Role of the Temporal Domain for Response Selection and Perceptual Binding

Most cognitive functions are based on highly parallel and distributed information processing by the brain. A paradigmatic example is provided by the vertebrate visual system where numerous cortical areas have been described which analyse different types of visual information. At present, it is unclear how information can be integrated and how coherent representational states can be established in such distributed systems. We suggest that this so-called 'binding problem' may be solved in the temporal domain. The hypothesis is that synchronization of neuronal discharges can serve for the integration of distributed neurons into cell assemblies and that this process may underlie the selection of perceptually and behaviourally relevant information. We review experimental results, mainly obtained in the visual system, which support this temporal binding hypothesis.

The Binding Problem in the Visual System and its Possible Solutions

The past two decades of research on the cerebral cortex have revealed an astounding organizational complexity. Cortical regions have been subdivided into ever smaller compartments, each of which is characterized by distinct response properties and connections to other brain structures. This parcellation is pronounced for regions like the somatosensory (Kandel and Jessell, 1991), auditory (Kelly, 1991) and motor cortex (Kalaska and Crammond, 1992). However, a particularly intriguing example is provided by the visual cortex, where, in the monkey, more than 30 different visual areas have been classified (Livingstone and Hubel, 1988; Zeki and Shipp, 1988; Felleman and Van Essen, 1991; Zeki, 1993; Bullier and Nowak, 1995). As in the other cortical systems, the anatomical compartmentalization of the visual cortex is related to a functional specialization. Neurons in each of the visual areas are, at least to some degree, selective for a characteristic subset of stimulus features. Some areas, for example, are dedicated to the analysis of motion, others compute colour and still others are involved in processing of textures and shapes. This functional subdivision has far reaching consequences for the way in which perceptual objects are represented in the visual cortex. A single visual stimulus always activates cells in many visual areas, and this raises the question of how such distributed activity can be integrated to yield unambiguous representations of visual objects. The proposal that we shall discuss in the present paper can be traced back to Hebb (1949), who suggested that representations should be instantiated by assemblies, i.e. by distributed populations of cooperatively interacting neurons which, as a whole, signal the presence of a particular object.

In accordance with physiological data, it can be assumed that in such a distributed coding scheme a group of neurons, or module (or visual area), may be reserved for encoding each feature dimension. Visual objects, corresponding to particular constellations of distinct features can then be represented as unique patterns of activation over all these modules. An important advantage of such a distributed representation strategy is the highly economical use of neurons since a particular feature-selective cell can participate in the representation of all visual stimuli that contain the respective feature. For example, neurons that are selective for the colour red can join assemblies representing red stimuli. Neurons that respond to another object. The responses only signal that a set of visual features is present in the image, but information about which feature belongs to which object is lost. This problem calls for a mechanism that selectively tags the responses evoked by a single object and distinguishes them from responses evoked by different objects. Contemporary theories of visual representation differ mainly in the way in which they attempt to cope with this binding problem (as it is now usually termed). These theories benefit from a long tradition of psychophysical research initiated at the beginning of our century by the gestalt psychologists, who investigated the rules the visual system employs for perceptual grouping and for linking the features belonging to a particular object (Köhler, 1930). They observed that, for example, image components with a similar shape or colour, components that are located in close vicinity or elements that are moving in the same direction are likely to be grouped together. These rules still guide the search for neuronal mechanisms that are capable of binding responses which originate from the same perceptual object and thus allow a disambiguation of the assembly code.

One possibility for removing ambiguities from a distributed representation is to endow the network with binding units, i.e. with neurons that are selective for conjunctions of features from different domains. These neurons should fire if a particular set of features, e.g. the colour red and the shape of an apple, are combined in a single object, but not if these features belong to different image components. An extreme version of this solution for the binding problem is the cardinal cell hypothesis, which proposes the existence of cells that are selective for very specific
Engel et al. needed is a binding mechanism which reliably disambiguates which respond to the various features of a single image needed for encoding objects, given the virtually infinite diversity unrealistically expensive in terms of the number of neurons further, this strategy is unrealistic for representing objects and their location in space, i.e., the ability to represent particular feature constellations does not warrant the potential for representing different combinations of the same features. Clearly, what is needed is a binding mechanism which reliably disambiguates distributed activity patterns, while avoiding the preposterous cell numbers required by the cardinal cell model.

