Large scale temporal coordination of cortical activity as prerequisite for conscious experience

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Summary

It is proposed that phenomenal awareness, the ability to be aware of one’s sensations and feelings, emerges from the capacity of evolved brains to represent their own cognitive processes by iterating and reapplying on themselves the cortical operations that generate representations of the outer world. Search for the neuronal substrate of awareness therefore converges with the search for the neuronal code through which brains represent their environment. The hypothesis is put forward that the mammalian brain uses two complementary representational strategies. One consists of the generation of neurons responding selectively to particular constellations of features and is based on selective recombination of inputs in hierarchically structured feed-forward architectures. The other relies on the dynamic association of large numbers of distributed neurons into functionally coherent cell assemblies which as a whole represent a content of cognition. Arguments and data are presented which favour the notion that the meta-representations supporting awareness are established according to the second strategy. The hypothesis is forwarded that such distributed representations self-organize through transient synchronization of the discharges of the participating neurons and evidence is presented that the prerequisites for the occurrence of these synchronization phenomena on the one hand and for awareness on the other are similar.

The term ‘consciousness’ has a number of different connotations ranging from awareness of one’s perceptions and sensations to self-awareness, the perception of oneself as an agent that is endowed with intentionality and free will. Here the position will be defended that these various manifestations of consciousness should be tractable within neurobiological description systems, provided that it is possible to reduce the problem to the question how brains perceive and represent the contents of perception. If one is conscious, one is always conscious of something. The respective contents of conscious experience can be perceptual objects of the outer world or states of one’s own organism, in which case information is provided to the brain by extero- and enteroceptive senses. However, the contents of consciousness can also be processes initiated within the brain itself and in the absence of any external stimuli. Thus, conscious experience appears to involve a cognitive process that monitors neuronal activation patterns irrespective of whether these result from sensory input or are internally generated. This suggests two conclusions: First, since sensory signals can be readily processed and influence motor responses without being consciously perceived, the cognitive operations leading to conscious experience must differ from straight forward sensory-motor processing either because they involve additional structures such as higher order cortical areas or because they are organized differently leading to more complex dynamical states of the involved networks. Second, because the primary sensory processes and the internally generated states can both be subject to conscious processing and then can coexist and be bound together, they must have the same format. In other words, the neuronal activation patterns representing the contents of conscious experience must have certain signatures in common, irrespective of whether they are due to sensory input or result from self-generated activity. These signatures should be identifiable by analyzing the differences in the spatio-temporal activation patterns associated with conscious and non-conscious processing, respectively.
Two non-exclusive possibilities may be considered. Conscious and non-conscious processes could involve the same anatomical substrate but differ with respect to certain state variables such as temporal coherence or synchrony or they could require recruitment of additional structures, conscious processing necessitating the engagement of particular cortical areas or a minimum number of cooperating cortical areas. In any case a mechanism is required that is capable of monitoring both the results of primary sensory processes as well as the results of computations based exclusively on information stored within the system. The most likely substrate for such cognitive processes of higher order are cortical areas that have been added in the course of evolution and that treat the results of lower order processes in the same way as these treat input from the sensory periphery. Part of the inner eye function of consciousness could thus be realized by an iteration of self-similar cortical functions. This interpretation is compatible with the neuroanatomical evidence that the phylogenetically more recent cortical areas are remote from primary sensory input and communicate mainly with one another and areas of lower order (Krubitzer, 1998). This scenario is also compatible with the graded emergence of the ability for conscious processing that is correlated with the graded expansion of the cerebral cortex during evolution and with the graded maturation of cortical areas during ontogeny. The evolutionary changes of the mammalian brain consist essentially of an apposition of new cortical areas and comparative behavioural studies suggest that this increasing corticalization goes hand in hand with the increasing ability to represent and combine information at a conscious level. During ontogenetic development the increasing differentiation of conscious processing from rudimentary awareness of sensations to the fully expressed self-consciousness of the adult goes in parallel with the gradual maturation of the phylogenetically more recent cortical areas.

Several arguments let it appear likely that the computational operations performed by cortical modules always obey the same basic principles irrespective of the type of input that is processed. These arguments are derived from the evidence that the microcircuitry of different cortical areas is strikingly similar and that auditory cortex, if supplied with visual input develops functional properties that closely resemble those of visual cortex. Thus, it can be assumed that the phylogenetically more recent cortical areas which are receiving their input mainly from the older areas treat this input in very much the same way as the latter treat the input that is provided to them by the sense organs. If so, the ability of brains to become aware of their own operations and states would have to be attributed to an iteration of the same cognitive operations that support primary sensory processing. The explanatory gap in the study of the neuronal correlates of consciousness would then be reducible to the general question of how the cerebral cortex processes signals and generates representations. If this question is answered with respect to primary sensory functions, the discovered strategies should be generalizable to the formation of the meta-representations, the coherent, global representations that are believed to be the basis of conscious experience.

