

Synchronization of oscillatory neuronal responses between striate and extrastriate visual cortical areas of the cat

(area 17/posteromedial lateral suprasylvian area/cross-correlation analysis/binding problem)

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ABSTRACT Recent studies have shown that neurons in area 17 of cat visual cortex display oscillatory responses which can synchronize across spatially separate orientation columns. Here, we demonstrate that unit responses recorded from the posteromedial lateral suprasylvian area, a visual association area specialized for the analysis of motion, also exhibit an oscillatory temporal structure. Cross-correlation analysis of unit responses reveals that cells in area 17 and the posteromedial lateral suprasylvian area can oscillate synchronously. Moreover, we find that the interareal synchronization is sensitive to features of the visual stimuli, such as spatial continuity and coherence of motion. These results support the hypothesis that synchronous neuronal oscillations may serve to establish relationships between features processed in different areas of visual cortex.

Anatomical and physiological evidence suggests that the visual system creates highly fragmented representations of objects present in the visual field. This is due to several characteristic features of cortical organization. (i) Neurons in the visual cortex integrate information only from a limited part of the sensory surface, and cells processing signals from adjacent parts of the visual field are not necessarily neighbors. (ii) Cortical neurons respond only to a limited range of feature constellations and again, cells preferring similar constellations may be nonadjacent. (iii) Within each sensory modality, different aspects of the afferent signals are processed simultaneously in a number of different cortical areas (1, 2). This fragmentary nature of sensory representations imposes the need to reintegrate the information that is distributed throughout the cortex and to “bind” together those attributes pertaining to a particular object (3–5).

It has been proposed (3, 6) that this binding may be accomplished in the temporal domain. According to this proposal, the relationship between features is encoded by the temporal correlation of neuronal discharges. Extending this hypothesis, von der Malsburg (7, 8) suggested that neuronal responses with a periodic temporal structure may be particularly advantageous as part of a temporal coding mechanism. According to this model, selective binding of features is expressed by the synchronization of oscillatory responses (8). Recent studies of cat visual cortex have provided evidence that a large fraction of area 17 neurons displays stimulus-induced oscillations in the frequency range of 40–60 Hz (9–11). These neuronal oscillations can synchronize across spatially separate orientation columns within area 17, depending on the configuration of the visual stimulus (10, 12, 13). Based on this evidence, we have suggested that synchronized oscillatory responses may indeed provide the physiological substrate for a mechanism of feature binding (12–15).

This hypothesis predicts that, because of the distributed nature of cortical processing, response synchronization should occur also between different visual areas. Cells located in different visual areas should fire synchronously if they are coactivated by different features of a single object (5, 14, 15). In the present study, we tested this hypothesis in the cat visual cortex. To this end, we looked for response synchronization between area 17 and the visual area in the posteromedial lateral suprasylvian (PMLS) sulcus (16). These two areas presumably process different aspects of visual stimuli in parallel. Area 17 appears to be devoted to the fine grain analysis of objects in the visual field (17), whereas area PMLS is considered as a visual association area involved in analysis of global motion and of the global structure of patterns (17–20). Therefore, we were interested in investigating (i) whether oscillatory responses occur in this extrastriate visual area, (ii) whether response synchronization can be observed between areas 17 and PMLS, and (iii) whether synchronization, if it occurs, depends on features of the visual stimuli used. Some of the results of this study have been presented in abstract form (21).

MATERIALS AND METHODS

We made simultaneous recordings of multiunit responses from area 17 and the ipsilateral area PMLS (16) in four adult cats. Preparation and maintenance of the animals have been described in detail (12, 13). Multiunit activity was recorded using arrays of four to six tapered and Teflon-coated platinum-iridium electrodes (25- μ m shaft diameter) with a spacing of 0.4–1 mm. One array was advanced down the medial wall of the suprasylvian sulcus between stereotaxic coordinates AP0 and A5, corresponding to the location of area PMLS (16). Another array was inserted into area 17, between AP0 and P5 and usually moved down the medial bank of the lateral gyrus.

Prior to quantitative measurements, the receptive field properties of the cells were assessed with hand-held stimuli. This enabled us to verify the location of the electrode array in area PMLS by two additional criteria: (i) The spatial arrangement of the receptive fields agreed with the characteristic retinotopy of area PMLS; i.e., during electrode penetrations at the AP level chosen, the receptive fields moved toward the center of the visual field along the horizontal meridian (16). (ii) The receptive field properties of the cells encountered were characteristic of area PMLS; i.e., the cells had large directionally selective receptive fields, exhibited pronounced binocularity, and showed broad velocity tuning but poor orientation selectivity (18–20). In most pairs of simultaneous area 17–PMLS recordings, both cell clusters had receptive fields in the paracentral region of the visual field (see Figs. 1 and 3). For all area 17–PMLS pairs, the

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Abbreviation: PMLS, posteromedial lateral suprasylvian.

largest distance between receptive field centers was 15 degrees.