An alternative solution for the binding problem, that is consistent with a distributed representation, uses a focus of attention for demarcating a region of the visual field from which responses are selected for further processing (Crick, 1984; Treisman, 1986, 1996; Olshausen et al., 1994). When this window of attention is positioned accurately, and the inclusion of more than a single object is avoided, the binding problem may be circumvented. However, positioning the window exactly around the object of interest is necessary, and may be a difficult problem in itself, in particular when its outline is erratic and different objects are in close proximity. Further limitations may result from restricting the window to a single perceptual object at a time. This causes severe problems when objects are partially occluded by others since, in this case, responses from non-contiguous parts of the visual field must be integrated into a coherent percept. Difficulties also arise in the representation of relations between different objects, since ambiguities are reintroduced as soon as more than a single object is included in the window of attention. In these situations, the successful segmentation of the image into the constituent objects and background is actually a prerequisite for the appropriate positioning of the attentional focus. Thus, the binding problem would have to be solved by another mechanism before the searchlight of attention can be adapted to the distributed activation pattern. The attention-driven mechanism can, therefore, only contribute to the stabilization of assembly representations once perceptual grouping and scene segmentation have occurred.

A third option for solving the binding problem has been proposed by von der Malsburg (1981, 1995), Abeles (1982a) and, in a preliminary form, also by Milner (1974). These authors suggested that ambiguities may be removed from a distributed representation by using the precise timing of action potentials as a label. This 'temporal binding model' predicts that neurons which respond to the various features of a single image component should synchronize their discharges on a fine temporal scale, whereas neurons that respond to different image components should not fire in synchrony (Fig. 1). A crucial advantage of this coding strategy is that it allows multiple assemblies to become active at the same time without becoming confounded (von der Malsburg, 1981, 1995; Engel et al., 1992; Singer and Gray, 1995). As illustrated schematically in Figure 1, the temporal relationship between neuronal discharges permits the unambiguous distinction of subsets of functionally related responses. Thus, the overall activity pattern in the respective cortical area exhibits a significant amount of additional structure that can be used for the fast and reliable selection of visual responses for further joint processing. This disambiguation strategy rests on the assumption that synchrony can be detected with appropriate precision by coincidence-sensitive neurons in other brain areas (Abeles, 1982b; Softky, 1994; Gerstner et al., 1992; König et al., 1996). If such a temporal mechanism were used to solve the binding problem the advantages of a distributed coding strategy could be preserved without running into the difficulties associated with the other representational models discussed above. In the following sections of this paper we shall review experimental evidence that supports the temporal binding hypothesis.

**Temporal Binding in the Visual System**

Numerous studies have shown that neurons in both cortical and subcortical centres can synchronize their discharges with a precision in the millisecond range (for review see Engel et al., 1992; Aertsen and Arndt, 1993; König and Engel, 1995; Singer and Gray, 1995). This has been demonstrated in particular for the visual system, but similar observations have been made for the auditory, somatosensory and motor systems, and related synchronization phenomena have also been found in cortical association areas (see the last section of this paper).

In the cat visual system, several studies have demonstrated that spatially separate cells within individual visual areas can synchronize their spike discharges (Toyama et al., 1981; Ts'0 et al., 1986; Eckhorn et al., 1988; Gray et al., 1989; Engel et al., 1990; Schwarz and Bolz, 1991; Brosch et al., 1995). Moreover, it has been shown that response synchronization can extend well to the temporal relationship between neuronal discharges permits the unambiguous division of subsets of functionally related responses. Thus, the overall activity pattern in the respective
Figure 2. Interhemispheric interactions in cat visual cortex. (A) In the anesthetized animal electrodes were placed in the primary visual cortex of left and right hemisphere (LH, RH), LAT, lateral sulcus; CC, corpus callosum. (B) Plot of the receptive field locations for the two recording sites. The neurons had identical orientation preferences. The receptive fields were located in the respective contralateral hemifield in the vicinity of the vertical meridian (dashed line). The cells were activated with bar-shaped stimuli moved in the same direction across the receptive fields. The circle represents the centre of the visual field. (C) Cross-correlogram computed for the recorded responses. The central maximum present in the correlogram indicates the coincident neuronal firing. The additional side maxima reflect an oscillatory temporal modulation of the neuronal responses (Modified from Engel et al., 1991a.)