**Two representational strategies**

If the argument is valid that the internal monitoring functions that lead to consciousness rest on the same cognitive operations as the sensory processes which deal with signals conveyed by the sense organs, the search for the neuronal substrate of phenomenal awareness converges with the search for the nature of the neuronal codes used by the cerebral cortex to represent and store perceptual objects. In the following paragraphs I shall, therefore, expose hypotheses on the putative nature of neuronal representations.
The hypothesis proposed here is that evolved brains use two complementary strategies in order to represent contents (see also Singer, 1995; 1999). The first strategy is thought to rely on individual neurons that are tuned to particular constellations of input activity. Through their selective responses, these neurons establish explicit representations of particular constellations of features. It is commonly held that the specificity of these neurons is brought about by selective convergence of input connections in hierarchically structured feed-forward architectures. This representational strategy allows for rapid processing and is ideally suited for the representation of frequently occurring stereotyped combinations of features; but this strategy is expensive in terms of the number of required neurons and not suited to cope with the virtually infinite diversity of possible feature constellations encountered in real world objects. The second strategy, according to the proposal, consists of the temporary association of large numbers of widely distributed neurons into functionally coherent assemblies which as a whole represent a particular content whereby each of the participating neurons is tuned to one of the elementary features of composite perceptual objects. This representational strategy is more economical with respect to neuron numbers because, as already proposed by Hebb (1949), a particular neuron can, at different times, participate in different assemblies just as a particular features can be part of many different perceptual objects. Moreover, this representational strategy is more flexible. It allows for the rapid de novo representation of constellations that have never been experienced before because there are virtually no limits to the dynamic association of neurons in ever changing constellations. Thus, for the representation of highly complex and permanently changing contents this second strategy of distributed coding appears to be better suited than the first explicit strategy.

The meta-representations postulated as substrate for conscious experience have to accommodate contents that are particularly unpredictable and rich in combinatorial complexity. In order to support the unity of consciousness, the computational results of a large number of subsystems have to be bound together in ever changing constellations and at the same rapid pace as the contents of awareness change. It appears then as if the second representational strategy that is based on the formation of dynamic assemblies would be more suitable for the implementation of the meta-representations that support consciousness than the explicit strategy. Further support for this view comes from considerations on the state dependency and the non-locality i.e. the distributed nature of mechanisms supporting conscious experience. If conscious experience depends on the ability to dynamically bind the results of subsystem computations into a unified meta-representation, conditions required for the formation of meta-representations ought to be the same as those required for awareness to occur. Neuronal codes that are readily observable in deep anesthesia, or during slow wave sleep, or in the absence of attention should not be accepted as sufficient correlates of awareness or consciousness although they are likely to be necessary components of the more global states required for the manifestation of consciousness. In this sense the local codes would be a subset but not the full set of correlates of consciousness. At low processing levels, the response properties of individual neurons tend to differ only little in awake and anesthetized brains. Therefore, it is unlikely that the explicit representations encoded by these neurons are the substrate of the meta-representations that support consciousness. However, neurons in higher cortical areas that are part of attention controlling networks or participate in executive functions undergo drastic changes of their response properties during states in which consciousness is absent. This suggests that the activity of these neurons depends on cooperative interactions that only come into play when the brain is awake and attentive. As discussed later, such cooperativity could be the result of the coordinating mechanisms that are required for the dynamic binding of distributed neuronal responses into coherent representations. One candidate mechanism for dynamic binding is the synchronization of neuronal responses with high temporal precision.
Such synchronization raises the impact that the activity of distributed neurons has on common target structures and thereby enhances responses to distributed inputs. As synchronization is abolished in the same brain states that are incompatible with conscious experience, it appears that the organizing mechanisms that bind distributed responses and thereby enhance responses of cells at higher processing stages play an important role in the maintenance of consciousness.

If the meta-representations postulated as substrate of conscious experience were indeed based on widely distributed codes rather than on responses of local groups of neurons then consciousness should be rather resistant to local lesions. While lesions in subsystems are expected to prevent conscious experience of the contents provided by the respective subsystem, consciousness per se should not be jeopardized. It should break down only if lesions interfere with the coordinating mechanisms that permit establishment of globally coherent cell assemblies. This prediction is by and large in agreement with the known consequences of circumscribed cortical lesions. They eliminate from conscious experience the specific contents processed by the lesioned areas but there is no distinct site of the neocortex whose destruction would lead to a loss of consciousness. It is only after lesions affecting the global coordination of cortical functions that consciousness is abolished.

