

DYNAMIC PREDICTIONS: OSCILLATIONS AND SYNCHRONY IN TOP-DOWN PROCESSING

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Classical theories of sensory processing view the brain as a passive, stimulus-driven device. By contrast, more recent approaches emphasize the constructive nature of perception, viewing it as an active and highly selective process. Indeed, there is ample evidence that the processing of stimuli is controlled by top-down influences that strongly shape the intrinsic dynamics of thalamocortical networks and constantly create predictions about forthcoming sensory events. We discuss recent experiments indicating that such predictions might be embodied in the temporal structure of both stimulus-evoked and ongoing activity, and that synchronous oscillations are particularly important in this process. Coherence among subthreshold membrane potential fluctuations could be exploited to express selective functional relationships during states of expectancy or attention, and these dynamic patterns could allow the grouping and selection of distributed neuronal responses for further processing.

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In cognitive neuroscience, we are witnessing a fundamental paradigm shift¹⁻³. Classical theories viewed the brain as a passive, stimulus-driven device that does not actively create meaning by itself, but simply reacts to sensory inputs and copies pre-specified information. In these theories, sensory processing was considered to consist mainly of the sequential extraction and recombination of features, leading to the veridical reconstruction of object properties⁴⁻⁷. As a result, perception was believed to deliver an internal ‘world model’ that provided general-purpose, context-invariant knowledge about the external environment. Accordingly, classical approaches have focused on serial ‘bottom-up’ processing in hierarchically organized neural architectures⁵⁻⁸. In this framework, each percept is considered to be synthesized *de novo* from elementary bits of information, requiring explicit computation of the complete set of structural details. This idea of serial processing implies further that the representational contents carried by individual neurons would increase in complexity as one moves up the processing HIERARCHY⁹⁻¹¹.

These concepts have received considerable support from electrophysiological studies of single-cell responses, but new data indicate that the brain should be regarded as a much more active and adaptive system^{3,12}. Therefore, current approaches emphasize the intimate relationship between cognition and action^{1,13} that is apparent in the real-world interactions of the brain and the rich dynamics of neuronal networks¹⁴⁻¹⁸. One of the new concepts is captured by the idea of ‘situatedness’^{1,13,19}. This assumes that cognition does not build on ‘universal’, context-invariant models of the world, but is subject to constraints imposed by an ever-changing environment that need to be coped with in an adaptive and context-dependent manner. The main task of cognition is the guidance of action; so, the criterion for judging the success of cognitive operations is not the ‘correct’ representation of environmental features, but the generation of actions that are optimally adapted to particular situations. Therefore, some authors propose that internal states should be viewed not primarily as representations of perceptual objects, but rather as ‘action-oriented pointers’; that is, as sensorimotor activity patterns that

HIERARCHY

A system of interconnected modules, in which 'higher' centres are activated later and contain more abstract representations than 'lower' areas.

ASSEMBLY

A spatially distributed set of cells that are activated in a coherent fashion and are part of the same representation.

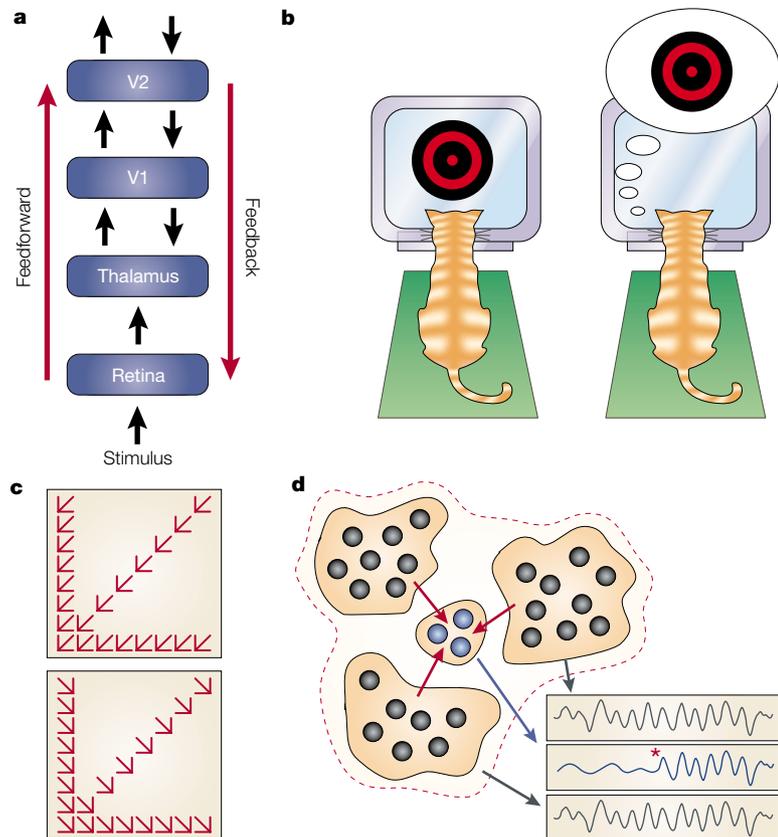
refer to aspects of the world in the context of possible behaviours^{1,13,19}. This new stance incorporates many of the concepts of mid-1980s connectionism²⁰: distributed processing, the lack of central control and the emphasis on context dependence. Accordingly, there is a shift towards explaining cognitive functions in terms of the coherent behaviour of large neuronal populations^{12,16–18} that are dynamically bound within and across subsystems. As a consequence of this conceptual reorientation, new research strategies are being developed to analyse the dynamic interactions between large numbers of neurons and to monitor the formation of functionally coherent ASSEMBLIES²¹ in complex sensorimotor contexts.