Beyond the borders of a single visual area. Thus, for instance, correlated firing has been observed between neurons located in different cerebral hemispheres (Engel et al., 1991a; Nowak et al., 1995). Figure 2 illustrates one of the measurements where this type of long-range interaction has been studied. In terms of the temporal binding hypothesis, this result is important because interhemispheric synchrony is required to bind the features of objects extending across the midline of the visual field. In addition, temporal correlations in cat visual cortex have been studied for neurons located in different areas of the same hemisphere (Eckhorn et al., 1988; Engel et al., 1991b; Nelson et al., 1992; Roelfsema et al., 1997). Of particular interest is the finding that interactions can occur between areas with quite different response properties, such as the primary visual cortex (area 17) and the posteromedial area in the lateral suprasylvian sulcus (PMLS), an extrastriate area involved in the processing of object motion (Engel et al., 1991b). As mentioned already, different areas are assumed to process different aspects of visual stimuli (Felleman and Van Essen, 1991; Bullier and Nowak, 1995), hence interareal synchronization could mediate binding across feature dimensions which presumably is required for the complete representation of visual scenes. Finally, recent evidence shows that synchronous firing is not confined to the cortex but occurs at the level of subcortical visual structures such as the retina, the lateral geniculate nucleus and the superior colliculus (Brechtt and Engel, 1996; Brecht et al., 1996; Neuenschwander and Singer, 1996). The majority of these studies on the cat visual system have been carried out in anesthetized preparations. However, the investigation of awake animals has yielded very similar results (Chiang et al., 1996; Fries et al., 1996; Gray and Viana Di Prisco, 1997; Roelfsema et al., 1997).

A key finding in these studies on cat visual cortex is that the neuronal synchronization depends on the stimulus configuration. It can be demonstrated that spatially separate cells show strong synchronization only if they respond to the same visual object. However, if responding to two independent stimuli, the cells fire in a less correlated manner or even without any fixed temporal relationship. Figure 3 gives one example for this effect that has been observed both for the synchrony within (Gray et al., 1989; Engel et al., 1991c; Freiwald et al., 1995) as well as across visual areas (Engel et al., 1991b). The experiments demonstrate that gestalt criteria such as continuity or coherent motion, which have been shown to support scene segmentation psychophysically, are important for the establishment of synchrony among neurons in the visual cortex. These data provide strong support for the hypothesis that correlated firing could provide a dynamic mechanism which permits binding and response selection in a flexible manner.

Studies performed in the visual system of other species suggest that the results obtained in the cat may be generalized.

Figure 3. Stimulus-dependence of long-range synchronization in the visual cortex. Data are from an experiment in which neuronal responses were recorded from two sites separated by 7 mm in the primary visual cortex of an anaesthetized cat. (A, C) Schematic plots of the receptive fields. At both recording sites the cells preferred vertical orientations. The colinear arrangement of the fields allowed the comparison of different stimulus paradigms. The neurons were activated with either a long continuous light bar moving across both fields (A) or two light bars moving in opposite directions (C). (B, D) The respective cross-correlograms obtained with each stimulus paradigm. Using the long light bar, the two responses were synchronized as indicated by the strong modulation of the correlogram (B). Synchrony disappeared with the two incoherently moving stimuli (D); n.s., not significant. The graph superimposed on the correlogram in (B) represents a damped cosine function that was fitted to the data to assess the strength of the modulation. (Modified from Engel et al., 1992.)
Neuronal synchronization with similar characteristics has been observed in the visual system of non-mammalian species as different as pigeon (Neuenschwander et al., 1996) or turtle (Prechtl, 1994). Of particular relevance is the demonstration of comparable synchronization phenomena in the visual system of primates. In monkeys, precise synchronization of spatially separate neurons has been demonstrated within both striate and extrastriate cortex (Ts’o and Gilbert, 1988; Kreiter and Singer, 1992; Friedman-Hill et al., 1995; Livingstone, 1996). In addition, correlated firing has been reported to occur between neurons of different visual areas (Roe and Ts’o, 1992; Frien et al., 1994; Salin and Bullier, 1995). Moreover, the stimulus-dependence of neuronal interactions has recently been confirmed in anaesthetized (Livingstone, 1996) and awake monkeys (Kreiter and Singer, 1996). Finally, EEG studies have provided evidence for precise synchronization in human visual cortex that is related to perception and reflects the subjective coherence of stimulus arrangements (Tallon et al., 1995; Tallon-Baudry et al., 1996). Taken together, these studies suggest that a temporal binding mechanism might be a general operating principle in the visual system of higher vertebrates.

