Visual Feature Integration and the Temporal Correlation Hypothesis

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Introduction

The Combinatorial Problem

The mammalian visual system is endowed with a nearly infinite capacity for the recognition of patterns and objects. To have acquired this capability the visual system must have solved what is a fundamentally combinatorial problem. Any given image consists of a collection of features, consisting of local contrast borders of luminance and wavelength, distributed across the visual field. For one to detect and recognize an object within a scene, the features comprising the object must be identified and segregated from those comprising other objects. This problem is inherently difficult to solve because of the combinatorial nature of visual images. To appreciate this point, consider a simple local feature such as a small vertically oriented line segment placed within a fixed location of the visual field. When combined with other line segments, this feature can form a nearly infinite number of geometrical objects. Any one of these objects may coexist with an equally large number of other possible objects. The problem becomes daunting when we expand this scenario to account for the wide array of possible local features and the fact that objects may appear in different spatial locations and orientations. The possible combinations that confront the visual system are virtually unlimited. Yet when faced with any new scene, the visual system usually has no problem in segmenting the image into its component objects within a fraction of a second. This observation suggests that the visual system has adapted a very efficient mechanism for the flexible integration of featural information.

Population Coding and the Binding Problem

Considering what is presently known about the anatomical and functional organization of the mammalian visual system, we can clearly see that the requirement for flexible integration presents a fundamental problem to our understanding. The mammalian visual cortex consists of numerous interconnected areas (Rosenquist 1985, Felleman and van Essen 1991, Sereno and Allman 1991, Payne 1993). These different regions possess numerous feedforward, feedback, and intrinsic connections and are thought to be devoted to the analysis of different but often overlapping attributes of visual images (DeYoe and Van Essen 1988, Livingstone and Hubel 1988, Merigan and Maunsell 1993). At early stages of processing, cortical areas are retinotopically organized; neurons have relatively simple receptive field properties; and cells with similar functional properties are grouped together into functional streams (DeYoe and Van Essen 1988, Livingstone and Hubel 1988). This organization gradually gives way to a largely nonretinotopic mapping at higher levels in the hierarchy, and the receptive field properties of cortical neurons concurrently increase in size and complexity owing to convergence and divergence of connections from cells in lower areas. Although the functional streams are preserved, in the sense that separate areas tend to have distinct functional properties, extensive cross-talk occurs among areas at every processing stage.

It is apparent from this organization that the representation of a perceptual object, and its attributes such as location in space or direction of motion, are not likely to be processed at a single location but rather involve a large population of cells distributed over several different cortical areas. This raises the question as to how relations are established among the spatially distributed responses occurring within and between different levels of processing. Similar binding problems are also likely to arise at lower levels. A common assumption is that the representation of a particular local feature is achieved by the graded responses of a population of neurons.
This notion is attractive because the relatively broad tuning of neuronal receptive fields suggests that single contours evoke simultaneous responses in many neurons. For the same reason, the response amplitude of any individual cell is an ambiguous descriptor of a particular feature because response vigor is equally influenced by the location of a contour and its orientation, contrast, and extent. Representation of a feature by a population of cells raises binding problems when nearby contours evoke graded responses in overlapping groups of neurons. Of the many simultaneous responses, those evoked by the same contour need to be distinguished and evaluated together to avoid interference with the responses elicited by neighboring contours. A similar need for response selection and binding arises in the context of perceptual grouping. Once the elementary features of a scene have been represented, some grouping operation must be performed to identify those neurons responding to the features of a particular object and to segregate the activity of neurons responding to the features of other objects or to the background. The implementation of units that receive converging inputs from cells whose responses require integration may allow this type of binding. The activity of such cells would then represent either elementary features or, at higher levels of processing, a particular constellation of elementary features. Finally, by iteration of this operation, units could be created that respond with high selectivity to single perceptual objects.

The analysis of single-cell receptive fields at different levels of visual processing suggests that the visual system does exploit the option of binding by convergence. Cells at higher levels of processing tend to have larger receptive fields and to respond selectively to rather complex constellations of elementary features, such as stereotypes of faces or patterns (Gross et al. 1972, Baylis et al. 1985, Desimone et al. 1985, Perrett et al. 1987, Sakai and Miyashita 1991, Fujita et al. 1992, Gallant et al. 1993). However, several observations indicate that binding is probably not achieved solely by the convergence of distributed signals onto specialized cells. Although such a mechanism could enable the rapid and unambiguous association of a limited set of key features, the number of units required to implement it as a universal mechanism scales very unfavorably with the number of possible patterns to be represented. Essentially, one cell would be required for every distinguishable feature, for each higher-order feature combination, and ultimately for every distinguishable perceptual object. Moreover, because of its inherent lack of flexibility, such a mechanism cannot easily cope with the representation of new or modified patterns. Experimental data also suggest that binding by convergence is probably not the only strategy for the association of distributed neuronal responses. The pattern-specific cells in the inferotemporal cortex are not selective for individual perceptual objects but for characteristic components of patterns (Fujita et al. 1992). Hence, these cells respond to a whole family of related patterns, and conversely, a particular pattern is likely to activate many neurons simultaneously (Young and Yamane 1992).

The representation of features and objects by the joint activity of neuronal populations has several undisputed advantages (Hebb 1949; Braitenberg 1978; Ballard et al. 1983; Singer 1985, 1990; von der Malsburg 1985; Edelman 1987; Gerstein et al. 1989; Grossberg 1980; Palm 1990; Abeles 1991). One essential feature of such assembly coding is that individual cells can participate at different times in the representation of different patterns. This strategy substantially reduces the number of cells required for the representation of different patterns and allows for greater flexibility in the generation of new representations. The assumption is that just as a particular feature can be present in many different patterns, the group of cells coding for this feature can be shared by many different representations in that they participate at different times in different assemblies of coactive neurons. The code is thus relational and the significance of an indi-
individual response depends entirely on the context set by the other members of the assembly.

To exploit the advantages of population coding, however, mechanisms are required that enable the flexible association of neuronal activity. Those active cells participating in a particular representation must be unambiguously identified as belonging together. One way to distinguish a given subset of cells is to enhance their saliency by increasing their relative firing rates (Olshausen et al. 1993). The output of these cells then has a greater impact because of temporal summation. However, selecting neurons solely on the basis of enhanced discharge rates has two potential disadvantages: First, it limits the option of encoding information about stimulus properties by the graded activity of neuronal groups. Second, it limits the number of populations that can be enhanced simultaneously without becoming confounded. Only those populations that are clearly defined by a place code would remain segregated. However, although place codes can in principle reduce ambiguity, they are again expensive in terms of neuron numbers, and most importantly, they sacrifice flexibility. To maintain the position code, interactions between assemblies in different areas must be forbidden, because they would reintroduce the ambiguity that one wants to overcome. It has been proposed, therefore, that response selection could be achieved by the synchronization of activity among a distributed population of neurons rather than by solely increasing their discharge rate (Milner 1974; von der Malsburg 1981, 1985; von der Malsburg and Schneider 1986).

