TARGET ARTICLE

Temporal Binding, Binocular Rivalry, and Consciousness

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Cognitive functions like perception, memory, language, or consciousness are based on highly parallel and distributed information processing by the brain. One of the major unresolved questions is how information can be integrated and how coherent representational states can be established in the distributed neuronal systems subserving these functions. It has been suggested 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 behaviorally relevant information. As we intend to show here, this temporal binding hypothesis has implications for the search of the neural correlate of consciousness. We review experimental results, mainly obtained in the visual system, which support the notion of temporal binding. In particular, we discuss recent experiments on the neural mechanisms of binocular rivalry which suggest that appropriate synchronization among cortical neurons may be one of the necessary conditions for the buildup of perceptual states and awareness of sensory stimuli.   © 1999 Academic Press

INTRODUCTION

This paper intends to contribute to the ongoing debate about the neural correlate(s) of consciousness from the viewpoint of a particular experimental approach: the study of distributed neuronal processing and of dynamic interactions which implement specific ''bindings'' in neural network architectures. The now-classical notion of binding and the search for potential binding mechanisms has received increasing attention during the past decade. Having been introduced first in the psychological discourse (for review, see Treisman, 1986, 1996), the issue of binding has now advanced also into the focus of research in other disciplines within cognitive science such as neural network modeling (e.g., Hinton, McClelland, & Rumelhart, 1986; Smolensky, 1990; Hummel & Biederman, 1992; Schillen & König, 1994), philosophy of mind (e.g., Fodor & Pylyshyn, 1988; van Gelder, 1990; Fodor & McLaughlin, 1990), and cognitive neuroscience (e.g., von der Malsburg, 1981, 1995; Crick, 1984; Sejnowski, 1986;

Damasio, 1990; Engel, König, Kreiter, Schillen, & Singer, 1992; Engel, Roelfsema, Fries, Brecht, & Singer, 1997; Singer, 1993; Singer & Gray, 1995; Roelfsema, Engel, König, & Singer, 1996).

In all these domains, the problem has been identified that encoding and retrieval of information in neuronal networks requires some sort of binding mechanism which allows the expression of specific relationships between elementary processors. This ''binding problem'' arises for several reasons: First, information processing underlying cognitive functions is typically distributed across many network elements and, thus, one needs to identify those neurons or network nodes that currently participate in the same cognitive process (Hinton et al., 1986). Second, perception of and action in a complex environment usually require the parallel processing of information related to different objects or events that have to be kept apart to allow sensory segmentation and goal-directed behavior. Thus, neuronal activity pertaining, e.g., to a particular object needs to be distinguished from unrelated information in order to avoid confusion and erroneous conjunctions (von der Malsburg, 1981). Third, it has been claimed that specific yet flexible binding is required within distributed activation patterns to allow the generation of syntactic structures and to account for the systematicity and productivity of cognitive processes (Fodor & Pylyshyn, 1988). Fourth, many cognitive functions imply the context-dependent selection of relevant information from a richer set of available data. It has been suggested that appropriate binding may be a prerequisite for the selection and further joint processing of subsets of information (Singer & Gray, 1995; Singer, Engel, Kreiter, Munk, Neuenschwander, & Roelfsema, 1997). These arguments suggest that cognitive functions require the implementation of binding mechanisms in the distributed networks subserving these functions.

In what follows, we want to focus on the idea that some kind of binding mechanism may also be critical for the establishment of conscious mental states. In recent years, several authors have emphasized a close link between binding and consciousness, following the intuition that consciousness requires some kind of integration, or coherence, of mental contents (von der Malsburg, 1997). Damasio (1990) has suggested that conscious recall of memory contents requires the binding of distributed information stored in spatially separate cortical areas. In various publications, Crick and Koch have discussed the idea that binding may be intimately related to the neural mechanisms of sensory awareness (Crick & Koch, 1990a,b; Koch & Crick, 1994; Crick, 1994). According to their view, only appropriately bound neuronal activity can enter short-term memory and, hence, become available for access to phenomenal consciousness. Llinas, Ribary, Joliot, and Wand (1994) have proposed that arousal and awareness require binding of sensory information which is implemented by interactions between specific and nonspecific thalamocortical loops. Recently, Metzinger (1995) has extended this discussion by speculating that binding mechanisms might not only account for low-level properties of phenomenal consciousness like the holistic character of perceptual objects, but also for the formation of a phenomenal self-model and its embedding into a global world model. Pöppel (1997) has suggested that binding is required for conscious time perception and establishment of subjective time frames.

Our discussion of the consciousness issue will be restricted to one particular aspect,

namely, sensory awareness. With many authors, we share the view that sensory awareness is one of those facets of consciousness that is (probably) most easily accessible both in terms of experimental quantification and theoretical explanation (Crick & Koch, 1990a; Farber & Churchland, 1995). Furthermore, there can be little doubt that we have this basic form of phenomenal consciousness in common with many other species (presumably with at least most other higher mammals). Thus, it is conceivable that research on animals can contribute substantially to explaining this aspect of consciousness, which may not hold for many higher order features of consciousness which, for instance, require a language system or an elaborated self-model.

There seems to be wide agreement that awareness as the basic form of phenomenal consciousness has the following prerequisites: First, generating sensory awareness seems to involve some form of attentional mechanism, i.e., a mechanism that selects relevant information and enhances its impact on subsequent processing stages (Crick & Koch, 1990a; Newman & Baars, 1993; Crick, 1994; Desimone & Duncan, 1995). Second, awareness presumably requires working memory, which allows the short-term storage of episodic contents (Goldman-Rakic, 1992; Moscovitch, 1995). Third, awareness seems to presuppose the capacity for structured representation, i.e., the ability to achieve coherence of the contents of mental states and to establish specific relationships between representational items. Our basic assumption is that all three capacities are, on the one hand, closely related to each other and, on the other hand, strongly dependent on binding mechanisms implemented in sensory systems. This is probably most obvious for the third capacity mentioned, the establishment of coherence in mental states. As will be further disussed below, attentional selection may also depend on appropriate binding of neuronal responses. Similarly, there is evidence that binding is important for inducing changes of synaptic efficacy and hence for the transfer of information into memory structures (for review, see Singer, 1993). With these issues in mind, we will discuss one particular candidate mechanism, namely, dynamic binding by transient and precise synchronization of neuronal discharges. As we will argue, there is now empirical evidence suggesting that such ''temporal binding'' may be crucial for generating functionally efficacious representational states and for the selection of perceptually or behaviorally relevant information.