Evidence for the Functional Relevance of Synchronization

Although the temporal binding model offers an attractive conceptual scheme for understanding the integration of distributed neuronal responses, definitive evidence that the brain actually uses synchronization in exactly this way has not yet been obtained. The first hint that neuronal synchronization might indeed be functionally relevant and related to the animal’s perception was provided by experiments on cats with divergent squint (König et al., 1993). Typically, humans and animals with a divergent strabismus develop a pattern of alternating fixation with the two eyes. Usually, monocular vision is undisturbed in these subjects, but they show a striking inability to combine information arriving simultaneously through the two eyes into a single percept. In animals with this malfunction, the perceptual deficit is accompanied by a loss of synchronization between neurons that receive information from different eyes (König et al., 1993). This correspondence between a functional deficit and loss of neuronal interaction argues for the importance of correlated neuronal firing in normal visual perception.

Further evidence for the functional relevance of synchrony among cortical neurons comes from a more recent correlation study in cats with convergent squint (Roelfsema et al., 1994). Unlike subjects with a divergent strabismus, convergent squinters often use only one eye for fixation. The non-fixating eye then develops a syndrome of perceptual deficits called strabismic amblyopia. Symptoms of strabismic amblyopia include a reduced acuity of the affected eye, temporal instability and spatial distortions of the visual image, and the so-called crowding phenomenon, i.e. the fact that discrimination of details deteriorates further if other contours are nearby. Clearly, at least some of these deficits indicate a reduced capacity of integrating visual information and an impairment of the mechanisms responsible for feature binding. The results of the correlation study by Roelfsema et al. (1994) indicate that these perceptual deficits may be due to a disturbance of intracortical interactions. As illustrated in Figure 4, clear differences can be observed in the synchronization of cells driven by the normal and the amblyopic eye respectively. Visually evoked responses of neurons activated through the amblyopic eye showed a much weaker correlation than the discharges of neurons driven by the normal eye. In addition, synchronization between neurons dominated by different eyes was virtually absent, confirming the results that had been obtained in cats with divergent squint.
further joint processing, permitting the selected responses to align. A striking observation made in many of the correlation studies is the reduction of synchronicity in the neuronal responses driven by the normal and amblyopic eye. Gray and Viana Di Prisco (1997) observed that synchronization is employed for feature binding and serves to disambiguate distributed response patterns.

Direct evidence for a relation between neural synchronization and perception comes from recent experiments in which neuronal responses were recorded from the visual cortex of strabismic cats under conditions of binocular rivalry (Fries et al., 1996). In contrast to the two studies mentioned above, these measurements were performed in awake animals with chronically implanted wire electrodes. The animals were subjected to dichoptic visual stimulation, i.e. different moving patterns were simultaneously presented to the left and the right eye. Under these conditions, rivalry occurs between the two stimuli and thus only one eye contributes to perception at a given moment (the dominant eye), the information arriving through the other eye (the suppressed eye) being excluded from perceptual experience and behavioural control. The experiments carried out with this experimental paradigm (Fries et al., 1996) show that visual cortical neurons driven by the dominant and the suppressed eye, respectively, do not differ in either the strength or the synchronicity of their response to monocular visual stimulation. They show, however, striking differences with respect to their synchronization behaviour when exposed to the rivalry condition. As illustrated in Figure 5, neurons representing the stimulus that wins in rivalry and is perceived increase their synchrony, whereas cells processing the suppressed visual pattern decrease their temporal correlation. However, no differences were noted under the rivalry condition for the discharge rates of cells responding to the dominant and the suppressed eye, respectively. We consider these data as direct support for the hypothesis that synchronization is used to select, among a large number of equally strong neuronal responses, a subset (in this case the responses of the dominant eye) for further joint processing, permitting the selected responses to control behaviour and contribute to perception.