In this review, we focus on one of the key elements of this new framework: the fundamental role of 'top-down' effects in sensorimotor processing. As opposed to the idea of bottom-up, the concept of top-down (BOX 1) refers to the fact that many aspects of cognition and behaviour are not stimulus driven in a reflex-like manner, but are to a large degree based on expectations derived from previous experience, and on generalized knowledge stored in the architecture of cortical and sub-

cortical networks^{22–28}. Intelligent behaviour presupposes that a cognitive system can detach itself to varying degrees from the current stimulus situation, and select — in agreement with intrinsic goals and motivational states — only those inputs that are meaningful for the control of action. In the real world, such computations must be both extremely fast and reliable. This seems to be possible only if the brain makes efficient use of top-down resources, allowing it to create predictions about forthcoming stimuli and to constantly match expectations against signals from the environment^{22,26,27,29}. As part of the emerging shift in assumptions towards the idea of an active and selective brain, this anticipatory nature of neural activity patterns is attracting increasing interest in systems neuroscience^{30–35}. We discuss recent evidence that predictions about forthcoming events might be implemented in the temporal structure of neural activity patterns. Specifically, we focus on spatiotemporal patterns of ongoing activity that translate the functional architecture of the system and the prestimulation history into dynamic states of anticipation.

Box 1 | Flavours of 'top-down'

The ideas of 'top-down' and 'bottom-up' are ambiguous and can, depending on the context, be used with substantially different meanings. Probably the most widely used variant is anatomical, in which top-down influences are equated with the activity of feedback connections in a processing hierarchy, whereas bottom-up denotes feedforward information flow^{23,24} (see part a of the figure). In cognitivist terms, the two concepts refer to the distinction between hypothesis- or expectation-driven processing, and stimulus-driven processing¹⁵. In this case, the behaviour of an experimental animal or subject can be controlled largely by a sensory stimulus (part b, left), or dominated by intrinsic factors such as attention, memory or expectation of forthcoming sensory events (right). In many situations, the properties of the 'whole' determine the perception of the 'parts'. In the stimulus arrangement shown in part c, it takes longer to identify the parts than to respond behaviourally to features of the whole¹¹⁶. This global-precedence effect, which provides one of many examples of the contextual modulation of perceptual items, can be considered as yet another type of top-down interaction (the gestaltist, or perceptual, idea of top-down^{117,118}). A fourth variant could be referred to as the 'dynamicist' idea of top-down, in which large-scale dynamics can have a predominant influence on local neuronal behaviour by 'enslaving' local processing elements¹¹⁹. For instance, already synchronized populations (part d, black) in a network might entrain other neurons (blue) to become part of the same overall assembly after some point in time (asterisk), resulting from the spread of synchronized activity through lateral connections. In functional terms, this could correspond to the incorporation of some contents (coded by the blue neurons) into a broader context (represented by the black neurons), leading to a reinterpretation of the represented item. This idea of top-down does not require a processing hierarchy, but the dynamic 'capture' of neurons into a larger assembly could occur between areas at the same processing level or within one area. Our concept of top-down is closest to the dynamicist view, as we assume that the intrinsic processing dynamics of a cognitive system are a crucial variable for expressing goals or expectations, and that these correspond to states of large-scale integration in the system^{18,49,105}. By comparing the different uses of the term, it is evident that the concept of top-down is richer than the mere idea of feedback signal flow, and encompasses a whole class of phenomena. These notions of top-down are by no means mutually exclusive, as they partly apply at different levels of description.