THE CONCEPT OF TEMPORAL BINDING

The concept of dynamic binding by synchronization of neuronal discharges has been developed mainly in the context of perceptual processing. One source of inspiration for this model has come from the insight that perception, like most other cognitive functions, is based on highly parallel information processing carried out by numerous brain areas. A paradigmatic case is provided by visual processing, which shows a highly distributed organization (Livingstone & Hubel, 1988; Zeki & Shipp, 1988; Felleman & Van Essen, 1991). In monkeys, anatomical and physiological studies have led to the identification of more than 30 distinct visual areas in the cortex. This parcellation is assumed to reflect some kind of functional specialization since neurons in each of these visual areas are, at least to some degree, selective for charac-
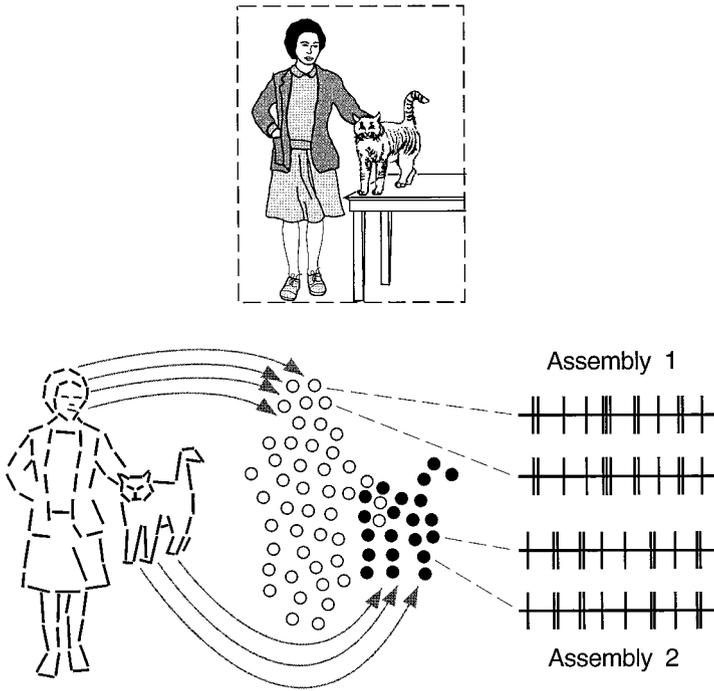
FIG. 1. Establishment of coherent representational states by temporal binding. The model assumes that objects are represented in the visual cortex by assemblies of synchronously firing neurons. In this example, the lady and her cat would each be represented by one such assembly (indicated by open and filled symbols, respectively). These assemblies comprise neurons which detect specific features of visual objects (such as, for instance, the orientation of contour segments) within their receptive fields (lower left). The relationship between the features can then be encoded by the temporal correlation among these neurons (lower right). The model assumes that neurons which are part of the same assembly fire in synchrony, whereas no consistent temporal relation is found between cells belonging to different object representations. Reproduced with permission from the publisher from Engel et al., 1997.

teristic subsets of object features. Thus, for instance, some areas contain cells responding to the color of objects, while others primarily process information about the form of an object or its direction of motion in the visual field. As a consequence of this functional specialization, any object present in the field of view will activate neurons in many cortical areas simultaneously. The highly complex organization of visual processing naturally raises the question of how distributed neuronal responses can be integrated, which seems necessary to enable the brain to represent and store information about the external world in a useful way.

It has been suggested that the binding problem arising in distributed sensory networks may be solved by a mechanism which exploits the temporal aspects of neuronal activity (von der Malsburg, 1981, 1995; for review, see Engel et al., 1992, 1997; Singer, 1993; Singer & Gray, 1995; Singer et al., 1997). The prediction is that neurons which respond to the same sensory object might fire their action potentials in temporal synchrony with a precision in the millisecond range (Fig. 1). However, no such syn-

chronization should occur between cells which are activated by different objects appearing in sensory space. Such a temporal integration mechanism would provide an elegant solution to the binding problem since, on the one hand, the synchrony would selectively tag the responses of neurons that code for the same object and demarcate their responses from those of neurons activated by other objects. This highly selective temporal structure would make it possible to establish a distinct representational pattern (a so-called assembly) for each object and, thus, would enable the visual system to achieve figure–ground segregation. On the other hand, such a temporal binding mechanism could also serve to establish relationships between neuronal responses over large distances and, thus, solve the problems imposed by the anatomical segregation of specialized processing areas.

This strategy of temporal binding exhibits a number of crucial advantages. First, it preserves the general advantages of distributed coding schemes such as robustness against loss of network elements and ''richness'' of representations which contain explicit information about object features and do not just signal the presence of the object (like a small set of ''cardinal cells'' would do; cf. Barlow, 1972). Second, this strategy enhances processing speed because binding can, in principle, occur using the very first spikes of a response (Singer et al., 1997; Fries, Roelfsema, Singer, & Engel, 1997a). Third, temporal binding alleviates superposition problems that occur in conventional distributed systems that operate solely on the basis of average firing rates (von der Malsburg, 1981). The reason is that using synchrony as an additional coding dimension allows the dissociation of the binding code from the feature code (object features being signaled by firing rates). This allows coactivation of multiple assemblies without confusion, because the temporal relationship between neuronal discharges permits the unambiguous distinction of subsets of functionally related responses. Fourth, temporal binding provides an efficient mechanism for selection of assemblies for further processing (Singer & Gray, 1995; Singer et al., 1997), because precisely synchronized spikes constitute highly salient events which can be detected by coincidence-sensitive neurons in other brain areas (Abeles, 1982; König, Engel, & Singer, 1996; Alonso, Usrey, & Reid, 1996).

It should be noted at this point that, although the temporal binding model has mainly been elaborated with respect to the visual modality, it can be generalized because binding problems similar to those described here for vision have to be coped with by other systems as well. Obviously, the problem of perceptual 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, 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 behavior of the organism (Roelfsema, Engel, König, & Singer, 1996). The hypothesis pursued here predicts, therefore, that temporal binding mechanisms should exist not only in the visual system, but in other cortical systems as well and, moreover, that synchrony should occur between different systems.