Two features of cortical connectivity suggest that synchronization may be a particularly effective way of enhancing response saliency. First, cortical cells contact each other with only a few synapses whose efficiency is usually low (Komatsu et al. 1988, Mason et al. 1991, Braintenberg and Schüz 1991, Nicoll and Blakemore 1993, Thomson and West 1993). Second, synaptic transmission among cortical neurons is characterized by pronounced frequency attenuation (Thomson and West 1993). Hence, increasing the summation of activity by synchronizing inputs may more effectively enhance transmission than raising discharge rates (see Abeles 1991). Another (and in this context) crucial advantage of synchronization is that it expresses unambiguous relations among neurons because it enhances selectively only the saliency of synchronous responses. Simulation studies by Softky and Koch (1993) suggest that the interval for effective summation of converging inputs is only a few milliseconds in cortical neurons. Thus, if synchronization of discharges can be achieved with a precision in the millisecond range, it can define relationships among neurons with very high precision. Moreover, if synchrony is established rapidly and maintained only over brief intervals, different assemblies can be organized in rapid temporal succession. In principle, a particular assembly can be defined by a single barrage of synchronous action potentials whereby each individual cell needs to contribute only a few spikes (Buzsaki et al. 1992). Such synchronous events are likely to be very effective in eliciting responses in target populations, and because they are statistically improbable, their information content is high.

In summary, the hypothesis predicts that the discharges of neurons undergo a temporal patterning and become synchronous if they participate in the encoding of related information. This synchronization is thought to be based on a self-organizing process that is mediated by a selective network of corticocortical and corticothalamic connections. Thus, distributed groups of coactive neurons that code for a particular feature, or at higher levels, for constellations of features corresponding to a perceptual object, would be identifiable as members of an assembly because their responses would contain episodes during which their discharges are synchronous. These theoretical considerations yield several predictions regarding the organization of neuronal assemblies in cortical networks. In the following paragraphs we enumerate these predictions.
and review the experimental evidence for their validation.

Predictions

The first requirement of the temporal correlation hypothesis, and the one with the most supporting evidence, predicts that cells recorded simultaneously should, under appropriate conditions, exhibit synchronous firing on a millisecond time scale. Specifically, correlated firing should occur between cells recorded in (a) the same cortical column of a given area to enable the coding of local features, (b) different columns within an area to enable the linking of spatially disparate but related features, (c) different cortical areas to provide for the binding of information across different feature categories and different locations in space, (d) the two cerebral hemispheres to link information present in the two visual hemifields, and (e) different sensory and motor modalities to contribute to the processes of sensorimotor integration. Second, the probability for intra- and interareal response synchronization should reflect some of the Gestalt criteria for perceptual grouping (Koffka 1935). Third, individual cells should be able to rapidly change the partners with which they synchronize their responses if stimulus configurations change and require new associations. Fourth, if more than one object is present in a scene, several distinct assemblies should form. Cells belonging to the same assembly should exhibit synchronous response episodes, whereas no consistent temporal relationships should exist between the discharges of neurons belonging to different assemblies. This prediction, however, may apply differently to different levels in the cortical hierarchy. In retinotopically organized areas synchronous assemblies of active cells can be spatially separated. In nonretinotopic areas, such as inferotemporal cortex, spatial segregation is less likely. Thus, few assemblies or even a single assembly of synchronously active neurons may be present at any given time. This could contribute to the serial nature of visual attention (Crick and Koch 1990). Fifth, the connections determining synchronization probability should be specific and yet modifiable according to a correlation rule whereby synaptic connections should strengthen if pre- and postsynaptic activity is often correlated, and they should weaken when there is no correlation. This is required to enhance grouping of cells that code for features that often occur in consistent relations, as is the case for features constituting a particular object. Finally, the patterns of synchronized activity should bear some specific relation to visual discrimination behavior.

Experimental Testing of Predictions

Intracolumnar Interactions

Multielectrode recording experiments have revealed neuronal response synchronization over each of the predicted spatial scales. The bulk of these studies have focused on the occurrence and properties of local (<1 mm) intra- and intercolumnar interactions. The literature contains many examples of temporal synchrony between cells recorded within the same cortical column (<200 μm separation) in different areas of the cat or monkey visual cortex (Toyama et al. 1981a,b; Michalski et al. 1983; Ts’o et al. 1986; Ts’o and Gilbert 1988; Aiple and Kruger 1988; Hata et al. 1988, 1991; Gochin et al. 1991; Schwarz and Bolz 1991; Gawne and Richmond 1993). These synchronous interactions occur among various cell types in different layers of cortex and are most often characterized by central peaks in cross-correlation histograms, which indicates a common excitatory or inhibitory input (Perkel et al. 1967). Occasionally, the correlograms exhibit peaks or troughs at specific latencies indicative of direct excitatory or inhibitory synaptic interactions.
In our own studies, the systematic search for dynamic, stimulus-dependent interactions between cortical neurons was initiated by the finding that adjacent neurons in area 17 of the cat visual cortex often transiently engage in highly synchronous discharges when presented with their preferred stimulus (Gray and Singer 1987, 1989). Groups of neurons recorded simultaneously with a single electrode discharge synchronously at intervals of 15–30 ms. These sequences of synchronous rhythmic firing occur preferentially when cells are activated with slowly moving contours of optimal orientation. They typically last a few hundred milliseconds and may occur several times during a single passage of a moving stimulus (figure 64.1). Accordingly, autocorrelation histograms computed from such response epochs often exhibit a periodic modulation (Gray and Singer 1987, 1989; Eckhorn et al. 1988; Gray et al. 1990; Schwarz and Bolz 1991). During such episodes of synchronous firing, an oscillatory field potential can be recorded by the same electrode; here, the negative phase of the signal coincides with the cells’ discharges (figure 64.1). The occurrence of the local field response indicates that many cells in the vicinity of the electrode synchronize their discharges (Gray and Singer 1989). This conjecture is supported by recent multiple single-unit recordings employing new spike extraction techniques (figure 64.2) (Gray and Viana Di Prisco 1993).