The active brain

In recent years, several neural theories have considered the functional importance of top-down mechanisms. Most of these models make use of the anatomical idea of top-down processing (BOX 1): they assume that predictions or hypotheses about the features of environmental stimuli are expressed by signals travelling along feedback connections from 'higher' to 'lower' areas in a processing hierarchy. One of the earliest examples of such a model is the 'adaptive resonance theory' developed by Grossberg and co-workers^{22,36}. The model was inspired by the insight that feedback in sensory systems is necessary to stabilize important representations selectively in a rich environment, where only subsets of input signals are relevant for learning. The theory assumes complementarity between ascending and descending pathways among sensory areas, the former allowing adaptive filtering of the input signals and the latter carrying predictive signals (templates of expected patterns that need to be matched by the current input). In this scheme, the lower area that is closer to the sensory periphery provides the interface where afferent data and learned feedback expectancies are compared. The assumption is that a mismatch between the two leads to extinction of the sensory responses in the early area, whereas a match causes their amplification, allowing broadcasting of the salient signals to other downstream areas. Related models that also postulate a key role of feedback influences in pattern recognition have been suggested by Mumford²³ and Ullman²⁴.

These models suggest that the comparison of sensory input with existing knowledge is essential for perception. A common trait of these theories is that the search for matching patterns is primarily triggered by external input, and not initiated by the system itself. Moreover, feedback control originates in the same sensory modality that processes the feedforward input. Both aspects are handled differently in more recent top-down models of attentional selection and cognitive control^{25–27,37–39}. Going beyond a single processing stream, these models consider cross-systems interactions and, in agreement with functional imaging^{37,38} and cellular^{25–27,39} data, indicate that top-down influences originate in prefrontal and parietal cortical areas. One crucial idea is that assemblies of neurons that represent action goals in the prefrontal cortex provide modulatory 'bias signals'^{26,39} to sensorimotor circuits that have to carry out response selection. So, prefrontal signals are assumed to exert top-down control over the routing of information flow through specific sensorimotor loops. Reward signals²⁹ are thought to gate learning processes that optimize functional connections between prefrontal and lower-order sensorimotor assemblies.

A different idea of how top-down influences might be implemented neurally — leading to what we call a 'dynamicist' view (BOX 1) — is suggested by another theory of perception: the temporal binding model^{16,17,40–43} (BOX 2). This model assumes that neural synchrony with precision in the millisecond range is crucial for object representation, response selection, attention and sensorimotor integration. Synchrony is supposed to enhance the

saliency of neural responses⁴², because correlated discharges have a much stronger impact on neuronal populations than temporally disorganized inputs^{44–46}. The core idea is that synchronization through the joint enhancement of response saliency can select and group subsets of neuronal responses for further joint processing. So, synchronization can be used to encode information about the relatedness of neural signals and is, therefore, likely to be causally relevant in neural processing. A crucial ingredient of the model is that synchrony can be intrinsically generated (not imposed on the system by external stimuli), and modulated by intrinsic signals that reflect experience, contextual influences and action goals^{16,17,31,34,43,47,48}. In this context, the search for the mechanisms of top-down control (BOX 1) becomes equivalent to the investigation of the influence of ongoing patterns of activity on the processing of sensory signals, and, in particular, on their selection and grouping through oscillatory patterning and synchronization. In contrast to the top-down models discussed above, the patterns relevant to the dynamic selection of input signals would be generated not only by assemblies in association cortices that carry more abstract, invariant representations, but as the result of continuous large-scale interactions^{17,18,49} between higher- and lower-order cortical areas. The patterns of coherent activity emanating from such large-scale interactions could bias the synchronization of input signals, leading to a selective enhancement of temporal correlations in subsets of the activated populations^{50,51}. This would result in enhanced saliency and a competitive advantage for the selected populations of neurons.