After amplification, multiunit activity was obtained by bandpass filtering of the signals between 1 and 3 kHz. The spikes were fed through a Schmitt trigger and digitized with a time resolution of 1 ms, the threshold being set to about twice the noise level. Prior to computer-controlled stimulation, the receptive fields for the two eyes were superimposed with a prism to permit binocular stimulus presentation. For each trial, light bar stimuli of appropriate velocity were moved forward and backward across the receptive fields. Whenever possible, the stimuli were moved in the cells, preferred direction. Orientation of the light bars was always perpendicular to the axis of motion. All stimulus trials lasted 10 s and were repeated 10 times.

Our methods for data processing have been described in detail (13). Auto- and cross-correlation functions were computed for all spike trains. As discussed (13), the periodic modulation of autocorrelograms indicates the oscillatory nature of the responses, and their synchronization is reflected by the periodic modulation of the respective cross-correlograms. To detect a significant periodicity, we fitted Gabor functions (damped sine waves) to the correlograms. The parameters of the respective function (i.e., amplitude, decay, phase shift, frequency, and offset) were then used to assess the correlogram modulation. To obtain a measure of the modulation amplitude that is independent of the absolute response strength, we determined the "relative modulation amplitude" by computing the ratio of the amplitude of the Gabor function over its offset (13) (see Figs. 1–3).

Cross-correlograms were considered as reflecting a significant synchronization of oscillatory responses if the amplitude of the Gabor function was significantly different from zero (at the 5% level), if the relative modulation amplitude exceeded a value of 0.1, and if the Gabor function displayed at least three distinct peaks (13) (see Fig. 1 *F* and *G*). The same criteria were applied to autocorrelograms to quantify the oscillatory nature of the responses (Fig. 1 *D* and *E*). As a control, we computed a shift predictor of the auto- and cross-correlation after shuffling the trial sequence (13). These shift predictors were flat for all correlograms included in this report.

RESULTS

We studied the interaction between cells in areas 17 and PMLS in 46 response pairs. Two of these response pairs are illustrated in Fig. 1. We recorded simultaneously from two different sites in the PMLS area and from one site in area 17 (Fig. 1*A*). Since the two PMLS recordings differed in their preferred axis of stimulus movement and in their receptive field location (Fig. 1*B* and *C*), we were able to compare two different recording constellations. In the first, the receptive fields of area 17 and PMLS cells were overlapping, preferred similar stimulus orientations, and thus could be coactivated with a single light bar (Fig. 1*B*). The autocorrelogram computed for the PMLS response showed a strong periodic modulation with a frequency of about 50 Hz, indicating the oscillatory temporal structure of the response (Fig. 1*D*, lower histogram). The response of the area 17 cell showed a weak, but significant periodicity (Fig. 1*D*, upper histogram). The cross-correlogram computed for the two responses also showed a significant periodic modulation indicating interareal synchronization (Fig. 1*F*). In a subsequent measurement, the cells at the second PMLS recording site were costimulated with the area 17 cell cluster. In this constellation, the two receptive fields were nonoverlapping and their orientation preferences differed (Fig. 1*C*). Therefore, we applied two independent stimuli of optimal orientation. As before, the PMLS and area 17 responses were oscillatory