In the present context, the most radical extension of the concept of temporal bind-

ing has been its application to the issue of consciousness by Crick and Koch. As has been mentioned already, they have argued for a close relationship between binding and sensory awareness (Crick & Koch, 1990a,b). Beyond that, they were the first to suggest that a temporal binding mechanism of precisely the kind discussed here could be required for the establishment of awareness. Inspired by the finding that visual stimuli can elicit synchronized oscillatory activity in the visual cortex (Eckhorn, Bauer, Jordan, Brosch, Kruse, Munk, & Reitboeck, 1988; Gray & Singer, 1989; Gray, König, Engel, & Singer, 1989; Engel, König, Gray, & Singer, 1990), they proposed that an attentional mechanism could induce synchronous oscillations in selected neuronal populations and that this temporal structure would facilitate transfer of the encoded information to working memory. The provocative scent of this hypothesis comes from the authors' implicit assumption that these are not just necessary, but indeed sufficient conditions for the occurrence of awareness. At the time it was published, Crick and Koch's speculative proposal was not supported by experimental evidence. In the present contribution, we will discuss more recent results which suggest that temporal binding may indeed be a prerequisite for the access of information to phenomenal consciousness. However, although largely in line with Crick and Koch's hypothesis, the present data do not seem to support the conclusion that synchronization of assemblies would constitute a *sufficient* condition for production of awareness.

EVIDENCE FOR TEMPORAL BINDING

By now, the synchronization phenomena predicted by the temporal binding hypothesis are well documented for a wide variety of neural systems. It is well established that neurons in both cortical and subcortical centers can synchronize their discharges with a precision in the millisecond range (for review, see Engel et al., 1992, 1997; Singer, 1993; Singer & Gray, 1995; König & Engel, 1995; Singer et al., 1997). This has been demonstrated in particular for the visual system, but similar observations have been made for the other sensory systems, for the motor system, and for cortical association areas. In the following, we will focus on experimental data suggesting that the observed synchrony does indeed serve for the binding and selection of functionally related responses. These data have been obtained mainly in experiments on cats and monkeys, but presumably the results can be generalized to the human brain, where recent EEG and MEG studies have provided evidence for similar synchronization phenomena (see Sauve, this issue).

For the case of the visual system, the temporal binding model predicts a synchronization of spatially separate cells within individual visual areas to account for the integration of perceptual information across different locations in the visual field. In addition, synchrony should occur across large distances in the cortex to allow for binding between visual areas involved in the analysis of different object features. According to the temporal binding model, this would be required for the full representation of objects. Both predictions have been confirmed experimentally. In cats and monkeys (in both anesthetized and awake preparations) synchrony has been observed within striate and extrastriate visual areas (Ts'o et al., 1986; Ts'o & Gilbert, 1988; Eckhorn et al., 1988; Gray et al., 1989; Engel et al., 1990; Kreiter & Singer, 1992;

Brosch, Bauer, & Eckhorn, 1995; Livingstone, 1996; Gray & Viana Di Prisco, 1997). Moreover, it has been shown that response synchronization can extend well beyond the borders of a single visual area. Thus, for instance, correlated firing has been observed between neurons located in different cerebral hemispheres (Engel, König, Kreiter, & Singer, 1991a; Nowak, Munk, Nelson, James, & Bullier, 1995). 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 have been studied for neurons located in different areas of the same hemisphere (Eckhorn et al., 1988; Engel, Kreiter, König, & Singer, 1991b; Nelson, Salin, Munk, Arzi, & Bullier, 1992; Roe & Ts'o, 1992; Frien, Eckhorn, Bauer, Woelbern, & Kehr, 1994; Roelfsema et al., 1997). Finally, recent evidence shows that synchronous firing is not confined to the cortex but occurs also in subcortical visual structures such as the retina, the lateral geniculate nucleus, and the superior colliculus (Meister, Lagnado, & Baylor, 1995; Neuenschwander & Singer, 1996; Alonso et al., 1996; Brecht, Singer, & Engel, 1996; Brecht, Singer, & Engel, 1998). It is important to note that, at the cortical and subcortical levels, synchrony can be both internally generated (non-stimulus-locked) and externally imposed (stimulus-locked). Most of the studies cited above have focused on the former type, which occurs predominantly with smoothly changing stimuli or during tonic response phases and is generated by lateral interactions within the respective structures (Engel et al., 1991a; Munk, Nowak, Nelson, & Bullier, 1995). In contrast, externally imposed synchrony is characterized by phase-locking to the stimulus, occurs in response to rapid stimulus transients (Kruse & Eckhorn, 1996; Rager & Singer, 1998), and is presumably mostly due to feed-forward signal flow from the periphery.

Studies in nonvisual sensory modalities and in the motor system have provided evidence for very similar synchronization phenomena. Synchronization 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 odor information (Freeman, 1988; Laurent, 1996). Moreover, in both the auditory (Eggermont, 1992; deCharms & Merzenich, 1996) and the somatosensory cortices (Murthy & Fetz, 1992; Nicolelis, Baccala, Lin, & Chapin, 1995; Steriade, Amzica, & Contreras, 1996) precise neuronal synchronization has been observed. Furthermore, neuronal interactions with a precision in the millisecond range have been described in the hippocampus (Bragin, Jandó, Nádasdy, Hetke, Wise, & Buzsáki, 1995; Buzsáki & Chrobak, 1995) and in the frontal cortex (Abeles, Vaadia, Bergman, Prut, Haalman, & Slovin, 1993; Vaadia, Haalman, Abeles, Bergman, Prut, Slovin, & Aertsen, 1995). Finally, similar evidence is available for the motor system, where neural synchronization has been discovered during both preparation and execution of movements (Murthy & Fetz, 1992, 1996a,b; Sanes & Donoghue, 1993; Kristeva-Feige, Feige, Makeig, Ross, & Elbert, 1993; Riehle, Grün, Diesmann, & Aertsen, 1997).

Although the temporal binding model offers an attractive conceptual scheme for understanding the binding and selection of distributed neuronal responses, definitive evidence that the brain actually uses synchronization in exactly this way has not yet been obtained. However, a number of findings strongly suggest that the synchrony is indeed functionally relevant. One important result supporting the temporal binding

model is that neuronal synchronization in the visual system depends on the stimulus configuration. Thus, it could 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 moving in different directions, the cells fire in a less correlated manner or even without any fixed temporal relationship. This effect has been documented for the synchrony within (Gray et al., 1989; Engel, König, & Singer, 1991c; Freiwald, Kreiter, & Singer, 1995; Livingstone, 1996; Kreiter & Singer, 1996; Brosch, Bauer, & Eckhorn, 1997) as well as across visual areas (Engel et al., 1991b; Engel, König, Roelfsema, Munk, & Singer, 1995). Along the same lines, it has recently been shown that precise synchronization in striate cortex is weakened if textures composed of spatially discontinuous elements (moving random-dot patterns) are applied as stimuli, rather than patterns comprising continous contours (Engel, Fries, Goebel, & Neuenschwander, 1998). In such cases, precise neuronal synchronization disappears completely if the texture elements move incoherently (i.e., if the dot patterns contain substantial fractions of noise). Taken together, these experiments demonstrate that Gestalt criteria such as continuity or coherent motion, which have psychophysically been shown to support perceptual grouping, are important for the establishment of precise synchrony among neurons in the visual cortex. These data strongly support the hypothesis that correlated firing provides a dynamic mechanism for feature binding and response selection.