A relationship between top-down influences and synchrony has also been suggested in the framework of two other theories: the 'convergence-zone' model of Damasio^{52,53} and the theory of 'neuronal group selection' proposed by Edelman^{12,54,55}. In the Damasio model, synchrony in specific cortical areas reflects the influence of top-down signals broadcasted from convergence-zone assemblies⁵³, which are presumed to be located in higher-order integrative cortices. These top-down signals can both reactivate and bind lower-level contents and so, for example, subserve the recall of stored memories. In the theory of neuronal group selection^{12,54}, top-down influences are captured in the idea of 'reentry', defined as recursive signal exchange along loops of reciprocal connections. Like our temporal binding model, this concept does not depend on the assumption of hierarchical architectures, but includes the effects of lateral connections at the same processing level, which also provide sources of contextual modulation. Moreover, the Edelman theory suggests that reentry leading to the synchronization of distributed neuronal populations is crucial for perceptual categorization, memory and consciousness¹². Emphasis is placed on the constructive nature⁵⁴ of reentrant interactions, which allow the evaluation and interpretation of new stimuli against the background of knowledge already acquired by the system. The processing of input data assumes the form of a BAYESIAN OPERATION on sensory signals, based on self-generated expectancies⁵⁶. Similar to our model of temporal selection and binding, the two theories predict that

BAYESIAN OPERATION

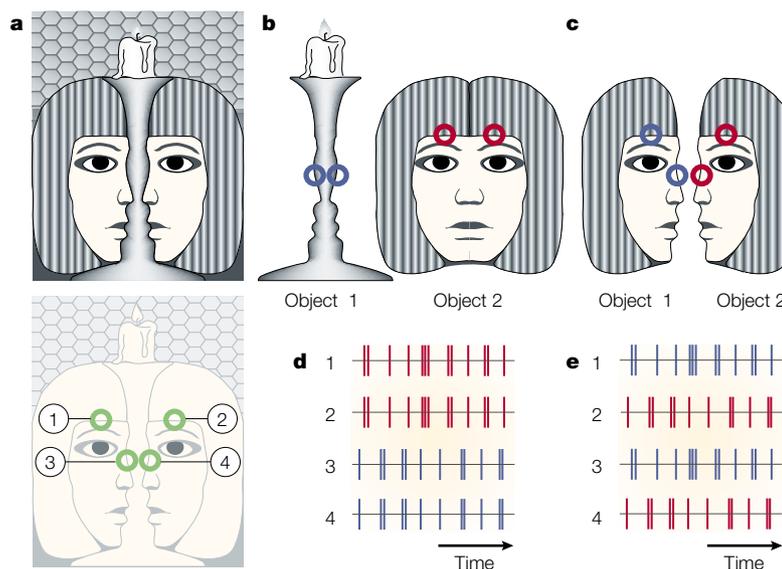
The estimation of conditional probabilities that can be used to quantify inferences about hypotheses, given certain input data. When implemented in a neural network, this can mean, for instance, that a neuron responds to feedforward input signals only if it previously received lateral inputs that convey an expectational bias from other neurons in the network.

Box 2 | The temporal binding model

Temporal binding has been suggested as a remedy to the problem of how to define dynamic functional relations between neurons in distributed sensorimotor networks. The proposal is that this 'binding problem' could be solved by exploiting the temporal aspects of neuronal activity^{16–18,40–43}. The model predicts that neurons that respond to the same sensory object might fire in temporal synchrony with a precision in the millisecond range. However, no such synchronization should occur between cells that are activated by different objects in sensory space. Such a temporal integration mechanism would provide an elegant solution to the binding problem, as 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 allow the system to establish a distinct representational pattern — an assembly²¹ — for each object, and so enable figure–ground segregation. Moreover, such a temporal binding mechanism could establish relationships between neuronal responses over large distances, solving the integration problem imposed by the anatomical segregation of specialized processing areas.

