proved to be much more complex (1, 3, 14, 42, 44, 54, 55–59, 62). In the cortex the manifestations of several types of interactions must necessarily be superimposed in the same correlograms, and a disentangling can only be successful if not only isolated easily interpretable examples are considered, but rather, if particular components of many pertinent correlograms can be systematically related to further neuronal parameters. Therefore, we recorded for long time spans during which the selectivities to a number of stimulus types were determined, and we recorded from many pairs of neurons so that sufficient numbers of cases were still available when the correlograms had to be segregated according to particular values of parameters.

*Origin of broad peaks*

It became apparent that the ~60-ms wide broad correlogram peaks (still broader ones were already noted in the cat, 44) differ in many respects from the theoretically more familiar narrow peaks a few milliseconds wide. In principle there are two types of explanation. First, the correlations may be transmitted to the cortex from elsewhere, as shown in Fig. 16A where an input shared by all neurons generates the correlation. (A similar correlational effect results when many neurons project in an overlapping way to a few neurons each; Fig. 16B). Second, the correlations may be generated intracortically.

We favor the first model, with the source of the correlations being located in the retina. A number of points corroborate this view, whereas extra assumptions would be required to support the intracortical model.

1 Intraretinal [or intra-LGN (lateral geniculate nucleus)] correlations have been observed in the cat (3, 42, 54). It is likely that they also exist in the monkey, and in that case one does not see how they could get lost on their way to the cortex. However, a temporal
blurring would be expected at each synaptic stage. In agreement with our observation, the strongest correlations are expected for neurons dominated by the same eye.

2) Correlation strength should depend on receptive field (i.e., retinal) rather than cortical distance. If there was strict retinotopy, these two cases could not be distinguished. However, at small distances, positional scatter dominates. Consider first the case that broad-peak interactions were generated intracortically, with strength directly depending on cortical distance. The decrease over the explored range of receptive-field distances could, on the average, only be smaller than that found for the available range of cortical distances.

On the other hand, if broad-peak interactions only depended on intraretinal distance, then the cortical distance decrease merely reflected the average retinotopic progression of receptive fields. In our infragranular recordings the peak areas for the case of similar eye dominance fall off to roughly half maximum at one cortical millimeter (Figs. 7C and 8B). As we have mentioned, this distance corresponds to ~10 min of arc, and indeed, there is an agreement with Fig. 11A where peak areas are shown to decrease to about half size at 10 min of arc. If this dependency was to result from entirely intracortical interactions, the neurons would have to “know” where their receptive fields are located.

3) The correlations induced by the visual stimulation, i.e., the shift predictors, have central structures whose peaks, if any, are never narrower than the broad peaks, and it sometimes occurs that the entire peak shapes are comparable, and only the magnitudes differ (e.g., the correlation C6/D4 in Fig. 5B). Because for stimulus-induced correlation, the origin of synchrony lies beyond the limits of the nervous system, a maximum of similarity to neurally generated synchronies would be obtained if the origin of the latter were at least located close to these limits, i.e., in the retina.

4) Visual stimulation drives many cortical neurons from very low spontaneous discharge rates to elevated frequencies. Therefore, most cortical spikes must stem from retinal spikes. Nevertheless, cortical neurons have lower average spike rates than retinal ganglion cells (24). Assuming excitation lev-

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3 This is because our data incorporate neurons separated by 160 μm whose receptive fields were, e.g., 10 min of arc apart, instead of 1.5 min of arc expected from retinotopy. In contrast, neuron pairs with the same receptive-field distance but a retinotopically expected separation of 20 min of arc were beyond the lateral extension of our recording array. If that were not the case, the dependency on receptive-field distances would simply be a strongly blurred version of the dependency on cortical distance, and the link would be the magnification factor.
els that are equal to each other in different retinal cells (or at least unrelated to the spike rates of the cortical cells to which they project), then different amounts of reduction lead to different cortical spike rates, and at the same time, to a reduced number of correlated spikes that is then proportional to both spike rates of a pair of cortical neurons. This is what we have observed. The point of the argument is that the interactions in question should occur before the retinocortical spike-rate reduction takes place. This points to an interaction site early in the visual pathway. The argument is only a suggestion, because other mechanisms could be invented showing the same proportionality.

The obvious retinal origin of most cortical spikes has still another consequence. The source of the correlations, if it is external to the cortex, must be in the retinogeniculate pathway, because other sources do not send enough spikes to build up the large broad peaks.

We do not propose that broad correlogram peaks are entirely unrelated to cortical processes. On the contrary, further evaluations of the present data (in preparation) show that the broad peaks systematically depend on intracortical signal propagation, but again, these findings can most easily be explained by the presence of the correlations already in the LGN input. For the origin of broad peaks the discussion below is relevant as well.