These considerations suggest that the contents of conscious experience are represented by distributed codes. The following sections will, therefore, focus on the evidence for such coding strategies.

**The signature of distributed codes**

In distributed coding an important constraint needs to be met. A mechanism is required that permits dynamic association of selected neurons into distinct, functionally coherent assemblies and labels grouped responses in a way that assures their joint processing. Numerous theoretical studies have addressed the question how assemblies can self-organize through cooperative interactions among distributed but interconnected neurons (Braitenberg, 1978; Edelman, 1987; Palm, 1990; Gerstein and Gochin, 1992). Here the focus will be on the question how responses of cells that have been grouped into an assembly can be tagged as related. Such tagging is equivalent with assuring that responses are processed together, and this is best achieved by jointly raising their saliency. In principle there are at least three non-exclusive options. First, non-grouped responses can be inhibited, second, the amplitude of the selected responses can be enhanced, and third, the selected cells can be made to discharge in precise temporal synchrony. All three mechanisms enhance the relative impact of the grouped responses. The first two strategies, which rely on the modulation of discharge rates, have been thoroughly investigated and appear to be common at all levels of processing. However, they have certain disadvantages when used for the labeling of assemblies because they may introduce ambiguities (von der Malsburg, 1985) and reduce processing speed (Singer et al., 1997). Ambiguities could arise because discharge rates of cells vary over a wide range as a function of the match between stimulus and receptive field properties and these modulations would not be distinguishable from those signaling the relatedness of responses. Processing speed would be reduced because rate coded assemblies can only be identified after a sufficient number of spikes have been integrated to distinguish high from low rates. Therefore, they need to be maintained for some time in order to be distinguishable, which reduces substantially the rate with which different assemblies can follow one another.

Both restrictions, the ambiguity and the slow processing speed can be overcome if the selection and labeling of responses is achieved through synchronization of individual discharges (von der Malsburg, 1985; Gray et al., 1989; Singer and Gray, 1995). Expressing the relatedness of responses by synchronization resolves the ambiguities resulting from stimulus-dependent rate fluctuations because synchronization can be modulated independently of rates.
Synchronization also accelerates the rate at which different assemblies can follow one another because the selected event is the individual spike or a brief burst of spikes and saliency is enhanced only for those discharges that are precisely synchronized. The rate at which different assemblies can follow one another without getting confounded is then limited only by the duration of the interval over which synaptic potentials summate effectively (for a detailed discussion see Singer, 2000).

**Experimental evidence for grouping by synchrony**
Following the discovery of stimulus related response synchronization among neurons in the cat visual cortex (Gray and Singer, 1987; 1989), numerous experiments have been performed in the search for a correlation between the occurrence of response synchronization and cognitive processes. One of the predictions to be tested was that synchronization probability should reflect some of the Gestalt-criteria according to which the visual system groups related features during scene segmentation. Among the grouping criteria examined so far are continuity, vicinity, similarity and colinearity in the orientation domain, and common fate in the motion domain (Gray et al., 1989; Engel et al., 1991a,c; Freiwald et al., 1995; Castelo-Branco et al., 2000 for the cat; Kreiter and Singer, 1996 for the monkey). So far, the results of these investigations are compatible with the hypothesis that the probability of response synchronization reflects the Gestalt criteria applied for perceptual grouping. Stimulus-specific response synchronization has been found within and across different areas, and even between hemispheres (for review see Singer, 1999). Most importantly, none of these synchronization phenomena were detectable by correlating successively recorded responses to the same stimuli. This indicates that synchronization was not due to stimulus locking but to internal dynamic coordination of spike timing. The observed temporal coherence among responses was much greater than expected from mere covariation of event related rate changes.

Studies involving lesions (Engel et al., 1991b; Nowak et al., 1995) and developmental manipulations (Löwel and Singer, 1992; König et al., 1993) indicate that the interactions responsible for these dynamic synchronization phenomena are mediated to a substantial extent by cortico-cortical connections. The criteria for perceptual grouping should then be reflected in the architecture of these connections and this postulate agrees with the evidence that cortico-cortical connections preferentially link neurons with related feature preferences (for review see Schmidt et al., 1997).