The locally synchronous firing has since been observed in recordings of multiple units and local field potentials (LFP) in several areas of the visual cortex of anesthetized cats (areas 17–19 and Posteromedial Lateral Suprasylvian (PMLS)) (Eckhorn et al. 1988, 1992; Gray and Singer 1989; Gray et al. 1990; Engel et al. 1991c; Schwarz and Bolz 1991), in striate cortex of awake, behaving cats (figure 64.2) (Raether et al. 1989, Gray and Viana Di Prisco 1993) and monkeys (Eckhorn et al. 1993), in the optic tectum of awake pigeons (Neuenschwander and Varela 1993), and in area 17 (Livingstone 1991) and area MT (Kreiter and Singer 1992, Engel et al. 1992) of anesthetized and awake, behaving monkeys, respectively. In each instance the activity is characterized by properties similar to those observed in the cat striate cortex:

1. The spike trains consist of repetitive burst discharges at semiregular 15- to 30-ms intervals.
2. Neither the onset latency nor the phase of the synchronous episodes are precisely related to the position of the stimulus within the neuron’s receptive field. When cross-correlation functions are computed between responses to identical stimuli, these shift predictors reveal no correlation (Gray and Singer 1989, Gray et al. 1990, Jagadeesh et al. 1992). This finding rules out the possibility that the synchronous firing is related to some fine spatial structure in the receptive fields of cortical neurons.
3. The locally synchronous firing often, but not always, results in the appearance of a correlated field potential signal at the same frequency (Eckhorn et al. 1988, 1993; Gray and Singer 1989; Engel et al. 1991c; Livingstone 1991; Kreiter and Singer 1992).

Although these properties appear to be general, several studies have found little or no evidence for rhythmic firing in single- and multiple-unit recordings from areas V1, MT, and the inferotemporal cortex of the macaque (Bair et al. 1992, Tovee and Rolls 1992, Young et al. 1992). The reasons for these conflicting results are not readily apparent. One possibility is suggested by data from the olfactory bulb (Freeman 1975, Gray and Skinner 1988) and the hippocampus (Alonso and Garcia-Austt 1987, Buzsaki et al. 1992) where rhythmic activity is prominent at the level of field potentials but often not apparent in the autocorrelograms computed from single-unit activity. In these systems, however, the timing of spike discharges are often well correlated with the phase of the LFP. Thus, even though little evidence supports rhythmicity in the discharge of single units, the cells do participate
Figure 64.1
Multiunit and local field-potential responses to the presentation of an optimally oriented light bar recorded from a single electrode in area 17 of an adult cat. Oscilloscope records show the response to the preferred direction of movement on a single trial. In the upper two traces, at a slow time scale, the onset of the response is associated with an increase in high-frequency activity in the local field potential. The lower two traces display the activity at an expanded time scale. Note the presence of oscillations in the local field potential correlated with the occurrence of the unit discharges. (b)–(e) Quantitative properties of multiunit and local field potential activity recorded on a single electrode in the striate cortex of a 6-week-old kitten in response to a moving light bar of optimal orientation. (b) Post-stimulus-time histogram (PSTH) of the multiunit activity. The light bar was first moved over the receptive field in one direction (1–4 s) and then in the opposite direction (6–9 s). (c) Compressed spectral array of the LFP recorded on a single trial illustrating the time course and frequency content of the oscillatory response. The signal was bandpass filtered between 20 and 100 Hz. (d) Autocorrelation histograms and associated shift predictor histograms computed from the multiunit activity. The unfilled bars are for the second direction of stimulus movement (4–9 s). The shift predictors are flat, indicating that the oscillatory signals are not time locked to the visual stimulus. (e) Spike-triggered average of the LFP demonstrating that spike activity occurs with the highest probability during the negative phase of the field potential oscillations. The thick line represents the second direction.
as members of a population that exhibits oscillatory behavior. The lack of rhythmicity in the spike trains is thought to be a consequence of the low firing rates of the cells, the frequency variability of the rhythmic population events, and the variation of phase differences between the single-unit discharges and the population oscillations. These sources of variance combine to produce a spike train that appears Poisson when analyzed using relatively short epochs of data.

Figure 64.2 shows an example of this effect. The sampling problem is alleviated with multi-unit recordings if several of the recorded cells are synchronized to the same rhythm. But variations in the frequency of the rhythm may yield autocorrelograms lacking any oscillatory modulation. Because the detectability of oscillatory activity in the gamma frequency range has become a major issue in the context of the correlation hypothesis, we emphasize that no conclusions regarding the formation of assemblies can be drawn from the presence or absence of oscillatory firing patterns in single-unit activity. First, oscillatory firing is in itself not thought to convey significant information regarding the stimulus. It is too variable in frequency and magnitude (Gray and Singer 1989; Engel et al. 1990; Gray et al. 1990, 1992; Ghose and Freeman 1992). Second, evidence for or against assembly formation can only be obtained with simultaneous recordings from two or more units or field-potential signals because the relevant parameter is the temporal correlation among the discharges of groups of neurons. Oscillations may provide an important mechanism for establishing synchrony, especially over large distances (König et al. 1994), but the nervous system contains many examples of nonrhythmic synchronous firing.

**Intercolumnar Interactions**

Measurements of intercolumnar correlations are fewer in number but have revealed similar pat-
terns of synchronous firing. The majority of these studies have been performed in area 17 and have sought to determine the relationship between receptive field properties and the occurrence of synchronous firing. Two general findings have emerged. First, the probability and strength of correlated firing falls off with distance in cortex (Michalski et al. 1983, Ts’o et al. 1986, Aiple and Kruger 1988, Ts’o and Gilbert 1988, Gray et al. 1989, Engel et al. 1990, Kruger 1990, Hata et al. 1991, Schwarz and Bolz 1991). Cells that have overlapping receptive fields and that are separated by less than 2 mm are far more likely to exhibit synchronous firing than cells with nonoverlapping fields that have a separation greater than 2 mm. Nevertheless, numerous examples of long-range synchronous firing have been observed over distances spanning several hypercolumns in area 17 (Ts’o et al. 1986, Ts’o and Gilbert 1988, Gray et al. 1989, Engel et al. 1990, Schwarz and Bolz 1991).

The second general finding obtained from these studies is that intercolumnar correlated firing occurs with greater probability for cells that have similar receptive field properties. Correlations tend to occur most often between cells with similar orientation preferences (Ts’o et al. 1986, Ts’o and Gilbert 1988, Gray et al. 1989, Hata et al. 1991, Schwarz and Bolz 1991), similar ocular dominances (Ts’o et al. 1986, Ts’o and Gilbert 1988), and similar color selectivities (Ts’o and Gilbert 1988). Moreover, cells with specific types of complex and simple receptive fields tend to interact with other cells of the same type (Ts’o et al. 1986, Schwarz and Bolz 1991), although there are exceptions to this, as yet, poorly defined rule (Schwarz and Bolz 1991). These long-range correlations have generally been thought to reflect the specificity of intracortical horizontal axonal connections that preferentially link functional columns with similar feature specificities (Ts’o et al. 1986; Ts’o and Gilbert 1988; Martin and Whitteridge 1984; Gilbert and Wiesel 1983, 1989; but see Matsubara et al. 1987). In most instances, however, inter-columnar correlation measurements have been performed using two stimuli, one optimal for each of the two recorded cells. Cells that have different receptive field properties are thus activated by stimuli that have different features. Within the context of the theory presented here, such a featural difference in the stimuli introduces a potential cue for the segregation of assemblies and the consequent absence of correlated firing. This point is discussed in detail below.