Additional evidence that neuronal synchronization is indeed functionally relevant and related to the animal's perception is provided by experiments on cats with convergent squint (Roelfsema, König, Engel, Sireteanu, & Singer, 1994). Subjects with this type of strabismus often use only one eye for active fixation. The nonfixating 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, 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 (Fig. 2). Thus, clear differences were observed in the synchronization of cells driven by the normal and the amblyopic eye, respectively. In the primary visual cortex, responses of neurons activated through the amblyopic eye showed a much weaker correlation than the discharges of neurons driven by the normal eye. Surprisingly, however, in terms of average firing rates the responses of neurons driven by the normal and the amblyopic eye were indistinguishable. These results indicate that strabismic amblyopia is accompanied by a selective impairment of intracortical interactions that synchronize neurons responding to coherent stimuli. As mentioned above, most of the problems in amblyopic vision result from an improper segregation of features and the formation of false conjunctions. Therefore, the fact that the only measurable abnormality correlating with the perceptual deficit was the reduced synchronicity is in good agreement with the hypothesis that synchronization is employed for feature binding and serves to disambiguate distributed response patterns.

Evidence for a functional role of neural synchrony is also provided by recent stud-
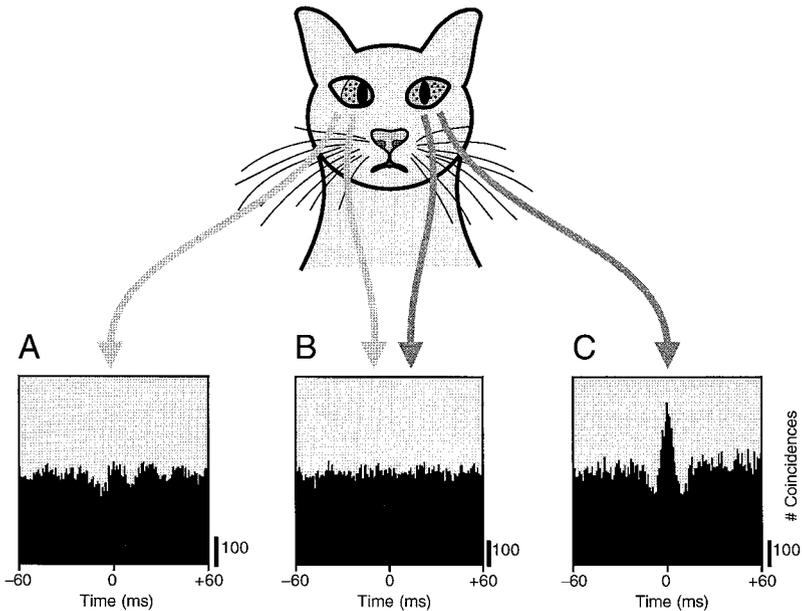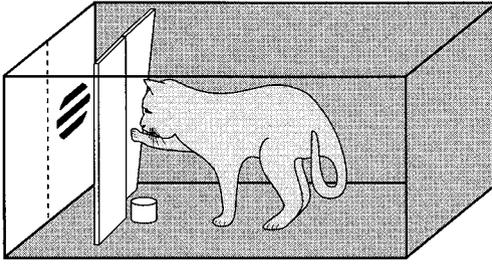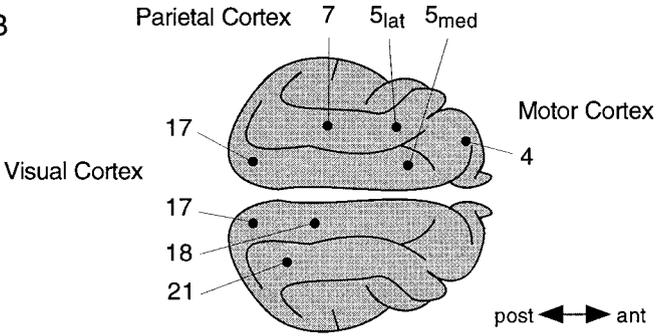
FIG. 2. Neuronal synchronization in the primary visual cortex of cats with strabismic ambylopia. The bottom panel shows examples of cross-correlograms between cells driven by the normal eye and by the amblyopic eye and between cells dominated by different eyes. Temporal correlation is strong if both recording sites are driven by the normal eye (C). Synchronization is, on average, much weaker between cells dominated by the amblyopic eye (A) and is in most cases negligible if the recording sites receive their input from different eyes (B) (modified from Roelfsema et al., 1994).

FIG. 3. Synchronization among visual, parietal, and motor cortices in awake behaving cats. Local field potentials were recorded with electrodes chronically implanted in several areas of the visual and parietal cortices as well as in the primary motor cortex. (A) The cats were situated unrestrained in a testing box and had to watch a screen through a transparent door. At the beginning of each trial, a grating was projected onto the screen. The cat had to respond by pressing the door with the forepaw and had to hold it until the grating was rotated. Upon change of the visual stimulus, the animal had to release the door. After correct trials, a reward was presented in a food well at the bottom of the box. (B) Location of the recording sites. Electrodes were implanted in areas 17, 18, and 21 of the visual cortex, in areas 5 and 7 of parietal cortex, and in area 4 of the motor cortex, where the forepaw is represented that the cat used for pressing the door. (C) Example of synchronization between areas 7 and 5 of the parietal cortex during the task period, i.e., the epoch where the cat was watching the grating and waiting for its rotation (left) and the reward period (right). The interactions are dependent on the behavioral context. Thus, during the task, zero-phase synchrony occurs between the areas. However, during the reward period the synchrony is lost and a large phase shift appears in the correlogram. (D) Summary of temporal correlation between the recorded areas during the task period. Thick lines indicate strong correlation (correlation coefficients larger than 0.10), and thin and hatched lines show weak, but still significant, interactions (correlation coefficients smaller than 0.10 or smaller than 0.05, respectively). Areas have been placed according to their position in the processing stream that links the visual cortex to the motor cortex. The diagram shows that precise synchrony is a global cortical phenomenon and is not restricted to the visual cortex (modified from Roelfsema et al., 1997).
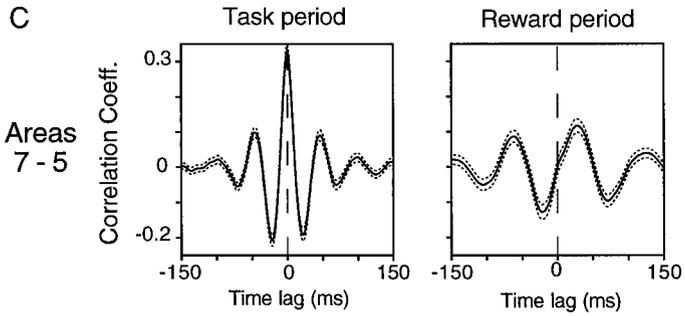
A

B

Parietal Cortex   7 5_{lat} 5_{med}

Motor Cortex

Visual Cortex

17

4

17

18

21

post ◄┈┈► ant

C

Task period

Reward period

Areas
7 - 5

Correlation Coeff.