**Response synchronization and behavioural states**
Evidence indicates that highly precise, internally generated synchrony is considerably more pronounced in the awake than in the anesthetized brain (for review see Singer, 1999). Of particular interest in this context is the finding that response synchronization is especially pronounced when the global EEG desynchronizes and when subjects are attentive. Stimulating the mesencephalic reticular formation in anesthetized animals leads to a transient desynchronization of the EEG, resembling the transition from slow wave sleep to rapid eye movement sleep. Munk et al. (1996) and Herculano-Houzel et al. (1999) have shown that stimulus-specific synchronization of neuronal responses is drastically facilitated when the EEG is in a desynchronized rather than in a synchronized state.

Direct evidence for an attention related facilitation of synchronization has been obtained from cats that had been trained to perform a visually triggered motor response (Roelfsema et al., 1997). Simultaneous recordings from visual, association, somatosensory and motor areas revealed that the cortical areas involved in the execution of the task synchronized their activity, predominantly with zero phase-lag, as soon as the animals prepared themselves for the task and focused their attention on the relevant stimulus.
Immediately after the appearance of the visual stimulus, synchronization increased further over the recorded areas, and these coordinated activation patterns were maintained until the task was completed. However, once the reward was available and the animals engaged in consumatory behaviour, these coherent patterns collapsed and gave way to low frequency oscillatory activity that did not exhibit any consistent phase relations. This close correspondence between the execution of an attention demanding visuo-motor performance and the occurrence of zero phase-lag synchrony suggests a functional role of the temporal patterning in the large scale coordination of cortical activity. It appears as if attentional mechanisms imposed a coherent subthreshold modulation on neurons in cortical areas that need to participate in the execution of the anticipated task and thereby permit rapid synchronization of selected responses. According to this scenario, the attentional mechanisms would induce what one might call a state of expectancy in the respective cortical areas by imposing on them a specific, task-related dynamic activation pattern. Once stimulus-driven input becomes available, this patterned activity would act like a dynamic filter that causes rapid synchronization of selected responses, thereby accomplishing the required grouping and binding of responses and in addition assuring rapid transmission of the synchronized activity (for more details see Fries et al., 2001).

**Conscious perception**

A close correlation between response synchronization and conscious perception and a remarkable dissociation between responses of individual neurons and perception has been found in experiments on binocular rivalry. When the two eyes are presented with patterns that cannot be fused into a single coherent percept, the two patterns are perceived in alternation rather than as a superposition of their components. This implies that there is a central gating mechanism which selects in alternation the signals arriving from the two eyes for further processing. Intercocular rivalry is thus a suitable paradigm for investigating the neuronal correlates of conscious perception.

Multiunit and field potential responses were recorded with chronically implanted electrodes from up to 30 sites in cat primary visual cortex while the animals were exposed to rivalrous stimulation conditions (Fries et al., 1997; 2001). In order to assure that the animals exhibited interocular rather than just figural rivalry they had been made strabismic shortly after birth as this is a condition that favours alternating use of the two eyes. Because the animal performs tracking eye movements only for the pattern that is actually perceived, patterns moving in opposite directions were presented dichoptically in order to determine from the tracking movements which signals were actually perceived by the animal. The outcome of these experiments was surprising as it turned out that the discharge rate of neurons in primary visual cortex failed to reflect the suppression of the non-selected signals. A close and highly significant correlation existed, however, between changes in the strength of response synchronization and the outcome of rivalry. Cells mediating responses of the eye that won in interocular competition and were perceived consciously increased the synchronicity of their responses upon introduction of the rivalrous stimulus while the reverse was true for cells driven by the eye that became suppressed. Thus, in this particular case of competition, selection of responses for further processing appears to be achieved by raising the saliency of responses through synchronization rather than enhancing discharge frequency. Likewise, suppression is not achieved by inhibiting responses but by desynchronization.

Thus, at least in primary visual areas, there is a remarkable dissociation between perception and the discharge rate of individual neurons. Cells whose responses are not perceived and are excluded from controlling behaviour respond as vigorously as cells whose responses are perceived and support behaviour. Another puzzling result of the rivalry study is that responses that win the competition increase their synchronicity upon presentation of the rivalrous stimulus.
This suggests the action of a mechanism that enhances the saliency of the selected responses by improving their synchronicity in order to protect them against the interference caused by the rivalrous stimulus.

In conclusion, evaluation of internally generated correlation patterns permits the extraction of information about stimulus configurations, behavioural states and perception that cannot be obtained by analyzing the responses of individual neurons sequentially. The relevant variable containing this additional information is the rather precise synchronization of a fraction of the discharges constituting the respective responses. The data indicate further that responses containing synchronized epochs have a higher probability of being processed further and, eventually, of being perceived consciously.