When interactions occur over larger tangential distances in the cortex, the cross-correlograms exhibit two other prominent features. First, the peak in the histograms is usually centered around zero delay. The half width at half height of this peak is often on the order of 2–3 ms, indicating that most of the action potentials occur nearly simultaneously (Ts’o and Gilbert 1986, Gray et al. 1989, Schwarz and Bolz 1991). Second, when cells engage in long-distance synchronization, the firing patterns of the local groups often exhibit synchronous repetitive discharges as described above. The central peak in the correlogram is thus often flanked on either side by troughs that result from refractory periods between the synchronous bursts. When the duration of these pauses is sufficiently constant throughout the episode of synchronization, the cross-correlograms show a periodic modulation with additional side peaks and troughs (Eckhorn et al. 1988, Gray et al. 1989, Engel et al. 1990, Schwarz and Bolz 1991, Livingstone 1991). Synchronous oscillations are readily apparent if the LFP is also recorded from each electrode (figure 64.3) (Engel et al. 1990, Gray et al. 1992). This pattern of rhythmic synchronization rarely, if ever, occurs in the absence of visual stimulation. Such intercolumnar synchronization has been observed over distances of up to 7 mm in the cat (Gray et al. 1989) and up to 5 mm in area V1 of the squirrel monkey (M. Livingstone, personal communication). In the cat, cells separated by more than 2 mm that have nonoverlapping receptive fields are more likely to exhibit synchronous firing if they have similar orientation...
preferences (Gray et al. 1989, Engel et al. 1990, Schwarz and Bolz 1991). If the cells are separated by less than 2 mm and have overlapping receptive fields, the synchronous firing occurs largely irrespective of the preferred orientation of the cells (Gray et al. 1989, Engel et al. 1990), provided that they can be activated with a single stimulus.

**Interareal and Interhemispheric Interactions**

In agreement with the predictions of the temporal correlation hypothesis, response synchronization has also been found between groups of cells located in different cortical areas. In the cat, stimulus-evoked synchronous firing has been observed between cells in areas 17 and 18 (Eckhorn et al. 1988, 1992; Nelson et al. 1992b); between cells in areas 17 and 19, and 18 and 19 (Eckhorn et al. 1992); between cells in area 17 and area PLMS, an area specialized for motion processing (figure 64.4) (Engel et al. 1991c); and between cells in area 17 of the two hemispheres (Engel et al. 1991a, Eckhorn et al. 1992, Nelson et al. 1992a). In the macaque, synchronous firing has been observed among neurons in areas V1 and V2 (Bullier et al. 1992, Roe and Ts’o 1992, Nowak et al. 1994).

In the studies of Nelson et al. (1992b) interareal synchronous firing in cats occurs spontaneously and during the presentation of visual stimuli. The interactions span a wide tripartite range of temporal scales, which produces correlograms with central peaks of narrow, medium, and broad width. The narrow coupling is most often seen between cells that have overlapping receptive fields with similar properties. The broader coupling encompasses a much wider range of receptive-field separations and orientation-preference differences (Nelson et al. 1992b). Synchronous interactions between cells in V1 and V2 in the monkey show similar broad peaks. Synchrony occurs between cells that have both overlapping and nonoverlapping receptive fields (Bullier et al. 1992, Nowak et al. 1994) and is most frequent between cells of similar color selectivity in the two areas (Roe and Ts’o 1992).

In the studies of Eckhorn et al. (1988, 1992) and Engel et al. (1991a,c), interareal and interhemispheric synchronous firing occurred primarily, if not exclusively, during coactivation of the cells by visual stimuli, and was particularly pronounced during periods of oscillatory firing. These data reveal several additional similarities to the intra- and intercolumnar oscillatory interactions. The occurrence of synchronous firing depends on, but is not locked to, the visual stimulus. The probability of occurrence and the magnitude of interareal temporal correlations are somewhat greater for cells that have overlapping receptive fields and similar orientation preferences. When receptive fields are nonoverlapping and cells are activated with two stimuli, synchronization probability is greatest when the stimuli move at the same speed in the same direction (Engel et al. 1991a,c). Interhemispheric synchrony also requires the integrity of the corpus callosum. Surgical sectioning of this structure markedly reduces the probability of synchronous firing between the two hemispheres (Engel et al. 1991a, Nelson et al. 1992a). These studies provide the first results demonstrating that corticocortical connections are critical for the establishment of synchronous firing.

**Evidence for Synchrony in Nonvisual Structures**

In the preceding discussion, we have reviewed the evidence for synchronous activity revealed by multielectrode recordings from visual cortical areas. Comparable multicell recordings are still rare in nonvisual structures, but considerable data are available from field-potential studies. The data indicate that synchronous rhythmic activity occurs over a range of spatial scales in several different cortical and subcortical systems throughout the brains of mammals (Basar and Bullock 1992, Gray 1993, Singer 1993).

In the mammalian olfactory system, for example, 40- to 80-Hz oscillatory activity is evoked
The local field potential and multiunit activity recorded at two sites in area 17 separated by 7 mm show similar temporal properties and correlated interactions. (A) Plot of the LFP responses (1–100 Hz bandpass) recorded on a single trial to the presentation of two optimally oriented light bars passing over the receptive fields of the recorded
during inspiration in both the olfactory bulb and piriform cortex (Adrian 1950; Freeman 1975, 1978; Bressler 1984). This activity is synchronous over a scale of several millimeters both within and between the two structures (Bressler 1984, 1987; Freeman 1987). The patterns of activity that emerge during these coherent states correspond to specific odors, the animal’s past experience with the odors, and their behavioral significance (Freeman 1987). The oscillatory activity by itself is not thought to convey any specific information; instead, it is viewed as a mechanism for establishing synchrony among large populations of coactive cells (Freeman 1987).