**Significance of Oscillatory Firing Patterns**

A striking observation made in many of the correlation studies described above is the emergence of synchronized states in the cortex that are frequently associated with oscillatory firing patterns of the respective neurons (Eckhorn et al., 1988; Gray et al., 1989; Engel et al., 1990, 1991a–c; Kreiter and Singer, 1992, 1996; König et al., 1993, 1995; Fries et al., 1994; Roelfsema et al., 1994, 1997; Broch et al., 1995; Freiwald et al., 1995; Brecht and Engel, 1996; Brecht et al., 1996; Engel and Brecht, 1996; Fries et al., 1996; Gray and McCormick, 1996; Livingstone, 1996; Neusenschwander and Singer, 1996; Neusenschwander et al., 1996; Gray and Viana Di Prisco, 1997). These temporal patterns, which induce troughs and additional peaks in correlograms (Figs 2, 3 and 5), were first described in the visual system by Gray and Singer (1987, 1989). They observed that, with appropriate stimulation, neighbouring neurons tend to engage in grouped discharges which recur at frequencies in the gamma range between 30 and 80 Hz (Fig. 6).

In the preceding sections, we have argued that synchronous firing may serve for the dynamic binding and selection of distributed neuronal responses. This, then, raises the question of what role the oscillatory firing patterns might play as part of such a temporal binding mechanism. Recently, this issue has been the subject of substantial controversy. Whereas some authors have questioned the existence of stimulus-induced gamma oscillations altogether (Young et al., 1992), others have, while acknowledging this phenomenon, doubted its functional relevance and considered it as an epiphenomenal by-product of cortical processing (Ghose and Freeman, 1992; Tovée and Rolls, 1992). Presumably, this issue cannot be settled based on the currently available experimental evidence. However, in the following we will argue that an oscillatory temporal structure of
neuronal responses may well be relevant for interactions of distributed neurons and assembly formation.

Possible functional roles of oscillatory discharge have been explored in simulation studies that have investigated the interactions in networks of coupled oscillatory elements (Schuster and Wagner, 1990; König and Schillen, 1991; Wilson and Bower, 1991; Sompolinsky et al., 1991; von der Malsburg and Buhmann, 1992; Ritz et al., 1994; Bush and Sejnowski, 1996; Tass and Haken, 1996; Traub et al., 1996). Some of these studies indicate that an oscillatory modulation of neuronal responses may have crucial advantages for the establishment of precise synchrony between widely remote sites in the cortex, and thus may be instrumental as a 'carrier signal' for temporal binding in the brain (Engel et al., 1992, König et al., 1995). Recent evidence shows that response synchronization is mediated by connections at the cortical level and not by synchronously driving subcortical input (Engel et al., 1991a; König et al., 1993; Munk et al., 1995). Interestingly, interareal and interhemispheric interactions have consistently been observed to occur with near-zero phase lag (Engel et al., 1991a, b; Nelson et al., 1992; Frien et al., 1994; Roelfsema et al., 1997; cf. Figs 2 and 7), although the underlying cortico-cortical connections are known to exhibit considerable transmission delays. As suggested by simulation studies, the establishment of synchrony without phase lag may be facilitated under these conditions if the respective neurons show oscillatory firing patterns (Schuster and Wagner, 1990; König and Schillen, 1991; Sompolinsky et al., 1991). These models demonstrate that, due to the recurrent temporal structure of such patterns, reciprocally coupled neurons can entrain each other and improve synchrony within a few oscillatory bursts. Further advantages of oscillatory activity suggested by these models are that oscillating neurons can be synchronized via polysynaptic linkages without accumulation of small phase-lags and that synchrony in such networks is robust despite considerable spatial variation of the conduction delays.

If the predictions suggested by these modelling studies hold true, cortical long-range synchronization should be closely

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**Figure 6.** Example of an oscillatory response in cat primary visual cortex. (A) In this experiment, the activity of a small group of neurons was recorded by means of a low-impedance electrode. (B) By filtering in different bandpasses, a local field potential (top, positivity upward) and multiunit spike activity (bottom) can be extracted from the raw electrode signal. As a light bar is passed through the cells' receptive field a clear oscillatory response is observed in the field potential, indicating that the neurons of the recorded cluster have engaged in a coherent and rhythmic firing pattern. Note the variability of both amplitude and frequency. The multiunit recording shows directly that different neurons (as indicated by spikes of different sizes) synchronize their discharges into a burst-and-pause firing pattern. Note that the spike bursts are in phase with the peak negativity of the field potential.