**Delay scale**

A particular feature of the broad peaks is that their lateral displacements have a large transitive component, i.e., if the displacements for the pairs of neurons 1 and 2 and 1 and 3 are observed, then that of pair 2 and 3 can be predicted. In this case we have shown that the data can be greatly reduced from the 435 original values belonging to each pair of neurons to the 30 values (position on the delay scale) belonging to each neuron. (Note that this result cannot be obtained from simultaneous recordings from only 2 neurons at a time.)

The pathway from the retina to the cortex is known to contain slower and faster fibers. As suggested by Fig. 16B, we propose that the delay scale is related to differences in signal transmission velocity from the retina, although the scale spans ~20 ms contrasting to 4 ms (maximally 7 ms) that can be deduced from electrostimulation measurements (12, 25, 29). Electrostimulation generates a non-physiological synchronization at the input of a target cell, but under natural conditions it is very rare that a spike in a termination of a given optic radiation fiber is successful in directly eliciting a spike in the recipient cell (55). The depolarization elicited by most incoming spikes will be integrated by the target cell until a later spike finally will be successful in firing the cell. Under the more natural conditions of the present experiment the measured delays are sensitive to integration of depolarization as well, and therefore, our results must be compared with those obtained from measurements of visual instead of electrical stimulation. Indeed, in the cat LGN Y cells have been shown to have 10- to 15-ms shorter latencies to visual stimuli than X cells of which only a small fraction is accounted for by the conduction velocity difference (50). A latency difference of the same magnitude is already observed in the cat retina (6). In the monkey LGN each millisecond increment of latency to electric chiasm shock was found on the average to correspond to a 25-ms increment in visual latency (41), but this has been observed in the parvocellular layers only, and the relationship to the X-Y subdivision is not clear. All these measurements show a large scatter of individual values, and, in addition, we have to extrapolate from cat to monkey as well as from LGN to cortex. Under these circumstances the span of our delay scale and the reported X-Y related differences between “natural” transmission times from retina to cortex may be considered not to be too discrepant.

An alternative explanation is that in principle any group of cells receiving precisely synchronous input would yield correlograms with displaced peaks if only their intracellular integration constants were different, and a delay scale reflecting these constants could be constructed. A decision between the alternatives cannot be reached by considering only the scale, but the arguments put forward to explain the origin of the broad peaks make the retinal model more likely.

A further argument in favor of the input to the cortical cells already carrying the delay property is that two cells distant on the delay scale have a smaller central correlogram
peak, i.e., they receive less shared input, than two neurons with similar positions on the delay scale. We have also observed that toward the fast end of our delay scale there is a pronounced increase in the responsiveness to moving noise patterns (unpublished observations). In the cat, this property has been related to complex cells (22) that in turn are much more akin to LGN Y cells than to X cells, if again, details of visual responses (11) are preferred to conclusions drawn from electrostimulation.

Interactions between fast and slow cells

We have shown (Fig. 15C) that pairs of neurons at opposite ends of the delay scale (having correlograms with pronounced broad-peak displacements) have a narrow bi-phasic structure at the abscissa zero point on the flank of the displaced peak. The interpretation of such a structure is difficult, since probably it results from several superimposed interactions. Our interpretation is, first, that there is some shared input filling the central bin. Second, we suggest that the lower contents of the two bins to the left of the center signify that slow neurons inhibit fast ones. (Remember that always the faster neuron of a pair was the reference neuron in the figure.) Third, the larger bin content to the right of the middle may signify that fast neurons excite slow ones (inset of Fig. 15C), but the latter feature could also be the right flank of a slightly wider central peak whose left flank is annihilated by the left dip).

It may seem surprising that the dip is so narrow, since most inhibitory actions are described to last longer (56). However, the shapes of correlogram structures do not reflect the time courses of postsynaptic potentials but they rather resemble their more rapidly varying temporal derivative (31). Indeed correlogram dips with brief phasic components followed by extended tails were observed in the LGN (43). In view of the small size of the dip in Fig. 15C it is possible that a longer tail extends to the left, which is difficult to outline on the slanting base line.

The size of the dip is ~0.001 signifying that in the average neuron one spike is suppressed every 10 min. Because there is a large number of input synapses to every cortical neuron (8) this is not a particular weakness.

Correlations related to orientation and direction selectivity

There is a predominantly steady variation of orientation angles in the cortical plane (26, 27), strongly suggesting that orientation selectivity is generated in a way involving strong neuronal interdependence. A theory (39, 40) explains the regular arrangement of orientation selectivity in such terms. Cells with similar orientations should excite each other at short distances but inhibit each other at greater distances of ~0.5 mm. This relationship is not easily accessible to intuition, but computer simulations have demonstrated that the relationships are adequate to interrelate orientation angles appropriately. Clearly, an anisotropy of interactions explaining the ultimate source of orientation selectivity must somehow enter the system, but the theory does not indicate it. However, this influence may be very small so that it would not be detectable by any present technique.