The model assumes that synchrony between neurons is subject to both bottom–up and top–down influences; that is, that synchrony is determined by both the stimulus and factors such as expectation, attention or knowledge about the current situational context. 'Bistable' images illustrate both aspects (see part a of the accompanying figure). Bistability means that two interpretations are possible — in this case, either the percept of one face that is partially occluded by a candlestick (b) or of two opposing faces (c). These perceptual situations mutually exclude each other, and most observers flip back and forth between the two. In this case, the temporal binding model predicts that neurons should dynamically switch between assemblies and, hence, that temporal correlations should differ for the two perceptual states. Consider four visual cortical neurons with receptive fields (positions 1–4 in a) over image components, the grouping of which changes with the transition from one percept to the other. As shown in part d of the figure, neurons 1 and 2 should synchronize if the respective contours are part of the one background face, and the same should hold for neurons 3 and 4, which represent contours of the candlestick. When the image is segmented into two opposing faces, the temporal coalition switches to synchrony between 1–3 and 2–4, respectively (e). Binding within the respective objects is facilitated by Gestalt criteria that lead to contour grouping. However, switching between the two perceptual constellations in terms of synchrony (d,e) cannot be explained with reference to low-level Gestalt criteria, but presumably requires interactions with higher-level assemblies carrying invariant object representations. Competition between such populations, representing high-level contents, is also likely to be involved.

The model does not assume that, at the level of early visual areas, the whole set of neurons representing the figure would synchronize homogeneously. It might suffice that specific temporal patterning occurs in those regions of interest in the image representation that are used in the respective perceptual epoch to support scene segmentation. In our example, important cues obviously include the contours around the midline of the image. In the representation of such regions, focused synchrony and — equally important — 'fractures' of desynchronization would then arise during parsing of the image. The assumption is that both bottom–up and top–down factors determine, in a context-dependent manner, which features are used and which neurons are incorporated into the region of interest where temporal patterning is most pronounced. Panel a modified with permission from REF. 120 © 1990 Palgrave Publishers Ltd.



self-generated activity should have a distinct spatiotemporal patterning, and should, in turn, bias the self-organizing process that leads to the temporal coordination of input-triggered responses and to their binding into functionally coherent assemblies. In the following sections, we discuss evidence that internally generated activity shows distinct temporal patterning against which input signals are matched.

Neural correlates of top–down processing

It is not yet clear how the brain expresses predictions and expectancy in terms of neural signals, or how it achieves efficient response selection. However, many studies have shed light on the effects of top–down influences on the neural processing of stimulus-related information. Much evidence shows how neuronal firing rates and response profiles can change under the influence of attention, working memory and behavioural context. Response

modulation by selective attention provides probably the best-studied example. Numerous studies, using unit recording or functional imaging, have established that attention shifts can influence neuronal activation levels (for review, see REFS 25,57,58), leading to a predominance of responses to attended locations or object features, and a suppression of responses to non-attended locations or features, respectively. An important aspect is that the modulatory effect of attention is present in the primary sensory cortices, although the extent of the top–down modulation of firing rates clearly increases as one moves up the cortical hierarchy. Functional imaging studies indicate that attention can also modulate the 'driving' effect that neuronal populations in one cortical area exert on cells in another area^{59,60}. In addition to attention, other top–down factors that modulate neuronal firing rates include familiarity with the stimulus²⁶ and cross-modal, task-specific influences⁶¹.

There is increasing evidence that modulatory top-down effects might influence not only average neuronal firing rates, but also the temporal structure of neural responses. This holds for both temporal correlations that can be measured between different neurons and oscillatory patterning of individual responses. The latter can occur in different frequency bands, and is particularly prominent in the beta and gamma band (frequency components above 20 Hz) in instances of top-down modulation. Recent data show that synchrony and/or gamma-band oscillations are enhanced during the attentional selection of sensory information. Steinmetz *et al.*⁶² investigated cross-modal attentional shifts in awake monkeys that had to direct attention to either visual or tactile stimuli that were presented simultaneously. For a significant fraction of the neuronal pairs in the second somatosensory area, synchrony depended strongly on the monkey's attention. If the monkey shifted attention to the visual task, temporal correlations typically decreased among somatosensory cells, as compared with task epochs in which attention was not distracted from the somatosensory stimuli. A strong attentional effect on temporal response patterning has also been observed in visual area V4 in the monkey⁵¹. In this study, two stimuli were presented simultaneously on a screen, one inside the receptive fields of the recorded neurons and the other nearby. The animals had to detect subtle changes in one or other stimulus. If attention was shifted towards the stimulus that was processed by the recorded cells, there was a marked increase in local coherence in the gamma band.