0.3

0

-0.2

-150   0   150
Time lag (ms)

-150   0   150
Time lag (ms)
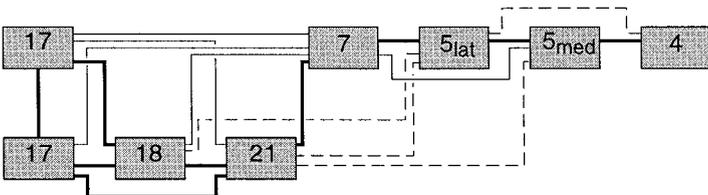
D

| 17 | | 7 | 5_{lat} | 5_{med} | 4 |

17   18   21

ies of sensorimotor interactions. Synchronization between sensory and motor assemblies has been investigated in a recent study on awake behaving cats that were trained to perform a visuomotor coordination task (Fig. 3) (Roelfsema et al., 1997). In these animals, neural activity was recorded with electrodes chronically implanted in various areas of the visual, parietal, and motor cortices. 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 cortices. Importantly, the interareal interactions changed dramatically in different behavioral situations. Precise neuronal synchronization between sensory and motor areas occurred specifically in those task epochs where the animal had to process visual information attentively to direct the required motor response. The observations of this study suggest that synchrony may indeed be relevant for visuomotor coordination and may serve for the linkage of sensory and motor aspects of behavior. The specificity of such interactions might allow, for instance, the selective channeling of sensory information to different motor programs which are concurrently executed (Roelfsema et al., 1996). Similar conclusions are suggested by recent studies in monkeys, where synchronization between sensory and motor cortical areas has also been reported (Murthy & Fetz, 1992, 1996a,b).

Complementing these animal experiments, supportive evidence for the notion of temporal binding comes from psychophysical studies in humans, where the role of external timing for buildup of coherent percepts has been investigated. Thus, it has been shown that small temporal offsets can induce figure–ground segregation (Leonards, Singer, & Fahle, 1996). As demonstrated in this study, a subset of elements in a flickered texture can be perceptually segregated if there is a temporal lag between figure and ground elements of more than 10 ms. Very similar effects of external timing on grouping of texture elements and on detection of colinear contours have recently been observed by Usher and Donnelly (1998). Moreover, it has been shown that perception of globally coherent motion is strongly enhanced if the contrast of stimulus components is synchronously modulated (Alais, Blake, & Lee, 1998). Finally, external timing can also enhance visual feature binding if the temporal cue is not present in the target display itself, but rather in a priming stimulus consisting of synchronously flickered figural elements (Elliott & Müller, 1998). In such cases, the detection of coherent features is facilitated in those locations where the synchronously flickered prime had been presented. The conclusion from these studies is that external timing cues can impose, via phase-locking of neuronal discharges to the respective stimulus transients, significant temporal structure on visual assemblies. Since the timing differences were on the order of 10–20 ms, these data clearly support the notion that sensory systems can exploit precise temporal structure (whether internally generated or externally imposed) for perceptual integration and the selection of coherent information. An important point is that in these experiments, the external timing cues leading to binding and figure–ground segregation *themselves* are usually not consciously perceived (Usher & Donnelly, 1998; Elliott & Müller, 1998).

BINDING AND PHENOMENAL CONSCIOUSNESS

The experimental data discussed in the preceding section clearly argue for the importance of precise neuronal synchrony in the establishment of coherent sensory

representations and for sensorimotor integration. Recent evidence indicates that these synchronization phenomena may also be relevant for the buildup of phenomenal states and the selection of visual information for access to awareness. This is suggested by experiments in which we recorded neuronal responses from the visual cortex of strabismic cats under conditions of binocular rivalry (Fries, Roelfsema, Engel, König, & Singer, 1997b). Binocular rivalry is a particularly interesting case of dynamic response selection which occurs when the images in the two eyes are incongruent and cannot be fused into a coherent percept. In this case, only signals from one of the two eyes are selected and perceived, whereas those from the other eye are suppressed (Blake, 1989). In normal subjects, perception alternates between the stimuli presented to the left and the right eye, respectively. The important point is that this shift in perceptual dominance can occur without any change of the physical stimulus. Obviously, this experimental situation is particularly revealing for the issue at stake, because neuronal responses to a given stimulus can be studied either with or without being accompanied by awareness (Crick & Koch, 1990a; Farber & Churchland, 1995), and thus there is a chance of revealing the mechanisms leading to the selection of perceptual information.

Previous studies have examined the hypothesis that response selection in binocular rivalry is achieved by a modulation of firing rate. In these experiments, a number of different visual cortical areas were recorded in awake monkeys experiencing binocular rivalry (Logothetis & Schall, 1989; Leopold & Logothetis, 1996; Sheinberg & Logothetis, 1997). With respect to early processing stages (visual areas V1, V2, V4, MT), the results of these investigations were not conclusive. The fraction of neurons that decreased their firing rates upon suppression of the stimulus to which they responded was about the same as the fraction of cells that increased their discharge rate, and altogether response amplitudes changed in less than 50% of the neurons when eye dominance switched (Logothetis & Schall, 1989; Leopold & Logothetis, 1996). A clear and positive correlation between firing rate and perception was found only in inferotemporal cortex, i.e., at a relatively late stage of visual processing (Sheinberg & Logothetis, 1997).