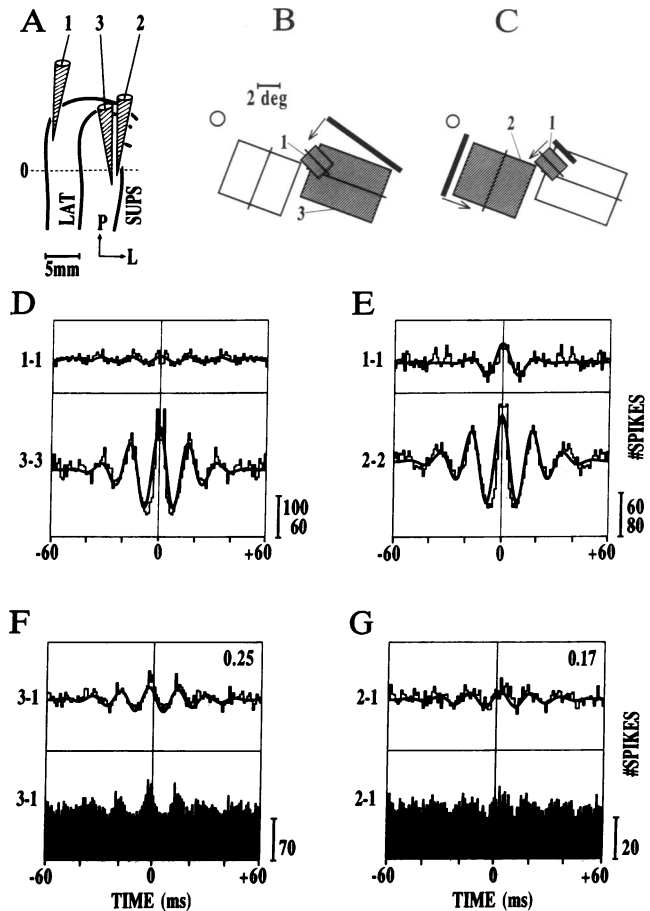


FIG. 1. Synchronization of oscillatory responses between areas 17 and PMLS. (A) Position of the recording electrodes in area 17 (site 1) and area PMLS (sites 2 and 3). Electrodes 2 and 3 were separated by 2 mm. LAT, lateral sulcus; SUPS, suprasylvian sulcus; P, posterior; L, lateral. (B and C) Plots of the receptive fields. The bar within each receptive field indicates the optimal orientation of the light bar stimulus, which is perpendicular to the preferred axis of stimulus motion. (B) In one recording situation, the cells at electrodes 1 and 3 (shaded area) were stimulated with a single light bar of near optimal orientation. (C) Subsequently, cells at sites 1 and 2 (shaded area) were coactivated using two independent bar stimuli of the respective optimal orientation. The circle represents the center of the visual field. (D and E) Autocorrelograms of the responses obtained for the two stimulus conditions. The correlograms were computed for a 1.5-s window centered on the peak of the response in the peristimulus time histogram (data not shown). The thick line represents the Gabor function that was fitted to the respective correlogram. Note that both PMLS responses (3-3, 2-2) display a strong oscillatory modulation. (F and G) Interareal cross-correlograms obtained for the two stimulus conditions. The cross-correlograms are computed for the same time window as the autocorrelograms. The upper parts of the figures show the same correlogram as the lower but superimposed with the respective Gabor function. The number in the upper right corner indicates the relative modulation amplitude of each Gabor function. Note that both response pairs (3-1, 2-1) show a significant degree of synchronization. However, the interaction between 2-1 is weaker, as indicated by the lower relative modulation amplitude.

(Fig. 1*E*). Cross-correlation analysis of the two responses revealed a significant interareal synchronization that was, however, weaker than that seen in the first measurement (cf., Fig. 1*F* and *G*).

These examples demonstrate clearly (i) that PMLS neurons exhibit oscillatory responses in the same frequency range as cells of area 17 (9–13) and (ii) that cells in area 17 and PMLS can synchronize their responses. In addition, the experiment shows that synchronization is not restricted to

cases where cells of the two areas match in their receptive field locations and directional preferences. However, the data suggest that synchronization is weaker if the recorded cells have nonoverlapping fields and different directional preferences. As will be demonstrated below, this may be related to the fact that cells with dissimilar receptive field properties were usually stimulated in a rather incoherent manner; i.e., two light bars were presented that moved in different directions (Fig. 1C; see Fig. 3).

Analysis of our remaining data sample confirms these observations. Of the 25 sites investigated in PMLS, 19 exhibited responses with a significant periodic modulation. The average of the oscillation frequency was 52 Hz (SD = ± 12 Hz; $n = 19$) and thus in the same range as that of responses in area 17 (11–13). In agreement with previous reports (18–20), most of the cell clusters (17 out of 25) showed a clear directional selectivity. Oscillatory responses occurred in both directionally selective and nonselective cells.