**Figure 7.** Long-range synchronization is accompanied by oscillatory firing patterns. (A) Data are from an experiment in which one of the recording sites was located in the primary visual cortex (A 17), the other in extrastratine area PMLS. LAT, lateral sulcus; SUPS, suprasylvian sulcus. (B) The cells at the two recording sites had nonoverlapping receptive fields but their response properties were sufficiently similar to allow for coactivation with a single moving stimulus. In this case, a large number of trials were recorded using the same stimulus. C and D show data from two representative response epochs. (C) Example of a trial where both cell groups showed narrow-banded oscillations, as indicated by the presence of multiple peaks and troughs in the autocorrelograms (middle and bottom). This is reflected in a strong modulation of the corresponding cross-correlogram (top). (D) Example of a trial where no temporal correlation was evident in the cross-correlation function (top). The two autocorrelograms (middle and bottom) showed only a centre peak without significant satellite peaks. As in Figure 3, the continuous line superimposed on the correlograms represents a damped cosine function fitted to the data.
correlated with the occurrence of oscillatory activity. However, such a relation would not necessarily hold for synchrony between closely spaced cells, since these tend to be strongly coupled without major delays in the respective connections. Recently, physiological evidence has been obtained in support of this hypothesis (König et al., 1995). Indeed, the physiological data demonstrate a close relationship between long-range synchronisation and oscillatory firing patterns. If synchronization occurs over large distances within striate cortex, between areas or across the hemispheres it is almost always accompanied by oscillatory response patterns (Fig. 7). In contrast, short-range interactions can occur both with and without oscillatory modulation of the responses. These data support the hypothesis that oscillatory firing patterns may facilitate the establishment of precise synchrony between widely separate neuronal populations in the brain (Engel et al., 1992; König et al., 1995). If so, these oscillatory discharge patterns may actually be a prerequisite for the binding of distributed neurons into assemblies and for the buildup of coherent representational states.

Implications for Visual Information Processing
The key assumption of the temporal binding model is that time constitutes an important variable for neural information processing. The evidence reviewed above suggests that synchrony is not a mere epiphenomenon of cortical circuitry as assumed in classical cross-correlation analysis. Rather, temporal correlations seem to reflect a dynamic coupling of distributed neurons which is causally efficacious in the system and serves for the integration and selection of coherent chunks of perceptual information. In the following, we will briefly highlight a number of implications that this model has for current views on sensory processing.

One interesting aspect of the temporal binding hypothesis is that it implies a firmly holistic view of the architecture of the visual system. The representational code implemented by synchrony is strictly relational: the activity of individual neurons — considered in isolation — has a rather limited causal efficacy, because the functional significance of a neuron depends on the context set by the other members of the assembly. In this sense, processing has ‘gestalt-quality’. This holistic stance, which converges with classical gestalt psychological notions (Köhler, 1930), is incompatible with the atomistic framework that emphasizes the single neuron as the relevant level of description (Barlow, 1972) — an idea pervading many of the contemporary views on sensory information processing.

Moreover, the temporal binding model conflicts with the now-classical assumption that the visual cortex is characterized by a strictly modular architecture comprising independent processing pathways (Livingstone and Hubel, 1988). Rather, the temporal binding hypothesis predicts strong interactions across different streams at all levels of visual processing. The interareal interactions reviewed above suggest that, at least in the cat, neurons in different processing pathways can, in principle, be tied into the same assembly (Eckhorn et al., 1988; Engel et al., 1991b; Nelson et al., 1992). For the primate visual system we are still lacking the experimental proof of synchrony between areas that are part of different processing pathways. However, according to the temporal binding model, synchrony across processing streams should also be observed in primates (in accordance with known anatomical cross-talk) which then would serve for the binding of different classes of features (Engel et al., 1992; Tononi et al., 1992; Singer and Gray, 1995).

In this context, it is of interest that some of the findings on temporal binding argue against the notion that the visual pathways are organized as a strictly serial hierarchy and that processing is predominantly feed-forward (Hubel and Wiesel, 1965; Livingstone and Hubel, 1988; Thorpe et al., 1996). For example, temporal correlations have recently been found between monkey primary (V1) and secondary (V2) visual cortex (Frien et al., 1994; Salin and Bullier, 1995). As in the case of intra-areal interactions, synchrony between these two areas occurs, on average, with zero phase lag. This finding suggests a parallel activation of V1 and V2 neurons rather than a serial-hierarchical transfer of information. Similar observations have been made in the cat, where areas 17, 18 and PMLS can show zero-phase synchrony (Eckhorn et al., 1988; Engel et al., 1991b; Nelson et al., 1992). Results of this kind, together with numerous additional anatomical and physiological data, suggest that the visual system may be organized in much more parallel fashion than assumed previously (for review see Bullier and Nowak, 1995).