In our study (Fries et al., 1997b) we have investigated the hypothesis that response selection in early visual areas might be achieved by modulation of the synchronicity rather than the rate of discharges. These measurements were performed in awake cats with wire electrodes chronically implanted in areas 17 and 18 (Fig. 4). The animals were subjected to dichoptic visual stimulation, i.e., patterns moving in different directions were simultaneously presented to the left and the right eye, respectively. Perceptual dominance for a given set of stimuli was inferred from the direction of eye movements induced by the drifting gratings (the so-called optokinetic nystagmus) which were recorded by periorbital electrodes (during correlation measurements, however, precautions were taken to minimize eye movements; for details, see Fries et al., 1997b). As a baseline, neuronal responses were also recorded under monocular stimulation conditions. The results obtained with this experimental approach show that visual cortical neurons driven by the selected and the suppressed eye, respectively, differ neither in the strength nor in the synchronicity of their response to monocular visual stimulation. They show, however, striking differences with respect to their synchronization behavior when exposed to the rivalry condition.
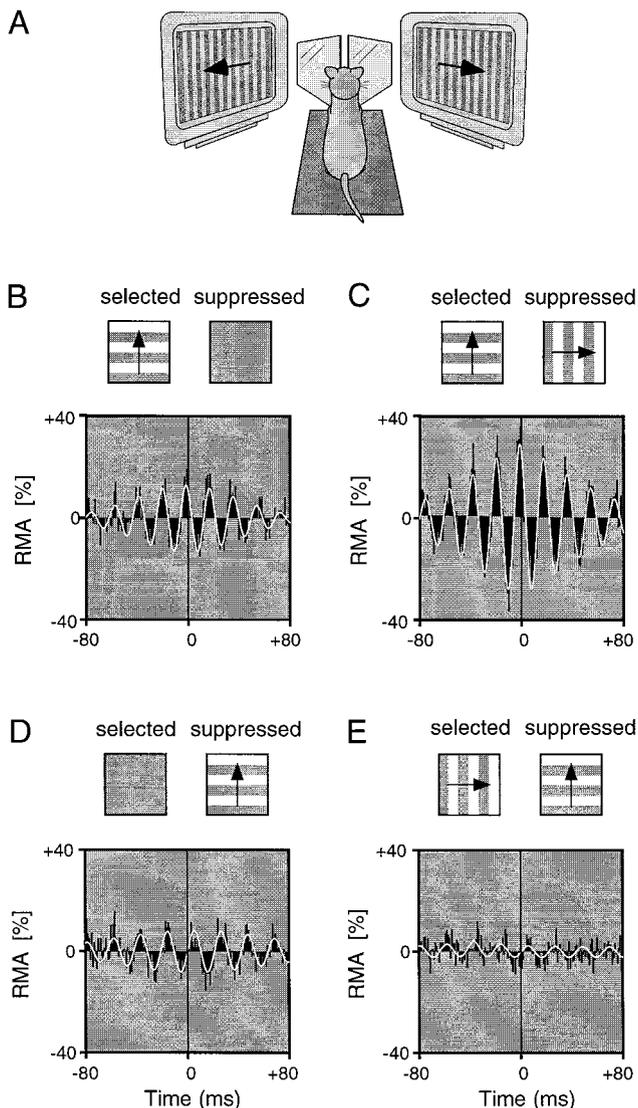
FIG. 4. Neuronal synchronization under binocular rivalry. (A) Cats were placed on a recording table and the head was fixed by means of an implanted bolt. In front of the animal's head two mirrors were mounted such that each eye was viewing a separate monitor. (B–E) Normalized cross-correlograms for two pairs of recording sites activated by the selected (B, C) and the suppressed eye (D, E), respectively. Insets above the correlograms indicate stimulation conditions. (B, C) Synchronization among neurons driven by the eye that is selected under rivalry conditions. Under monocular stimulation applied as a control (B), the cells showed a significant temporal correlation. Under rivalry conditions (C) these cells, which were representing the perceptually selected stimulus, increased their synchrony. (D, E) Correlation among cells driven by the nonperceived stimulus. In the monocular control condition (D), these neurons also showed significant synchronization. However, under dichoptic stimulation (E) the cells (which were responding to the suppressed stimulus) decreased their temporal correlation. The white continuous line superimposed on the correlograms represents a damped cosine function fitted to the data. RMA, relative modulation amplitude of the center peak in the correlogram, computed as the ratio of peak amplitude over offset of correlogram modulation (modified from Fries et al., 1997b).

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 selected and the suppressed eye, respectively.

These results show that, in areas 17 and 18 of awake, strabismic cats, dynamic selection and suppression of sensory signals are associated with modifications of the synchrony rather than the rate of neuronal discharges. This suggests that at an early level of visual processing, it is the degree of synchronicity rather than the amplitude of responses that determines which of the input signals will be processed further and then support perception and oculomotor responses. Changes in synchronicity at early stages of processing are bound to result in changes of discharge rate at later stages. Thus, the rate changes observed with perceptual rivalry in higher cortical areas (Sheinberg & Logothetis, 1997) could be secondary to modifications of neuronal synchronization at lower levels of processing. An interesting aspect of our results is that the synchronicity of responses representing the dominant stimulus even increased when the rivalry condition was introduced, suggesting the action of a mechanism that enhances the saliency of the selected responses. One possibility is that both the increase in synchronicity of the selected and the reduced synchronicity of the suppressed signals are due to local competition among the populations of neurons responding to the right and the left eye, respectively. However, it is also conceivable that attention-related top-down processes contribute to the selection of input signals by controlling their synchronicity. The possibility that attentional mechanisms act by modulating not only the rate but also the synchronicity of responses is supported by the evidence that neuronal synchronization increases during states characterized by arousal and focused attention (see next section).

In the present context, the important conclusion from these experiments is that only strongly synchronized neuronal responses can contribute to awareness and conscious phenomenal states. The data suggest that activation of feature-detecting cells is, as such, not sufficient to grant access to consciousness of the encoded information (note that the cells representing the suppressed stimulus are still responding well). Rather, to be functionally effective and to be selected for perception, neurons have to be strongly synchronized and bound into assemblies. In this respect, our data support the proposal by Crick and Koch (1990a,b) that neuronal synchronization may be a necessary condition for the occurrence of awareness. Admittedly, our conclusion rests on the assumption that sensory awareness of the stimulus correlates well with the oculomotor behavior that we have used as an indirect measure of the cat's perceptual state. However, this correspondence has been well established in humans, where a nearly perfect correlation has been found between the direction of the pursuit phase of the optokinetic nystagmus and the perceived direction of motion (Enoksson, 1963; Fox, Todd, & Bettinger, 1975), meaning that it is impossible, in the rivalry situation, to track one of the patterns with the eyes but consciously perceive the other.

At this point, we wish to add a brief comment on the issue of oscillations. As in many studies on correlated activity in the visual cortex, the synchrony observed in our rivalry experiments was associated with a strong oscillatory modulation of the responses at frequencies in the gamma range, i.e., between 30 and 80 Hz (Fries et

al., 1997b; for a review on gamma oscillations, see Engel et al., 1992, 1997; Singer & Gray, 1995). Under rivalry conditions, these oscillations show the same changes as the synchrony across recording sites, i.e., the power in the gamma band increases for neurons representing the dominant stimulus, while it decreases for cells responding to the suppressed stimulus. At present, the function of these oscillations is unresolved and it seems possible that selection of perceptually relevant information could also occur on the basis of nonoscillatory synchronized activity. However, as discussed in detail elsewhere, the oscillations may at least be of indirect relevance for response selection because they seem to facilitate the establishment of synchrony among distributed neurons (Engel et al., 1992, 1997; Singer, 1993; König, Engel, & Singer, 1995; Singer et al., 1997).