Evidence for the attentional modulation of neural synchrony is also provided by studies of sensorimotor interactions. Synchronization between sensory and motor assemblies has been investigated⁶³ in awake, behaving cats as they perform a visuomotor coordination task (FIG. 1Aa–d). Neural activity was recorded with electrodes that were chronically implanted in various areas of the visual, parietal and motor cortices. The results show that the 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 markedly in different behavioural situations. Precise neuronal synchronization between sensory and motor areas occurred during those task epochs in which the cat expected the appearance of the stimulus, and increased further in phases when the animal had to process visual information attentively to direct the required motor response (FIG. 1Ac,d). This study points to two important conclusions on the nature of top-down processing: it can be expressed through the modulation of synchronization and it can involve interactions between multiple areas, supporting our hypothesis that large-scale coherence could be one of the correlates of top-down control. This issue has been addressed explicitly by König and colleagues^{34,64}, who recorded simultaneously from the primary visual cortex and a parietal visual area in cats performing a VISUOMOTOR GO/NO-GO TASK (FIG. 1Ba). Interareal synchrony

was strongly task dependent at lower frequencies in the theta and alpha range (4–12 Hz), being more prominent in the GO than in the NO-GO condition. The phase relationship between signals from the different areas indicated a top-down-directed interaction. If novel rather than trained stimuli were used in the task, gamma-band synchrony was enhanced between the recorded areas (FIG. 1Bb). These findings support the hypothesis that interareal synchronization can reflect the anticipatory coordination of internal brain states in the context of top-down processing.

Further support for a role of temporal coordination in top-down processing comes from investigations of attention- and memory-related changes of electroencephalographic (EEG) activity in humans. Motivated by the animal experiments that indicated a functional relevance of high-frequency oscillations, several studies have focused on changes in gamma-band signals in conditions requiring selective attention. They have shown the enhancement of high-frequency components during attentive listening⁶⁵, visual search⁶⁶ and attention to moving visual stimuli^{67,68}. Moreover, gamma-band activity is enhanced in task situations involving object recognition⁶⁹, learning⁷⁰, language processing⁷¹ and emotional evaluation⁷². In agreement with the animal studies, these investigations show that the effects are most prominent for the so-called 'INDUCED' fraction of gamma activity. This, in turn, is evidence that the observed synchrony is the result of intrinsic dynamic interactions in the involved sensorimotor loops. As suggested^{48,49,68,69,73}, modulation of these induced gamma components, particularly of those occurring more than 200 ms after stimulus onset, could reflect top-down processing. In addition to changes of spectral power, some of these studies have specifically looked at the coherence across EEG recording sites and found clear evidence of large-scale integration during epochs in which processing was modulated by top-down information^{69,70,74}.

Temporal patterns in ongoing activity

The data discussed above are compatible with the idea that the top-down modulation of sensory information processing could be mediated by context-dependent modifications of the temporal patterning of neuronal responses and, in particular, by influencing their coherence. In addition to modulating activity evoked by a stimulus, top-down factors can also act before stimulus appearance, or during states of expectancy or anticipation^{32,33,35}. Top-down factors can even act in the complete absence of any external stimulus, as shown, for example, in imaging studies of normal subjects during mental imagery^{38,75} and of patients with schizophrenia during auditory hallucinations⁷⁶. These investigations provide evidence that neuronal activity can be modulated by purely intrinsic factors. Until recently, 'spontaneous' fluctuations of ongoing activity have been considered as noise⁷⁷, not conveying any information. However, if the brain is constantly creating predictions, as required by continuous engagement in real-world sensorimotor contexts, self-generated activity should

VISUOMOTOR GO/NO-GO TASK
A task involving the control of behaviour by two alternative visual stimuli, one allowing and the other preventing a trained motor response.

INDUCED RHYTHMS
Oscillatory signals that are not phase-locked to the stimulus that is presented to the subject.

always have some significance, at least in the awake, attentive brain. This does not challenge the idea that noise might be important in signal transduction by enhancing the sensitivity of transmission channels⁷⁷. Rather, it attributes significance to the internally generated, coherent

fluctuations of excitability. These fluctuations are assumed to serve as ‘bias signals’ that prime stimulus-evoked responses, thereby permitting rapid selection among multiple events or inputs. Below, we review data that support this interpretation.