A synchronization of oscillatory responses between the two areas was observed in 24 of 46 response pairs (52%). In 10 out of 24 response pairs, a strong synchronization was observed; i.e., the relative modulation amplitude of the cross-correlogram exceeded a value of 0.2. However, it never exceeded a value of 0.5 suggesting that, at least in the anesthetized animal, interareal interactions are weaker than the interactions observed within the primary visual area (13). For pairs of area 17 cells with overlapping receptive fields, we readily obtained correlograms with modulation amplitudes close to 1.0 (e.g., see figure 6 in ref. 13). Statistical evaluation of the whole data set revealed a significant dependence of response synchronization on the degree of receptive field overlap. Synchronization occurred more often if the cells had overlapping receptive fields ($P < 0.025$; U-test) (Fig. 2A). However, it did not depend on differences in orientation preference (Fig. 2B). On the average, the oscillation in area 17 had a phase lag of 2 ms relative to that in PMLS (SD = ± 2.5 ms; $n = 24$).

We have demonstrated (12–15) that interactions between area 17 cells not only depend on the cells' receptive field properties but also are markedly influenced by properties of the stimulus used. We wondered, therefore, whether this also holds true for interareal interactions. Fig. 3 illustrates an experiment in which we tested whether the interareal synchronization is sensitive to global stimulus features such as continuity of contours and coherence of motion (12). The cells at the two recording sites had nonoverlapping receptive fields but similar orientation and velocity preferences (Fig. 3B–D). This enabled us to evoke simultaneous responses at the two sites with a single continuous light bar (Fig. 3B), two light bars moving colinearly at the same velocity (Fig. 3C), or two bars moving in opposite directions (Fig. 3D). In all three stimulus conditions, we obtained similar peristimulus time histograms (Fig. 3E–G) and autocorrelograms (Fig. 3H–J) indicating that neither the amplitude nor the oscillatory nature of the local responses was affected by changing the global composition of the stimulus. However, the cross-correlograms showed that response synchronization was strongest with a continuous long light bar (Fig. 3K). The synchronization was weaker for two colinearly moving stimuli (Fig. 3L) and disappeared with the two light bars moving in opposite directions (Fig. 3M). This result was confirmed in one additional area 17–PMLS response pair in which the alignment of the two receptive fields allowed us to perform this test. These results clearly suggest a stimulus dependence of the interareal response synchronization.

DISCUSSION

The results of this study extend our previous findings on stimulus-induced oscillatory activity in cat visual cortex and

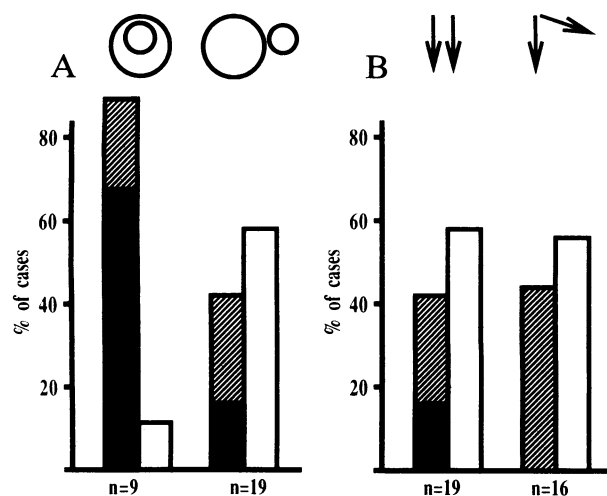


FIG. 2. Quantitative analysis of cross-correlograms. (A) Comparison of area 17–PMLS pairs with overlapping (on the left) and nonoverlapping (on the right) receptive fields. The histogram columns indicate the percentage of cases (response pairs) that show strong (relative modulation amplitude > 0.2), weak (relative modulation amplitude between 0.1 and 0.2), or no synchronization (solid, hatched, and open bars, respectively). Pairs with overlapping receptive fields correlate significantly more often than pairs with nonoverlapping fields ($P < 0.025$; U-test). Only response pairs were included in which the orientation preferences of the area 17 and PMLS recording differed by less than 22 degrees. This is because our data sample showed a relative lack of area 17–PMLS pairs with overlapping receptive fields plus widely differing preferred orientations. (B) Comparison of area 17–PMLS pairs with differences in preferred orientation of less (on the left) or more (on the right) than 22 degrees. Only pairs with nonoverlapping receptive fields are included. The two groups do not differ significantly ($P > 0.05$; U test). For testing whether the data samples compared in A and B differed significantly, a U test was applied to the respective distribution of the relative modulation amplitudes (for correlograms that lacked a significant modulation, this value was set to zero).

demonstrate (i) that PMLS cells oscillate in the same frequency range as striate cortical neurons, (ii) that cells in PMLS and area 17 can fire synchronously, and (iii) that this interareal synchronization can depend on features of the visual stimulus.