RELATION TO AROUSAL AND ATTENTION

The data on the changes of neuronal synchronization under rivalry conditions seem to provide, at this point, the most direct evidence for a relation between synchrony and perceptual awareness. However, a number of other studies also support the idea that synchronization is related to awareness and to attentive processing of information. These studies suggest that neuronal synchronization increases during states characterized by arousal and focused attention and, moreover, that high-frequency (gamma) oscillations are also particularly prominent during epochs of higher vigilance. Thus, experiments in rats (Franken, Dijk, Tobler, & Borbély, 1994) and cats (Steriade et al., 1996; Steriade, 1997) have shown that gamma-band synchronization is enhanced during REM sleep and waking compared to deep sleep. Moreover, electrical activation of the midbrain reticular formation (one of the structures responsible for change of vigilance states) has been shown to induce a shift from low to high oscillation frequencies and an increase of stimulus-induced synchronization in the visual cortex (Munk, Roelfsema, König, Engel, & Singer, 1996). In addition, studies in awake behaving animals demonstrate that precise neuronal synchronization and fast oscillations are enhanced in the cortex during epochs of focused attention (Rougeul, Bouyer, Dedet, & Debray, 1979; Roelfsema et al., 1997).

Further support for a relationship between temporal binding and attentional mechanisms comes from recent work on the superior colliculus, a midbrain structure with important integrative functions which mediates orienting responses toward a target of interest (Stein & Meredith, 1993). Lesions of the colliculus lead to neglect, i.e., a severe impairment of spatial attention and phenomenal awareness for events in the space contralateral to the lesion. Based on lesion studies and other physiological evidence, it has been assumed that the colliculus is involved in shifting of attention to new locations (Posner & Petersen, 1990; Kustov & Robinson, 1996). Recent experiments suggest that temporal structure in collicular activity patterns may play a crucial role for the target selection performed by this structure. In the cat, it could be shown that neurons in visual cortical areas can synchronize, via the corticotectal pathway, with cells in the superficial layers of the colliculus (Brecht et al., 1998). Moreover, synchrony occurs within the colliculus itself if the neurons are responding to a coherent visual stimulus (Brecht et al., 1996). These findings suggest that potential targets for attentional shifts and associated orienting behavior may be represented in the
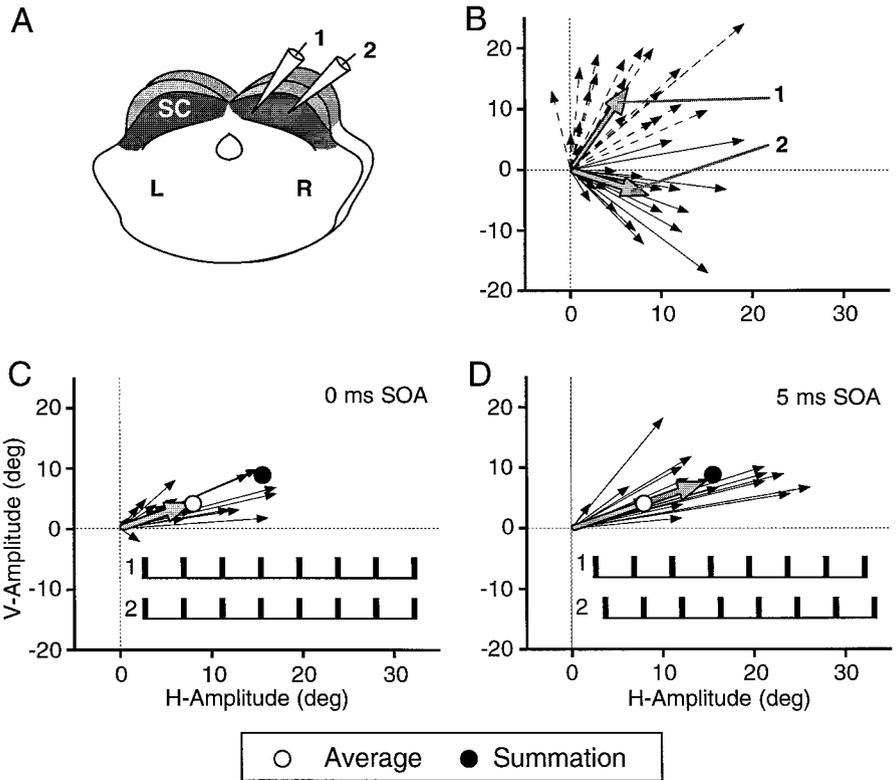
FIG. 5.   Effects of time-varied microstimulation in the superior colliculus on saccade vectors with different directions. (A) Position of the stimulation electrodes. Both electrodes were located in the deep layers of the right superior colliculus (SC). (B) Saccade vectors evoked by stimulating the two sites individually. Small dashed arrows refer to the individual saccades evoked by electrical microstimulation at site 1, whereas the continuous arrows refer to effects of stimulating site 2. The thick arrows indicate the respective mean vectors. (C, D) Saccade vectors obtained with different microstimulation timing protocols. Small arrows display the vectors of individual saccades, and the thick arrow represents the mean vector. The pattern of microstimulation bursts is schematically indicated below each set of sac-cades. (C) Synchronous microstimulation of the two sites leads to vector averaging, i.e., to movements along a vector corresponding to the mean of the saccades evoked by stimulating the two sites individually (white dot indicates the average of vectors 1 and 2, cf. B). (D) Slight temporal offsets of, e.g., 5 ms between the microstimulation pulses delivered to the two sites result in a completely different movement pattern: in this case, the saccades correspond to the sum, rather than the average, of the individual vectors (black dot indicates the sum of vectors 1 and 2 as shown in B), i.e., they have the same direction as those evoked by synchronous pulse trains, but show approximately double amplitude. SOA, stimulus onset asynchrony (from Brecht et al., 1997).

colliculus by assemblies of synchronously firing cells. More recent experiments have attempted a more direct test of the idea that temporal binding may play a role in target selection in the colliculus (Brecht, Singer, & Engel, 1997). In these experiments, it was investigated how electrically evoked saccadic eye movements were affected by varying the temporal relation between microstimulation trains applied at two different sites in the colliculus. As shown in Fig. 5, small temporal phase shifts lead to a motor

output radically different from that evoked by synchronous stimulation. Thus, these data strongly suggest that synchrony in the millisecond range is an important determinant for target selection in the corticotectal pathway and hence, also for the role of this system in directing spatial attention.