We wish to emphasize that the temporal binding hypothesis is fully compatible with the idea that ‘top-down’ influences (such as, for instance, attentional mechanisms) play an important role for visual processing and perceptual integration (Treisman, 1986, 1996). This aspect has largely been neglected in some of the more classical approaches which have elaborated mainly on the ‘bottom-up’ components of perceptual function (Barlow, 1972; Marr, 1982). In a recent study (Munk et al., 1996) it was shown that stimulus-induced synchrony in visual cortex is not fully determined by the peripheral stimulus and by the binding criteria implemented in the architecture of the respective visual area. Rather, the experiments demonstrated a profound influence of central modulatory systems which participate in the control of arousal and attention. Similarly, recent measurements in awake behaving cats suggest that precise temporal correlation between cortical cell populations depends on the behavioural situation the animal is engaged in and is observed only in episodes during which attentive processing of sensory information occurs (Roelfsema et al., 1997). These studies are compatible with the notion that temporal relationships among visual cortical neurons are induced in a ‘bottom-up’ manner, but are subject to ‘top-down’ modulation by contextual and attentional influences.

Finally, we would like to mention some implications for the modeling of perceptual and other cognitive processes in connectionist approaches (Rumelhart et al., 1986; McClelland et al., 1986). By making time available as an additional coding dimension, the binding mechanism suggested here enables the expression of specific relationships, and thus the endowment of neuronal activity patterns with a complex internal structure. In the current debate about the implementation of representational states in connectionist models it has been pointed out that a combinatorial or ‘syntactic’ structure of internal states is required to encode complex objects and to represent conjunctions of facts or events in the network (Fodor and Pylyshyn, 1988). Fodor and Pylyshyn have argued that connectionist models could not, on principle, account for the productivity and systematicity of cognitive processes if average firing rates or activation levels serve as the only coding dimension in such networks. This problem can be settled by temporal binding because appropriate synchronization can establish specific relations among the constituents of neural representations. If endowed with such a combinatorial code, connectionist models could — at reasonable costs — account for
productivity (i.e. the capacity of generating, in principle, infinitely many representational states by changing the relations between finite sets of neurons) and systematicity (i.e. the association of the capacity for representing particular feature constellations with the potential for representing different combinations of the same features).

**A General Mechanism for Integration and Response Selection**

In this paper we have reviewed experimental evidence suggesting the existence of a temporal binding mechanism. The available data support the hypothesis that correlated firing may be functionally relevant in the brain for the binding of distributed neurons into coherently active assemblies and the dynamic selection of their responses for joint processing. Moreover, the results suggest that oscillatory firing patterns with frequencies in the gamma range may be instrumental as carrier signals for the establishment of synchrony. So far, we have restricted our discussion to evidence obtained in the visual system. However, binding problems similar to those described here for vision have to be coped with by other systems as well. The problem of visual feature integration just exemplifies a much more general problem of integration that always occurs in neuronal networks operating on the basis of ‘coarse coding’ and distributed representation (Sejnowski, 1986; Damasio, 1990).

Since information processing in other sensory modalities and in the motor system is also highly parallel (Kandel and Jessell, 1991; Kelly, 1991; Kaas and Crammond, 1992; Georgopoulos, 1995), the needs to organize and bind distributed responses are similar to those encountered in the visual system. Furthermore, information must be flexibly coordinated both across sensory modalities and between sensory and motor processes in order to allow for adaptive behaviour of the organism. The hypothesis pursued here predicts, therefore, that temporal binding mechanisms should exist in other cortical systems and, moreover, that synchrony should occur between different systems.

Indeed, several recent findings suggest that the temporal binding model can be generalized to other functional neural systems. Studies in non-visual sensory modalities and in the motor system indicate that synchrony and oscillatory activity may actually be quite ubiquitous in the nervous system. Synchronization with prevalence of the gamma frequency range is well known to occur in the olfactory system of various vertebrate and invertebrate species, where these phenomena have been related to the processing of odour information (Freeman, 1988; Laurent, 1996). In the auditory cortex, synchronized gamma oscillations have been described by several groups. In humans, these phenomena have been observed with EEG and MEG (magneto-encephalographic) techniques (Galambos et al., 1981; Madler et al., 1991; Pantel et al., 1991; Joliot et al., 1994). In addition, temporal correlations in auditory cortex have been observed in animal experiments (Frigermont, 1992; deCharms and Merzenich, 1996). In the somatosensory system, synchronized oscillatory firing has recently been described in rats (Nicolelis et al., 1995), cats (Sternade et al., 1996) and monkeys (Murthy and Fetz, 1992, 1996a,b). Furthermore, such rhythmic interactions have been observed in the hippocampus (Bragin et al., 1995; Buzsáki and Chrobak, 1995).