Similar rhythmic activities have been discovered in both the somatosensory and motor cortices of cats and monkeys. In the studies of Bouyer and colleagues, field potential oscillations in the beta and gamma ranges occur in the somatosensory cortex when animals are in a state of focused attention (Bouyer et al. 1981). These rhythmic activities are synchronous over relatively large areas of cortex (Bouyer et al. 1981), occur in phase with similar activity in the ventrobasal thalamus (Bouyer et al. 1981), and are regulated by dopaminergic input from the ventral tegmentum (Montaron et al. 1982). Oscillatory field potential and unit activities in the range of 20–40 Hz have also been observed in the motor cortex of alert monkeys (Murthy and Fetz 1992, Sanes and Donoghue 1993). These signals are synchronous over widespread areas of the motor cortical map within and between the two cerebral hemispheres, between the visual and motor cortices (E. Fetz, personal communication), and between the motor and somatosensory cortices. They are also enhanced in amplitude when the animals are performing new and complicated motor acts (Murthy and Fetz 1992). The rhythms are suppressed, however, during the execution of trained movements (Sanes and Donoghue 1993).

The hippocampus exhibits several forms of synchronous rhythmic activity that are associated with particular behavioral states. Foremost among these is the theta rhythm, a 4- to 10-Hz oscillation of neuronal activity that occurs during active movement and alert immobility. Theta field potentials are often synchronous between the two hemispheres and over distances extending up to 8 mm along the longitudinal axis of the hippocampus (Bland et al. 1975). Local populations of cells also exhibit a high degree of synchronous firing during theta activity (Kuperstein et al. 1986). Furthermore, two other hippocampal neuronal rhythms have been discovered. One has a frequency of 30–90 Hz, occurs during a variety of behavioral states (Buzsaki et al. 1983, Leung 1992, Bragin et al. neurons at each site. The peaks of the responses overlap in time but are not in precise register. (B) The average cross-correlogram computed between the two LFP signals (20–100 Hz bandpass) at a latency corresponding to the peak of the oscillatory responses. The thick horizontal line represents the 95% confidence limit for significant deviation from random correlation. (C) PSTHs of the multiunit activity recorded over 10 trials at the same two cortical sites as shown in panel A. Again the responses overlap but are not in precise register. (D) Auto- (1–1, 2–2) and cross- (1–2) correlograms of the multiunit activity recorded at each site. Note the presence of clear periodicity in each correlogram, which indicates that the responses are oscillatory and that they show a consistent phase relationship. (E) Plots of the spike-triggered averages of the LFP signals at each site computed over all 10 trials. The thick and thin lines correspond to electrodes 1 and 2 respectively. Note that the peak negativity of the waveform is correlated with the occurrence of neuronal spikes at 0-ms latency. (F) Normalized average power spectrum of the LFP signals computed from periods of spontaneous (thick line) and stimulus-evoked (thin line) activity. The frequency of the activity is similar in both the autocorrelograms of the multiunit activity (MUA) and the power spectra of the LFPs. (From Gray et al. 1992.)
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. (b1–3) Plots of the receptive fields of the PMLS and area 17 cells. The diagrams depict the three stimulus conditions tested. The circle indicated the visual field center. (c1–3) PSTHs for the three stimulus conditions. The vertical lines indicate 1-s windows for which auto- and cross-correlation histograms were computed. (d1–3) Comparison of the autocorrelation histograms computed for the three stimulus paradigms. (e1–3) Cross-correlation histograms computed for the three stimulus conditions. Note that the response amplitudes are minimally affected by changes of stimulus configuration, whereas the synchronization of activity is largely absent for stimuli moving in opposite directions. (From Engel et al. 1991c.)
1994), and is both locally and bilaterally synchronous. Another more recently discovered signal with a frequency around 200 Hz is associated with alert immobility and the presence of sharp waves in the hippocampal EEG (Buszaki et al. 1992, Ylinen et al. 1994). These events have been termed population oscillations because single cells do not exhibit high-frequency periodic firing. Rather they fire at low rates in synchrony with the surrounding population of cells, which in the composite yields a periodic signal that is synchronous over distances up to 2.1 mm (Buszaki et al. 1992, Ylinen et al. 1994).

Oscillatory components in the beta- and gamma-frequency ranges have also been documented in humans. In several early studies, depth recordings of the local EEG from several cortical and subcortical sites revealed episodes of synchronous rhythmic activity during particular behavioral states (Sem-Jacobsen et al. 1956, Chatrian et al. 1960, Perez-Borja 1961). Surface EEG and MEG recordings have revealed gamma-frequency components in the auditory evoked potential (Galambos et al. 1981, Basar 1988, Sheer 1989, Pantev et al. 1991, Tiitinen et al. 1993), the somatomotor cortex (Murphy et al. 1994), and a broad distribution over the entire cerebral mantle (Ribary et al. 1991). Recently, however, direct surface recordings of the EEG over the somatosensory cortex in humans have revealed that gamma-band activity does not predominate over activity in other frequency ranges (Menon et al. 1994). In spite of this there is ample evidence from animals and humans that brain structures other than the visual cortex engage in synchronous rhythmic activity in the beta- and gamma-frequency ranges.

**Stimulus Dependence of Response Synchronization**

Another important prediction of the temporal correlation hypothesis is that the probability for distributed cells to join an assembly should reflect the Gestalt criteria, according to which, features in images tend to be grouped together into objects. Described early this century (see Koffka 1935), these criteria include the categories of proximity, similarity, continuity, and common fate, reflecting the fact that objects typically consist of features that exist in close proximity; that have common properties such as form, color, and depth; that are spatially contiguous; and that, when they move, tend to do so with a common or linked direction of motion. Evidence reviewed in the previous section supports the notion that response synchronization satisfies the criteria of proximity and similarity.

Additional evidence suggests that response synchronization fulfills the criteria of continuity and common fate. In one study, Gray et al. (1989) recorded multunit activity from two locations separated by 7 mm in striate cortex. The receptive fields of the cells were nonoverlapping, had nearly identical orientation preferences, and were spatially displaced along the axis of preferred orientation. This arrangement enabled stimulation of the cells with bars of the same orientation under three different conditions: two bars moving in opposite directions, two bars moving in the same direction, and one long bar moving across both fields coherently. Under these conditions, no significant correlation was found in the first case; a weak correlation was seen in the second; and a robust synchronization was found in the third case. This effect occurred in spite of the fact that the firing rates of the two cells and the oscillatory patterning of the responses were similar in the three conditions (Gray et al. 1989). Further support for the notion that response synchronization is influenced by stimulus continuity was obtained in a study by Schwarz and Bolz (1991). They demonstrated that the probability of detecting intercolumnar synchronization between standard complex cells in layer 5 and simple or complex cells in layer 6 is highest not only when the cells have the same orientation preferences but when their receptive fields are aligned colinearly.
In a related experiment, Engel et al. (1991c) obtained evidence that the criteria of continuity and common fate are also satisfied by interareal interactions. They made simultaneous recordings from cells in areas 17 and PMLS (a motion-sensitive area in the lateral suprasylvian sulcus of the cat) that had nonoverlapping receptive fields with similar orientation preference and colinear alignment. This technique allowed them to examine the effects of continuity and coherent motion on response synchronization using the paradigm described above. They found little or no correlation when the cells were activated by oppositely moving contours, a weak but significant correlation in response to two bars moving in the same direction, and a robust synchronization when the cells were coactivated by a single long bar moving over both fields (figure 64.4) (Engel et al. 1991c). Recently, Sillito et al. (1994) demonstrated an analogous influence of stimulus continuity and coherent motion on the synchronization of activity in the lateral geniculate nucleus (LGN). They showed that cells having nonoverlapping receptive fields displayed little or no evidence of synchronization when activated by a pair of stationary spots. If, however, the cells were driven by a single long bar or an extended grating drifting over both receptive fields, the cells often engaged in synchronous firing. This effect was abolished by removal of the overlying visual cortex, suggesting that the thalamic synchronization is controlled by feedback from the visual cortex.