Specific changes of neural synchronization with arousal and attention are also demonstrated by EEG and MEG studies in humans. Thus, high-frequency components of sensory evoked potentials, which indicate precise neuronal synchronization when recorded in the awake state, have been shown to disappear under deep anesthesia (Schwender, Madler, Klasing, Peter, & Pöppel, 1994; note that under such conditions the neurons are—in terms of their average firing rate—still responding well to sensory stimuli). Furthermore, EEG measurements have provided clear evidence that synchronization in the gamma band is enhanced during arousal and during focused attention (Sheer, 1989; Desmedt & Tomberg, 1994). Finally, recent results suggest that gamma synchronization is correlated with conscious perception of distinct auditory events (Joliot, Ribary, & Llinas, 1994) and with perception of coherent visual stimuli (Tallon, Bertrand, Bouchet, & Pernier, 1995; Müller, Junghöfer, Elbert, & Rockstroh, 1997), in particular during attentive visual search (Tallon-Baudry, Bertrand, Delpuech, & Pernier, 1997). Taken together, these data demonstrate that arousal (as one of the prerequisites for awareness) and selective attention (as a focused form of sensory awareness) are characterized by an enhancement of synchrony in the relevant neuronal populations. This evidence seems to agree well with our results on binocular rivalry, further corroborating the notion that temporal binding may be required to grant access of information to phenomenal consciousness (Crick & Koch, 1990a,b).

CONCLUSIONS

In this paper, we have discussed the concept of temporal binding and its application to the issue of sensory processing and perceptual awareness. The basic assumption is that synchrony is introduced as an additional coding dimension which complements the conventional rate code. While the latter serves for the coarse coding of representational contents, the former may permit the dynamic expression of specific relations within a network. In this way, the combination of two different coding strategies could allow the multiplexing of different types of information within the same activity patterns and thus could enhance the representational power of distributed systems. As discussed above, the available data suggest that a temporal binding mechanism may indeed exist in the brain. Rather than being a futile epiphenomenon of network connectivity, precise synchronization of neuronal discharges seems to be functionally relevant for the binding of distributed responses in a wide variety of neural systems. In sensory systems, temporal binding may serve for perceptual grouping and thus constitute an important prerequisite for scene segmentation and object recognition. Moreover, temporal binding may be involved in sensorimotor integration, i.e., in establishing selective links between sensory and motor aspects of behavior.

The crucial advantage of temporal binding is that it could permit the rapid and reliable selection of perceptually or behaviorally relevant information. Because precisely synchronized discharges have a high impact on the respective postsynaptic

cells, the information tagged by such a temporal label could be rapidly and preferentially relayed to other processing centers (Singer & Gray, 1995; Singer et al., 1997). We propose that such a process of response selection, which is based on temporal correlation among subsets of activated neurons, may be an integral part of the mechanisms responsible for perceptual awareness. As shown by our experiments on binocular rivalry, selection of visual information for perception is associated with an enhanced synchronization of the respective neuronal populations. Therefore, temporal binding may indeed be a necessary condition for the occurrence of awareness and the establishment of conscious phenomenal states.

In the present context, a question of obvious interest is why selection based on temporal binding would lead to awareness in some cases but not in others. Thus, for instance, both the attentive search for a particular object and the visuomotor coordination in a frequently practiced task like driving require context-dependent selection that, according to our hypothesis, may be implemented by synchronization of appropriate neural assemblies. However, while in the former case the selection process usually leads to awareness, this does not necessarily hold for the latter. What makes the difference, and what would be a *sufficient* condition for the instigation of awareness? A suggestion that we would like to make at this point is that the difference may relate to the ''routing'' (or targeting) of the selected information to processing centers downstream of the visual system. It might be, for instance, that sensory contents reach awareness only if the perceptual information is transferred to prefrontal areas and, thus, becomes part of short-term memory and is available for extended action planning. In contrast, if the ''loop'' leading to action is different, mainly involving a direct coupling of the sensory information to premotor/motor areas or to subcortical centers, then the same information might be less available for global control and thus less accompanied by awareness (Newman & Baars, 1993). Clearly, further studies are required that elaborate on the ''readout'' of temporally bound sensory information and on the routing of selected information in different behavioral contexts.

Other unresolved problems relate to the mechanisms leading to a specific enhancement of synchrony in subsets of distributed neuronal populations. Presumably, multiple factors can contribute to such an enhancement as a prerequisite for selection. First, the binding criteria implemented in the network architecture of sensory areas and, in addition, reentrant interactions between different modules in a sensory system are of basic importance. If binding criteria residing in different areas are consistently met, this may lead—via mutual augmentation—to a high degree of coherence within distributed assemblies (Tononi, Sporns, & Edelman, 1992; Schillen & König, 1994). Second, sensorimotor interactions and modification of the processing by sensorimotor loops may be important (for a more detailed discussion, see Roelfsema et al., 1996). We suggest that attentional selection of information for awareness is never ''purely sensory,'' but is always determined by the integral sensorimotor state of the system. Third, central modulatory systems can contribute to enhancement by upregulation of synchronizing influences (Munk et al., 1996). Fourth, as already discussed above, synchronization is very likely subject to attentional influences (Crick & Koch, 1990a,b). Finally, interactions with memory structures will very likely have a profound influence on selection. Thus, for instance, dynamic interactions with working

memory (Goldman-Rakic, 1992; Moscovitch, 1995; Desimone & Duncan, 1995), implemented by assemblies in prefrontal areas, are conceivable. These considerations indicate that an enhancement of synchronization leading to selection of neuronal populations may be based on a combination of both ''bottom-up'' and ''top-down'' influences, but further studies are required here as well to fully resolve the nature of these mechanisms.

In summary, we wish to suggest that studying the dynamics of neuronal interactions may be particularly rewarding in search for the neural correlates of consciousness. The important point of the results presented here is that, at least at early stages of sensory processing, the degree of synchronicity predicts reliably whether neural activity will contribute to conscious experience or not. We propose that experiments designed to investigate neuronal synchronization may help to identify the selection mechanisms that are required for phenomenal consciousness. At this point, we have deliberately restricted our discussion to the issue of awareness because it seems, based on the present data, that one can hardly argue about a relevance of binding mechanisms for other forms of consciousness. However, it has been speculated that temporal binding may also account for higher order properties of phenomenal consciousness (Metzinger, 1995)—an exciting possibility that clearly awaits future research.

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