Stimulus-evoked neuronal oscillations in a frequency range of 40–60 Hz have also been observed in areas 18 and 19 of cat visual cortex (10, 22). Neurons in both areas can synchronize their oscillatory responses with those of area 17 cells (10, 22). The present results extend these findings to a nonprimary visual area and suggest that the ability to generate oscillatory responses in the γ range may be a general property of cortical networks. This hypothesis gains further support from the observation of oscillatory response patterns in the olfactory bulb and entorhinal cortex (23).

The occurrence of response synchronization between striate and extrastriate visual cortical areas supports the hypothesis that this synchronization is achieved by cortico-cortical connections rather than by common input from specific thalamic nuclei (12–14). The visual projections to areas 17 and PMLS are largely relayed through different thalamic nuclei (24). Therefore, reciprocal cortico-cortical connections between areas 17 and PMLS appear as the most likely substrate for interareal synchronization (24). However, an additional possibility, which cannot be ruled out on the basis of available evidence, is that cortico-thalamo-cortical projections via thalamic association nuclei contribute to interareal synchronization. It has been shown that areas 17 and PMLS are also connected indirectly via the lateral portion of the lateral posterior nucleus of the thalamus, which itself

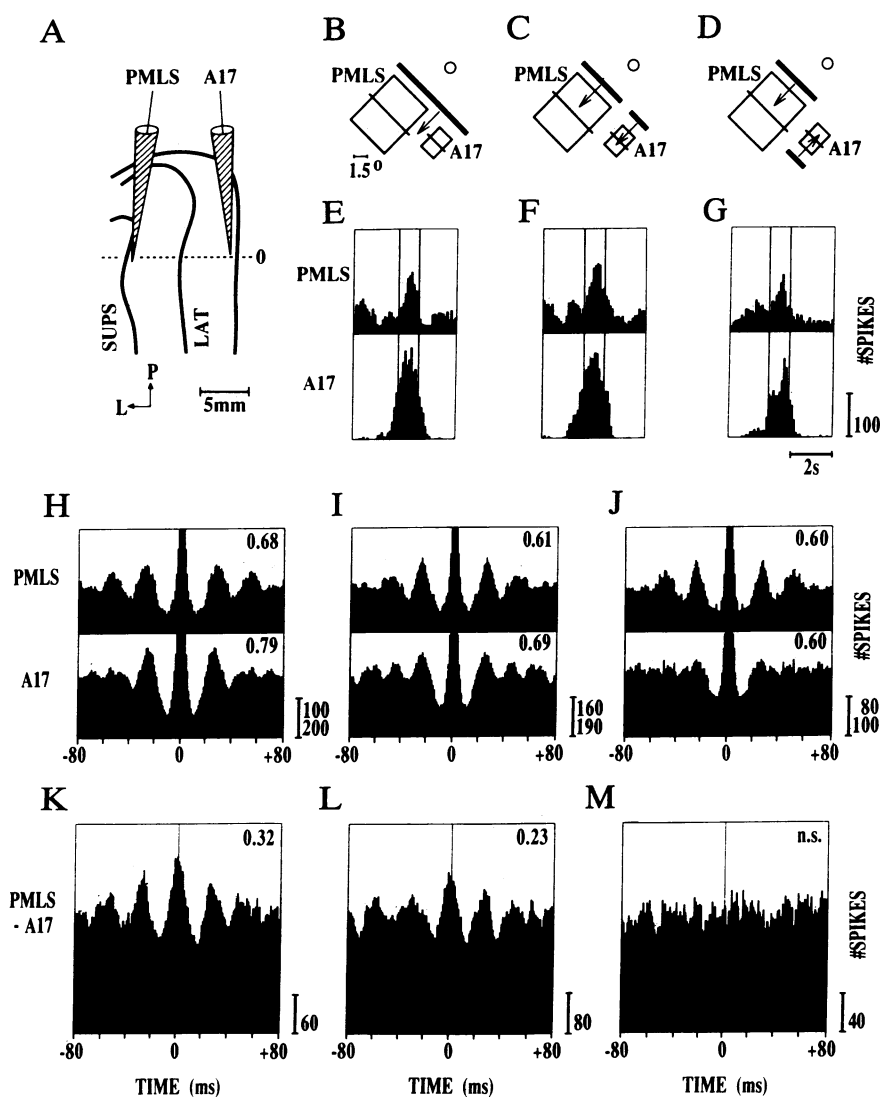


FIG. 3. Interareal synchronization is sensitive to global stimulus features. (A) Position of the recording electrodes. A17, area 17; LAT, lateral sulcus; SUPS, suprasylvian sulcus; P, posterior; L, lateral. (B–D) Plots of the receptive fields of the PMLS and area 17 recording. The diagrams depict the three stimulus conditions tested. The circle indicates the visual field center. (E–G) Peristimulus time histograms for the three stimulus conditions. The vertical lines indicate 1-s windows for which autocorrelograms and cross-correlograms were computed. The PMLS recording was directionally selective. Therefore, in D we reversed the direction of the bar stimulating the area 17 field. (H–J) Comparison of the autocorrelograms computed for the three stimulus paradigms. Note that the modulation amplitude of the correlograms is similar in all three cases (indicated by the number in the upper right corner). (K–M) Cross-correlograms computed for the three stimulus conditions. The number in the upper right corner represents the relative modulation amplitude of each correlogram. Note that the strongest correlogram modulation is obtained with the continuous stimulus. The cross-correlogram is less regular and has a lower modulation amplitude when two light bars are used as stimuli, and there is no significant modulation (n.s.) with two light bars moving in opposite direction.

does not receive visual input (24, 25). Oscillatory activity has now been observed in a number of thalamic nuclei (26–28). Thus, it seems conceivable that neurons in the lateral posterior nucleus might exhibit oscillatory firing patterns and participate in a synchronizing link between areas 17 and PMLS. Obviously, further experiments are needed to identify with certainty the substrate of interareal response synchronization. However, using a different experimental paradigm, we have recently obtained direct evidence for the hypothesis that reciprocal cortico-cortical connections are sufficient for response synchronization. We could demonstrate that oscillatory responses can also synchronize between the two cerebral hemispheres (21, 29). In this case, lesion experiments show directly that cortico-cortical connections, through the corpus callosum, mediate the interhemispheric synchronization (29). Therefore, we suggest that also the interareal synchronization observed within one hemisphere is likely to be accomplished by cortico-cortical connections.