These findings, combined with the earlier results, suggest that the global properties of visual stimuli can influence the magnitude of synchronization between widely separated cells located within and between different cortical areas and thalamus. Single contours, but also spatially separate contours, which move coherently and therefore appear as parts of a single figure, are more efficient in inducing synchrony among the responding cell groups than oppositely moving contours that appear as parts of independent figures. This finding demonstrates that synchronization probability and magnitude depends not only on the spatial separation of cells and on their feature preferences, but also on the configuration of the stimuli.

A central prediction of the correlation hypothesis posits that individual cells must be able to change the partners with which they become synchronized in order to join different assemblies at different times. Thus, as the features in an image change, the relationships among the activity patterns of the cells responding to those features should change in a way that reflects the Gestalt properties of the image.

Tests of this prediction have been conducted by Engel et al. (1991b) in cat area 17 and by Kreiter and colleagues in area MT of the anesthetized monkey (Kreiter et al. 1992). In the cat, multiunit activity was recorded from up to four electrodes that had a spacing of approximately 0.5 mm. The proximity of the electrodes yielded recordings in which all the cells had overlapping receptive fields and covered a broad range of orientation preferences. This configuration enabled these investigators to compare the correlation of activity among cells coactivated by either one or two moving bars. In the majority of cases, cells with different orientation preferences fired synchronously when coactivated by a single bar of intermediate orientation. But when the same cells were activated by two independent bars of differing orientation, moving in different directions, the responses were not synchronized (Engel et al. 1991b).

Kreiter and Singer (1994) recently demonstrated that this process is a general property of the visual cortex and is not confined to the visual cortex of anesthetized cats. Recordings of multiunit activity were made from two electrodes in area MT of an alert macaque. The electrode separation was less than 0.5 mm, which yielded cells with nearly completely overlapping receptive fields but often differing directional preferences. This setup enabled them to repeat the earlier experiment conducted in the cat (Engel et al. 1991b) by coactivating the cells with one
bar and then with two independently moving bars. The firing of the cells was synchronized when responses were evoked by a single bar moving over both fields but not when the responses were evoked by two independent bars (figure 64.5) (Kreiter and Singer 1994). Repeated measurements of the responses from the same cells under identical conditions revealed that the effect was stable.

Taken together, these data (Engel et al. 1991b, Kreiter and Singer 1994) demonstrate that two overlapping, but independent, stimuli evoke simultaneous responses in a large array of spatially interleaved neurons. The active neuronal populations can become organized into two assemblies that are distinguished by the temporal coherence of activity within and the lack of coherence between the cell groups responding to the two different stimuli. Cells representing the same stimulus exhibit synchronized response epochs, while no consistent correlations occur between the responses of cells that are activated by different stimuli. This observation suggests that the pattern of temporal correlation among the responses of individual cells provides additional information to signal that two objects are present in nearby or overlapping regions of the visual field. More generally, these examples demonstrate that under appropriate conditions visual stimulus properties can influence the synchronization of activity of two or more groups of neurons, thus supporting the hypothesis that response synchrony can serve to establish relations between spatially distributed features in a visual image. It must be pointed out, however, that there do exist examples in which the correlated firing of neurons in visual cortex is not influenced by changes in the pattern of visual stimulation (Schwarz and Bolz 1991). Thus, further experiments are required to rigorously determine the conditions under which this type of dynamic correlation occurs.

The theoretical arguments put forth here with respect to visual processing also apply to tactile and auditory processing, motor control, and higher cognitive functions. Hence, transient synchronization of distributed neuronal responses should also occur within and across other regions of cortex. Moreover, these temporal correlations of neuronal firing should be flexible. Single cells or populations of cells should be able to participate in different assemblies at different times depending on stimulus properties or the context of a particular behavioral task. Supporting this prediction are recent studies in the alert monkey that were based on multineuron activities in the auditory and frontal cortex (Ahissar et al. 1992, Vaadia and Aertsen 1992) and on field potential signals in sensory, motor, parietal, and frontal cortices (Bressler et al. 1993). These investigators found instances in which changes in either stimulus properties or behavioral-task conditions led to marked changes in the correlated firing of two neurons without an appreciable change in their firing rate (Ahissar et al. 1992, Vaadia and Aertsen 1992) or a change in the pattern of multiregional coherence of activity between different cortical areas (Bressler et al. 1993). These findings suggest that dynamic, stimulus- and context-dependent modulations of response synchronization are a general property of cortical networks.

Experience-Dependent Influences on Intraareal Synchronization

The temporal correlation hypothesis implies that assemblies based on synchronous firing patterns form as a result of the synaptic interactions among the constituent cells. The experiments on interhemispheric synchronization have confirmed this supposition by identifying corticocortical connections as the anatomical substrate for synchrony. Therefore, the criteria by which particular features are grouped together must be built into the functional architecture of the corticocortical connections. If this architecture is specified entirely by genetic instructions, perceptual grouping criteria will have to be regarded
Stimulus-dependent synchronization in area MT of an awake macaque. (a, e) Plots of the receptive fields and the stimulus configurations. Panels (a)–(d) illustrate the single-bar configuration, while panels (e)–(h) show the results when two bars are moved simultaneously but in different directions over the two receptive fields. Both stimulus conditions were applied in six alternating blocks, each containing 10 trials. Cross-correlation histograms and PSTHs computed for the single-bar condition appear in panels (b), (c), and (d) and those for the dual bar condition in panels (f), (g), and (h). The thin vertical lines in the PSTHs mark the time window in which the cross-correlation histograms were computed. The scale bars correspond to 40 spikes. Note that the single-bar stimulus results in a clear synchronization, as shown by the pronounced peaks in the cross-correlograms, while no synchronization occurs with the two-bar stimulus. (From Kreiter and Singer 1994.)
as genetically determined. If the architecture is modifiable by activity and hence experience, some of these criteria could be acquired by learning. The numerous similarities in the layout of cortical connections indicate that some of the basic principles of cortical organization are determined genetically. But extensive evidence also supports epigenetic modifications. In mammals, corticocortical connections develop mainly postnatally (Innocenti and Frost 1979, Price and Blakemore 1985, Luhmann et al. 1986, Callaway and Katz 1990) and attain their final specificity through an activity-dependent selection process (Innocenti and Frost 1979, Luhmann et al. 1990, Callaway and Katz 1991).