Similar evidence is available for the motor system, where neural synchronization in the gamma frequency range has been discovered in cats (Sternade et al., 1996), monkeys (Murthy and Fetz, 1992, 1996a,b; Sanes and Donoghue, 1993) and humans (Kristeva-Feige et al., 1995). It is interesting to relate these findings to the dynamics of so-called central pattern generators,
i.e. networks of coupled oscillators found in the spinal cord of vertebrates and in the nervous system of invertebrates which are involved in the execution of basic motor programmes (Grillner et al., 1991). Although the frequency of rhythmic activity is far below the gamma range in these systems, the principles of pattern generation appear similar. The same sets of neurons can be used to generate a large diversity of different patterns by changing the coupling strength among oscillatory modules and by modulating oscillation frequencies.

Remarkably, there is evidence suggesting that synchrony may also play a role for sensorimotor integration. In monkeys, synchronization between sensory and motor cortical areas has been reported (Murthy and Fetz, 1992, 1996a,b; Bressler et al., 1993). Similar results have been obtained in a recent study on awake behaving cats that were trained to perform a visuomotor coordination task (Fig. 8; Roelfsema et al., 1997). In these animals, neural activity was recorded with electrodes chronically implanted in various areas of the visual, parietal and motor cortex. The results of this study show that synchronization of neural responses occurs not only within the visual system, but also between visual and parietal areas as well as between parietal and motor cortex. Moreover, the interareal interactions changed dramatically in different behavioural situations (Fig. 8). Both findings suggest that synchrony may indeed be relevant for visuomotor coordination and may serve for the linkage of sensory and motor aspects of behaviour. The specificity of such interactions might allow, for instance, the selective channelling of sensory information to different motor programmes which are executed concurrently (Roelfsema et al., 1996).

These sensorimotor interactions observed at the cortical level provide one example of how motor systems could ‘read’ the information carried by sensory assemblies. Another important mechanism for ‘readout’ could be provided by interaction of cortical assemblies with subcortical integrative structures such as the superior colliculus. This possibility is suggested by the fact that neurons in visual cortical areas can also synchronize, via the corticotectal pathway, with cells in the superficial layers of the colliculus (Brecht and Engel, 1996; Brecht et al., 1996; Engel and Brecht, 1996). As illustrated in Figure 9, correlation analysis has demonstrated the existence of precise temporal relationships between cortex and colliculus in the cat. In these experiments, it could be shown that corticotectal interactions are strongly dependent on the temporal coherence of cortical activity. This finding is consistent with the idea that the temporal organization of activity patterns determines the output of the visual cortex. Further studies are underway to clarify the role of synchrony for the selection of targets during orienting responses of the animal, which are mediated by the superior colliculus.

Taken together, the available studies suggest that comparable synchronization phenomena are found in a large number of different functional systems. Thus, it seems justified to generalize the results obtained in the visual cortex and to suggest that temporal coordination of discharges may be of general relevance for neural information processing. Importantly, there is increasing evidence that dynamic synchronization, in
particular at frequencies in the gamma band, occurs also in the human brain. Yet, it must be kept in mind that for most of the functional systems the available data demonstrate merely the presence of synchronized neural activity whereby the relationship with behaviour is not always evident or even sought after. To prove that these temporal patterns do indeed serve for binding and response selection, data are required that establish causal relations between the occurrence of synchrony and perceptual or behavioural task. Ideally, one would like to manipulate selectively the synchronizing mechanisms without disturbing other functions. For most of the systems discussed here it is not, at present, obvious how this can be achieved (but see MacLeod and Laurent, 1996). Current experimental efforts therefore focus on close and, if possible, predictable correlations between neural synchrony and perceptual or behavioural context (Abeles et al., 1993; Bressler et al., 1993; Vaadia et al., 1995; Chiang et al., 1996; Fries et al., 1996; Murthy and Fetz, 1996a; Roelfsema et al., 1997).

Notes

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