To overstate the idea, one may imagine a single neuron that receives appropriate orientation-generating interactions, and all remaining cortical neurons create their orientations

4 An alternative explanation for a dip in a correlogram might be that it appears when one cortical neuron receives preferentially on-center, and the other off-center, excitation. However, it will be difficult to observe the anticorrelation described between the afferents (3, 42, 54) when these are stimulated, because when on-center cells are excited, off-center cells with coincident receptive fields are inhibited so that there may not be much occasion for a truly neural anticorrelation to manifest itself. We have examined the rare cases where the response properties of the cortical neurons suggested a predominant off-center input, but no peculiarities with respect to dips could be seen. In strongly coupled neurons a dip adjacent to a narrow correlogram peak can also result from the intraneuronal refractory period (43). However, for quantitative reasons this does not apply to the generally weak couplings observed in the cortex. To see this, we subdivide the spike train of the partner neuron into two trains. The first is the original spike train from which only the small number of spikes contributing to the correlogram peak has been eliminated. If there is no inhibition the correlogram formed with the reference neuron is flat. The eliminated spikes form the second train. Its correlogram with the reference neuron contains the central peak, absolutely no counts in the directly adjacent bins, and an extremely low lateral chance level, because of the low rate of correlated spikes (typically 0.01 or 0.001 Hz). The total correlogram is the sum of both components, and this sum would have its far lateral bins only slightly higher than the bins adjacent to the peak.
by interacting with each other, and thereby indirectly with that neuron.

Indeed, for neurons with parallel preferred orientations, we and others (44, 58, 62) found that in the cat, correlogram peaks a few milli-seconds wide are largest at short distances, but, in addition, we found that such peaks are weak or absent for separations ~ 350 μm, and most correlogram troughs are encountered at about that interneuronal separation.

Inhibition as a shaping mechanism for orientation and direction selectivity has also been demonstrated by iontophoretic application of antagonists to known inhibitory transmitters (51, 52, 60), but this method could not reveal the precise role of inhibition. From our results it follows that when inhibition is removed, it is the network of orientation interrelations that is disrupted but not necessarily the orientation generating mechanism.

Most excitatory as well as inhibitory postsynaptic potentials were detected when oriented stimuli were presented in the optimal condition (13, 17). This is not helpful to explain the generation of orientation selectivity, but it is in agreement with our findings; The different types of potentials reflect interactions over different lateral distances.

It is remarkable, and in correspondence to an observation in the cat (58), that the prominent narrow peak observed at short interneuronal distances and parallel orientation preferences is also present when both neurons are strongly selective to opposing movement directions. On the other hand, the inhibition exerted by slow neurons onto fast neurons, being approximately equivalent to an inhibition of directional neurons by nondirectional ones, is not observed when the property of direction tuning is replaced by orientation tuning, indicating that it is truly related to the former, and probably involved in its generation. Although at present our material may not be sufficient to clarify all pertinent questions, our data suggest that direction selectivity is not generated by delayed inhibition between two neurons with appropriately displaced receptive fields but rather by a mass action of many neurons whereby the receptive-field scatter is averaged out and only the cortical locus, related to the retinotopy dependent average receptive-field position is the relevant variable. In that case the available differences of visual field positions are very small, namely in our case ~1.5 min of arc/160 μm. Certainly the direction selectivity observed with noise patterns requires such fine-grain interactions, since presumably pairs of elements must react individually to each structural detail of such a pattern. The moving bar used in our study takes already 15 ms to travel through 1.5 min of arc so that an inhibition coming from a laterally displaced locus would have to be delayed at least by that time span in order to suppress a response for the nonoptimal direction. If our view is correct that slow neurons inhibit fast neurons, then the latency difference between these subtypes must be added to the delay of the inhibition. Thus our results suggest that the differential delay is exploited for the generation of direction selectivity. We do not believe that the description given here is complete. Presumably larger intracortical distances are put into relation by mechanisms involving several steps and also other layers (16).

Correlogram troughs

Most individual correlograms show peaks rather than troughs. This has already been noted and commented by Aertsen and Gerstein (2). For a neuron with a low firing rate, a weak excitatory input will suffice to raise the rate, but a very strong continuous inhibition will be required if a zero firing rate shall be attained, and all potential spikes be eliminated with certainty. This uneconomical process would be improved if the neurons participating were approximately synchronized, so that increases and decreases of firing rates can manifest themselves equally well. This may be an important function of the broad-peak correlations.