Direct evidence for experience-dependent modifications of synchronizing connections comes from experiments with strabismic kittens (Löwel and Singer 1992). The primary visual cortex of kittens raised with artificially induced strabismus is split into two subpopulations of cells of about equal size, each responding rather selectively to stimulation of one eye only (Hubel and Wiesel 1965b). The changes in the thalamocortical connections elicited by squint suggest that input to cells driven by different eyes is only rarely correlated. A recent study showed that horizontal intercolumnar connections were reorganized in strabismic kittens, and unlike in normal animals, no longer connected neurons receiving input from different eyes (Löwel and Singer 1992). This finding suggests that experience-dependent selection of cortical connections occurs according to a correlation rule in a manner similar to other levels of the visual system (for review, see Stryker 1990). Moreover, in strabismic cats response synchronization does not occur between cell groups connected to different eyes, whereas the incidence and magnitude of synchronization appears normal between cell groups connected to the same eye (König et al. 1993). Because strabismic subjects are unable to bind signals conveyed by different eyes into coherent percepts (von Noorden 1990), this result also supports the hypothesis that response synchronization serves binding.

Further indications for a relation between response synchrony and visual function come from a recent study of strabismic cats that had developed amblyopia, a condition in which the spatial resolution and perception of patterns through one of the eyes is impaired. The identification of neuronal correlates of these deficits in animal models of amblyopia has remained inconclusive because the contrast sensitivity and spatial acuity of neurons in the retina and in the lateral geniculate nucleus were found to be normal, and evidence for correlates of the perceptual deficits in the visual cortex has remained controversial (see Crewther and Crewther 1990, Blakemore and Vital Durand 1992). However, multielectrode recordings from the striate cortex of cats exhibiting behaviorally verified amblyopia have revealed significant differences in the synchronization behavior of cells driven by the normal and the amblyopic eye. The synchronization of activity among cells connected to the amblyopic eye was much less than that observed between cells responsive to the normal eye (Roelfsema et al. 1994). This difference was even more pronounced for responses elicited by gratings of high spatial frequency. Apart from these differences, the response properties of the cells appeared normal. Thus, cells connected to the amblyopic eye continued to respond vigorously to gratings whose spatial frequency had been too high to be discriminated with the amblyopic eye in the preceding behavioral tests. These results suggest that disturbed temporal coordination of responses may be one of the neuronal correlates of the amblyopic deficit.

**Mechanisms Controlling Oscillations and Their Functional Importance**

As reviewed above, synchronous activity is often associated with oscillatory firing patterns. This common finding raises the question of how oscillatory processes are generated and whether
Figure 64.6

PSTHs (left panels) and associated cross-correlograms (right panels) computed from the activity recorded in response to the presentation of gratings of different spatial frequencies in cats with strabismic amblyopia. (a)–(d) Neuronal responses to low (a, b) and high (c, d) spatial frequencies gratings, recorded simultaneously from two cell groups driven by the normal eye (N-sites) (a, c) and two groups driven by the amblyopic eye (A-sites) (b, d), respectively. Note that response amplitudes decrease at the higher spatial frequency in both cases, while the relative modulation amplitude of the cross-correlogram increases for the N-N pair but decreases for the A-A pair. (e) Cumulative distribution functions of the differences in response amplitudes to low and high spatial frequency gratings of optimal orientation. N-sites, squares (n = 53); A-sites, triangles (n = 35); abscissa, responses to high spatial-frequency minus responses to low spatial-frequency gratings. Note the similarity of the two distributions (P > 0.1). (f) Cumulative distribution functions of the differences between relative modulation amplitudes (DRMA) of cross-correlograms computed from responses to high and low spatial-frequency gratings of N-N pairs (squares; n = 24) and A-A pairs (triangles; n = 11). DRMA values (abscissa) were calculated by subtracting the relative modulation amplitude obtained with the low spatial frequency from that obtained with the high spatial frequency. The difference between the DRMA distributions of N-N pairs and A-A pairs is significant (P < 0.001). (From Roelfsema et al. 1994.)
they contribute to synchronization. Our discussion of these mechanisms focuses on activity in the gamma-frequency band (30–80 Hz) because this is the range in which the majority of synchronous activity in the visual cortex has been described. There are three basic mechanisms likely to underlie the generation of oscillatory firing in the visual cortex. The first and most obvious mechanism to consider is oscillatory afferent input. The periodic temporal structure of cortical responses could result from rhythmic input from the lateral geniculate nucleus (LGN) or other thalamic nuclei. Support for this notion has come from studies demonstrating robust oscillatory activity in the frequency range of 30–80 Hz in both the retina and the LGN (Doty and Kimura 1963, Fuster et al. 1965, Laufer and Verzeano 1967, Arnett 1975, Ariel et al. 1983, Munemori et al. 1984, Ghose and Freeman 1992). In both structures, the rhythmic activity is present in a subpopulation of roughly 10–20% of the cells, and it occurs spontaneously, in response to diffuse changes in illumination or specific stimulation of the receptive field (Laufer and Verzeano 1967, Arnett 1975, Robson and Troy 1987, Ghose and Freeman 1992). In some cases, however, neuronal oscillations in the LGN or perigeniculate nucleus are suppressed or not influenced by visual stimuli (Ghose and Freeman 1992, Pinault and Deschenes 1992). In spite of its prevalence, and surprising regularity, it is unlikely that oscillatory activity in the LGN can account for the cortical oscillations and their long-range synchronization. Rather, the data of Sillito et al. (1994) indicate that one form of thalamic synchronization depends on corticofugal influences.