The data presented in this paper may resolve the notorious puzzle concerning the function of reciprocal cortico-cortical connections. Several lesion studies indicate that neuronal responsiveness as well as the basic receptive field properties are essentially unchanged in area PMLS after ablation of the primary visual areas (30, 31). Thus, the massive cortico-cortical connections between areas 17 and PMLS do not seem to contribute to the formation of visual receptive fields. This is expected if—as our results suggest—these connections serve to create temporal relations between responses in the two areas. Simulation studies have demonstrated that reciprocal connections can effectively synchronize spatially distributed cell groups without affecting the neuronal response properties (32, 33).

In functional terms, response synchronization between areas 17 and PMLS is of particular interest, since neurons of the two areas show remarkable differences in their receptive field properties, suggesting that they process different as-

pects of visual stimuli. In contrast to area 17 cells, neurons in area PMLS have large receptive fields and are strongly directionally selective but poorly tuned for stimulus orientation (18–20). Accordingly, area PMLS has been hypothesized to be involved in global pattern analysis (17), figure-ground segregation (19), and global motion processing (20). Area 17, on the other hand, is considered to perform a high-resolution fine grain analysis of local features (17). Thus, synchronization of responses between the two areas may serve to bind the local with the global features of a visual object (e.g., the different orientations of its outlines and their coherent motion). Thereby, response synchronization may achieve binding across different feature domains. The observation that the area 17–PMLS interaction can depend strongly on the stimulus configuration and is not confined to cell pairs with strictly matching receptive field properties supports the hypothesis that synchronization of oscillatory responses provides a versatile and highly flexible mechanism for the binding of different features of a visual object (12–15).

The establishment of synchrony between remote cortical areas demonstrates that a temporal coding mechanism of this kind is capable of integrating widely distributed representations. Therefore, the mechanism proposed here may solve the problem of how information processed in separate and parallel cortical pathways is reintegrated (1, 2). By means of temporal coding, this is possible without “grandmother neurons” or the anatomical convergence of processing pathways onto an integrating “higher” area (5, 7). Dynamic representation of objects by assemblies of synchronously oscillating cells may avoid the combinatorial explosion that results if fixed sets of rigidly interconnected neurons were to represent the near infinite variety of possible feature constellations (7, 12–15).

In conclusion, this study demonstrates a temporal correlation of responses between striate and extrastriate visual areas that possibly represent different feature domains. These results further support the hypothesis that a temporal coding mechanism involving response synchronization may solve the general problem of integration in neuronal networks with highly parallel and distributed organization.

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