Shared-input peaks

A remarkable feature of many correlograms is a relatively large contents in the central millisecond bin, compared with the directly adjoining bins. Usually one concludes that shared input is particularly important. The question is whether very general network properties can explain its origin. It has been argued (58) that in a group of highly interconnected neurons the correlating effect of shared input is more influential than that of monosynaptic connections. We feel, however that this alone is not sufficient to explain the prominence of central peaks. Consider a
group of nine neurons, each one linked monosynaptically to each other one. Then indeed a given neuron pair receives shared input from seven other neurons, but there are only two direct links between the members of the pair. However, if the total number of spikes is conserved over time, the likelihood of a presynaptic spike to generate a postsynaptic one must be \(\frac{1}{8}\) at each synapse and that is the probability to detect the effect of a monosynaptic interaction between the members of the pair. The probability, however, that a spike of a third neuron generates a spike in both neurons simultaneously is only \(\frac{1}{8}\), and since there are seven such sources, shared input manifests itself with a probability of \(\frac{7}{8}\), which is comparable to the above \(\frac{1}{8}\). We conclude that, in addition, shared input from neurons outside the observed network is required to account for the abundance of central correlogram peaks.

Relations to anatomical projections

Shared input leading to the dependency of narrow peaks on orientation angles, as depicted in Fig. 14, spreads over areas with radii of 200–250 \(\mu\)m. It could result from nonobserved oriented neurons that would have to be located either in other, probably neighboring layers (35), or laterally beyond the limits of our recording area, as suggested by the findings of Ts’o et al. (58) in the cat. An alternative source could consist of more strongly overlapping LGN input in the case of similarly oriented neurons. However, examples such as the one given in Fig. 7B are difficult to reconcile with any present knowledge.

The lateral range of eye dominance dependent, shared input was found to be 200–250 \(\mu\)m in both layers V and VI. By magnitude it was prominent in layer VI but barely detectable in layer V. Indeed LGN input is reported for layer VI but not V (23). In the latter layer, however, an input from layer IVc has been described (38). It is difficult to match the above average ranges to the examples found in the literature of anatomically determined arborization diameters. Some fibers from the LGN to layer IVc give off collaterals in layer VI that are described to be sparse and extremely fine, but in one example the arborization covers an area of 800 \(\mu\)m across (5).

The eye independent shared input observed in layer V has a greater lateral range than the interactions in layer VI. It falls off to half its 160-\(\mu\)m value at a distance of \(~400\) \(\mu\)m, and it may be related to the presence of many laterally running fibers forming the inner band of Baillarger. At interneuronal distances \(<200\) \(\mu\)m bifurcating axons from layer III, whose ramifications are short (53, 61), may also contribute. The greater number of processing steps between LGN and layer V cells is presumably the reason for the loss of eye dominance dependency observed for the layer V input. Because we have only one animal with adequate recordings from layer V, it cannot be entirely ruled out that some apparently layer-related findings are due to interanimal variability.

The lateral interactions manifesting themselves as broad correlogram peaks, assumed to originate in the retina, fall off in the cortex to half maximum at lateral distances of \(~1\) mm, corresponding in our monkeys to angular distances between 9 and 11 min of arc. This in turn corresponds to \(~35–45\) \(\mu\)m in the retina (48). According to Boycott and Dowling (7) amacrine cells, [also suggested by Mastronarde (42) as sources of correlation] even with arborization diameters of 100 \(\mu\)m, were quite common in the central retina of the monkey.

Considerations of synaptic contribution

The matter is simple if only a narrow laterally displaced peak is observed as shown in Fig. 15F. The number of spikes contained in the peak compared with the number of spikes of the recipient neuron is the synaptic contribution, although in reality the interaction may be distributed over several parallel correspondingly weaker synapses. At distances of not \(<160\) \(\mu\)m most contributions were found to be \(<0.01\).

However, if there is a symmetrical correlogram peak, (interpreted as originating from shared input) then, as a first step, an assumption for the synaptic input probabilities (“efficacies”) at the two observed neurons is necessary, usually that they are equal. Furthermore the spike rate of the unknown input neuron must be assumed to be of the order of the observed neurons. Then the probability that a spike is elicited simultaneously in both neurons is the square of that efficacy, and this is what is determined in a correlogram. The contribution values thus obtained are only gross estimates, and they can be quite high; 0.1 is not rare. However, since the source is
not observed in this case it can well consist of many neurons, each with a lower contribution, and this is even the most likely case. Thus individual contributions, e.g., from the LGN to the firing of layer IV cells, are not necessarily different from contributions of other sources, as was also concluded by Tanaka (55).

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