A second mechanism likely to underlie the generation of cortical oscillations relies on intracortical network interactions. In this scenario, cyclical changes in firing probability are thought to arise through synaptic interactions of populations of excitatory and inhibitory neurons (Freeman 1968, 1975; Wilson and Cowan 1972; Bush and Douglas 1991; Wilson and Bower 1992; Bush et al. 1993). Evidence supporting this hypothesis has come from intracellular recordings in cat striate cortex in vivo (Jagadeesh et al. 1992, Bringuier et al. 1992). These studies have revealed both high (30–60 Hz) and low (10–20 Hz) frequency oscillations of membrane potential closely resembling the properties of neuronal oscillations observed extracellularly (Gray and Singer 1989). The membrane potential oscillations occur during visual stimulation: They are orientation specific, and occur less often in cells receiving monosynaptic input from the LGN (Jagadeesh et al. 1992). Moreover, spike discharges occur on the depolarizing phase of the oscillation, which mirrors the extracellularly observed negativity (figure 64.7) (compare to figure 64.1). When the cells exhibiting these fluctuations are hyperpolarized below the firing threshold by current injection, the visually evoked oscillations increase in amplitude but do not change in frequency (figure 64.7) (Bringuier et al. 1992, Jagadeesh et al. 1992). These data suggest that the rhythmic fluctuations of membrane potential reflect a synchronous pattern of excitatory synaptic input onto the cells that arises in the cortex.

These data do not, however, rule out the possibility that cortical oscillations may arise as a
consequence of activity in a subpopulation of cells that are intrinsically oscillatory (Llinas 1988). Support for this conjecture has been obtained from both in vitro and in vivo intracellular recordings. In the former case, a subpopulation of inhibitory interneurons in layer 4 of the rat frontal cortex exhibited subthreshold, voltage-dependent, 10- to 50-Hz oscillations in membrane potential in response to depolarizing current injection (Llinas et al. 1991). These cells, if present in the visual cortex, would be expected to produce rhythmic hyperpolarizing potentials in their postsynaptic targets, a result for which the experimental evidence is currently limited (Ferster 1986). Recent intracellular recordings in vivo from cat striate cortex have revealed a subpopulation of cells that fire in regular repetitive bursts at 20–70 Hz in response to visual stimulation and intracellular depolarizing current injection (McCormick et al. 1993). The firing properties of these cells are very similar to the burst-firing cells observed extracellularly in cat visual cortex (Hubel and Wiesel 1965a, Gray et al. 1990, Gray and Viana Di Prisco 1993), and they are distinct from the previously defined class of intrinsic bursting cells known to be present in layer 5 (Connors 1982, McCormick et al. 1985).

Whether these cells are excitatory or inhibitory is unknown, but in either case their activation might serve to drive a local network of cells into a pattern of synchronous oscillation.

Conclusions

Visual scenes are inherently complex and can exist in a nearly infinite combinatorial variety. In spite of this complexity, mammalian species have evolved a virtually unlimited capacity for the rapid recognition of patterned visual information, which suggests that the visual system possesses effective mechanisms to enable the flexible integration of featural information. Anatomical and physiological evidence indicates that the featural attributes of visual images are processed in different parts of the visual cortex. Therefore, the representation of perceptual objects is not likely to take place at a single location but rather to involve the concerted action of large populations of cells distributed throughout the visual cortex. This raises the fundamental question, often referred to as the binding problem, of how the visual system establishes the appropriate relationships among the large number of neurons that respond to the many features in any given visual scene. Such relationships must be specific and yet flexible in order to cope with the combinatorial variety of features constituting visual images.

The experimental results reviewed in this chapter are compatible with the hypothesis that synchronization of neuronal activity on a millisecond time scale may be exploited to link featural information that is represented in different parts of the cortex (Milner 1974; von der Malsburg 1981, 1985). In this view the identification of related features, for example those belonging to the same perceptual object, is achieved by the temporal coincidence of the neuronal discharges evoked by those features. In a distributed network, such as the neocortex, where any given cell contacts any other cell with only a few synapses, but where individual cells receive converging input from many thousands of different cells (Braitenberg and Schüz 1991), synchronization may also be a particularly efficient mechanism to increase the saliency of activity. Thus, synchronization can, in principle, be used to select with high spatial and temporal resolution those activity patterns that belong together and to enhance the effect of this activity so it may be evaluated for further processing. The proposal presented here is that this selection is achieved in a distributed and parallel fashion by the system of corticocortical association fibers. In this context, the function of these connections consists largely of adjusting the timing of discharges rather than modulating discharge rates. Synchronization will of course affect discharge rates by enabling more effective summation than asynchronous inputs.
Hence, modulation of response amplitude and synchronization of discharges can operate as complementary mechanisms for the selection and binding of responses.

In consideration of these functional issues, the fundamental question also arises as to how, at a cellular level, synchrony can be established on a millisecond time scale over the broad range of spatial scales that are required. One possibility is that during development those connections having a conduction velocity appropriate for the generation of synchrony get selectively stabilized. The fact that synchronizing connections are selected according to a correlation rule supports this possibility. Additional temporal patterning of discharges may further facilitate the establishment of synchronous firing. The evidence presented here suggests that this requirement may be met in many instances by discharge patterns in which bursts and pauses follow one another with a certain degree of rhythmicity. The refractory period following a burst will produce a brief period of decreased sensitivity, making synaptic inputs arriving at that time less likely to have an effective influence on the overall pattern of activity.

In this context, the question arises as to why the observed oscillations are so irregular and cover such a broad frequency range (Gray et al. 1992). Functionally, such variation could facilitate the desynchronization of activity and thereby prevent the cortical network from entering global states of synchrony that would be inappropriate for information processing. Furthermore, the number of assemblies that can coexist in the same cortical region increases if the oscillation frequencies are variable, because spurious correlations arising from aliasing effects would be rare and only of short duration. Thus, a broad-banded oscillatory signal appears as a reasonable compromise between several opposing constraints. However, synchronous activity may arise in cortical networks without oscillatory firing, and the presence or absence of a regular oscillatory time structure in single-cell activity neither proves nor disproves that spatially segregated cells discharge in synchrony. Oscillations per se are thus of little diagnostic value for the testing of the temporal correlation hypothesis. The synchronization of activity is the relevant issue.

To directly test the hypothesis that correlated activity contributes to the integration of distributed featural information, experiments are needed in which the dependence of the occurrence and the magnitude of synchronized activity on stimulus configuration and behavioral performance can be assessed. This minimally requires the simultaneous recording of activity from several locations in the brain of awake, behaving animals and the evaluation of temporal correlations of activity at high resolution. With the techniques currently available, the number of recording sites that can be examined simultaneously is bound to remain small, which poses a severe sampling problem. For the brain, a brief sequence of correlated activity may be a highly significant event if it occurs in a large number of cells (Bressler et al. 1993). However, for the experimenter, who can only look at a few cells (most often 2; occasionally as many as 100) (Wilson and McNaughton 1993), such brief synchronous events may pass undetected. They will only be recognized as significant if they recur. Thus, until new techniques become available, the relationships between synchronized neuronal activity and behavior are likely to be detectable only for conditions that maintain synchronization for longer periods of time. This limitation may confine the behavioral conditions suitable for such analyses to problem-solving tasks that are difficult, fraught with ambiguity, and require periods of sustained, focused attention.

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