**The generality of synchronicity**

Studies in non-visual sensory modalities and in the motor system indicate that synchrony and oscillatory activity are ubiquitous phenomena in the nervous system. Synchronization occurs in a variety of distinct frequency bands and has been found in all sensory modalities. Synchronization in the high frequency range (beta and gamma oscillations) has been observed in the olfactory system, the auditory cortex, the somatosensory system, the pre-frontal cortex, the motor cortex and the hippocampus (for review see Singer, 2004).

Synchronization also seems to play a role in the linkage between cortical assemblies and subcortical target structures such as the superior colliculus. This possibility is suggested by the existence of precise temporal relationships between the discharges of neurons in areas of the visual cortex and the superior colliculus (Brecht et al., 1998). In these experiments, it could be shown that corticotectal interactions are strongly dependent on the temporal coherence of cortical activity. If cortical neurons engage in synchronous oscillatory activity either with partners within the same cortical area or with cells in other cortical areas, their impact on tectal cells is enhanced, indicating that tectal cells are driven more effectively by synchronous than by asynchronous cortical activity. This finding is consistent with the idea that the temporal organization of activity patterns plays an important role in defining the output of the cortex.

Taken together, the available evidence suggests 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 now abundant evidence that precise synchronization such as that associated with oscillations in the beta and gamma band occurs also in the human brain. EEG and MEG studies have provided evidence that these synchronous high frequency oscillations are related to cognitive functions such as feature binding, visual search, focussed attention, short- and long term memory and conscious perception (for reviewing see Tallon-Baudry and Bertand, 1999; Varela et al., 2001; Engel et al., 1999a,b; Tononi et al., 1998).

**Conclusion**

The hypothesis proposed here is based on the following assumptions: i) phenomenal awareness emerges from the formation of meta-representations, ii) these are realized by the evolutionary addition of higher order cortical areas that process the output of lower order areas in the same way as these process their respective input, iii) in order to account for the required combinatorial flexibility these meta-representations are likely to consist of the coordinated responses of dynamically bound assemblies of distributed neurons rather than of the responses of individual specialized cells, iv) the selection and binding mechanism that groups neurons into assemblies and labels their responses as
related is the transient synchronization of discharges with a precision in the millisecond range, v) the 
formation of such dynamically associated, synchronized cell assemblies requires activated brain states 
characterized by „desynchronized“ EEG and is facilitated by attentional mechanisms. The data 
reviewed above support these premises and define conditions that need to be fulfilled in order to allow 
for conscious experience.

Obviously, for a content to be perceived consciously it is a prerequisite that neurons coding for this 
content are active. However, by measuring responses of individual neurons it is impossible to decide 
whether a recorded response is just a necessary or whether it is a sufficient condition for conscious 
experience. If neurons in a particular transmission chain stop responding, the content conveyed by that 
group of neurons cannot be perceived. Hence, correlations between perceptual awareness and cellular 
responses indicate only that the discharges of cells at a particular processing stage are necessary for a 
particular content to reach the level of awareness. In order to find out whether additional prerequisites 
have to be fulfilled, e.g. the binding of these responses into widely distributed assemblies, variables 
need to be determined that permit assessment of order parameters beyond the level of single units. This 
can only be achieved with recording techniques that disclose the spatio-temporal activation profile of 
large numbers of neurons. In this context it is noteworthy that methods such as EEG and MEG 
recordings which assess global activation patterns and monitor only activity that is sufficiently 
synchronous to add up to a measurable signal, differentiate best between brain states where 
consciousness is or is not possible. This favors the hypothesis that the generation of the meta- 
representations that support conscious experience requires temporal coordination of activity well 
beyond the level of single cell firing. Consciousness manifests itself only during brain states 
characterized by „desynchronized“ EEG. These states, in turn, favour the occurrence of high frequency 
oscillations and long distance synchronization of neuronal responses with a precision in the millisecond 
range. It seems not unreasonable, therefore, to pursue the hypothesis that the meta-representations 
required for consciousness to manifest itself consist of large assemblies of distributed neurons whose 
signature of relatedness is the internally generated synchronicity of discharges. Thus, consciousness, 
rather than being associated with the activation of a particular group of neurons in a particular region of 
the brain, appears to be an emergent property of a particular dynamical state of the distributed cortical 
network – a state that is characterized by a critical level of precise temporal coherence across a 
sufficiently large population of distributed neurons.
References cited