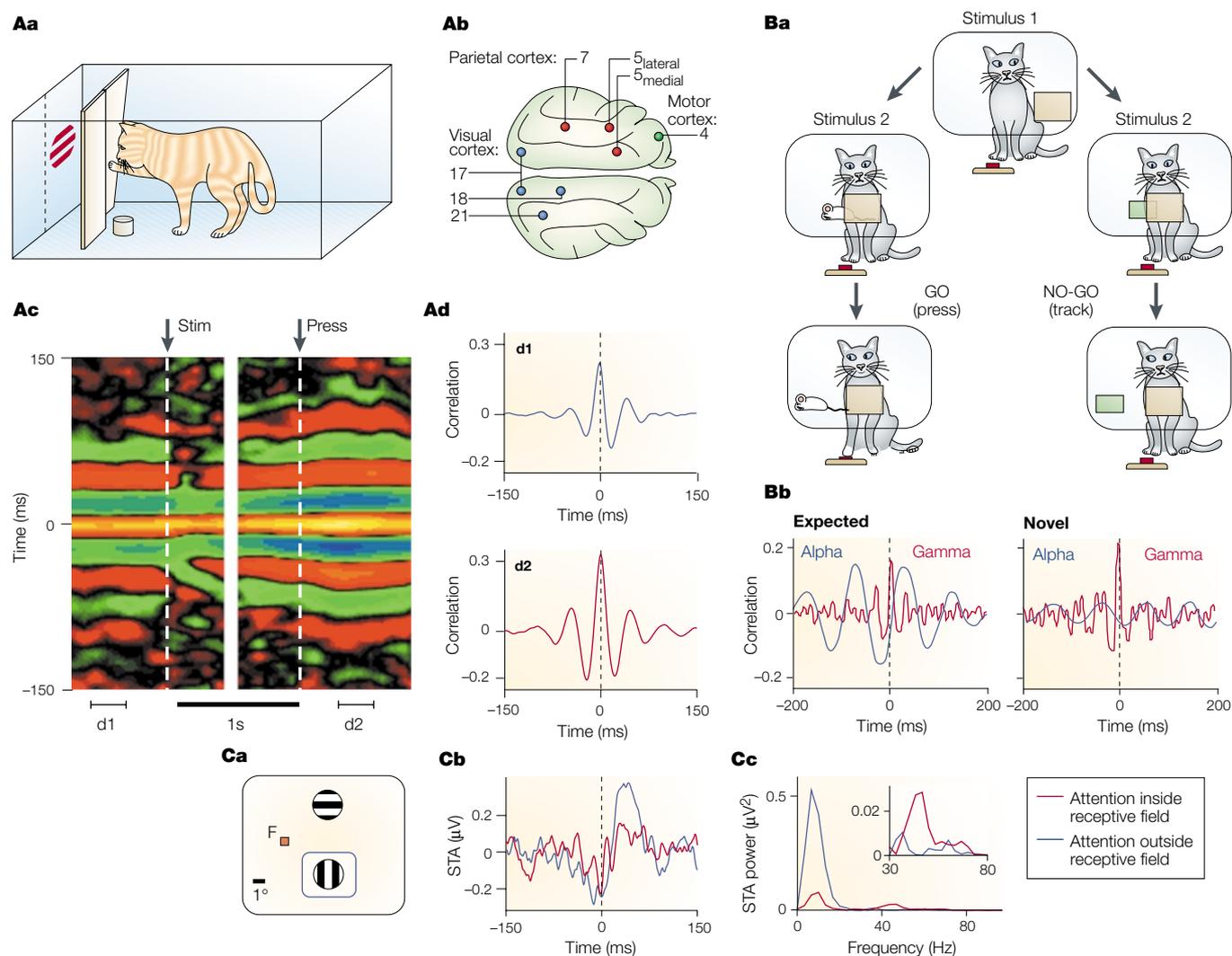


Figure 1 | Expectation-related synchrony in visual cortex. Aa–d | Synchrony in awake cats during a visuomotor coordination task⁶³. **Aa** | Cats had to respond to a visual stimulus by pressing and holding a transparent door as they waited for a rotation of the stimulus. **Ab** | Local field potentials (LFPs) were recorded from visual, parietal and motor cortex. **Ac** | The contour plot shows how the temporal correlation between parietal areas 5 and 7 evolves over time. Abscissa: time relative to stimulus appearance (Stim) or motor response (Press). Zero on the ordinate indicates synchrony between the recording sites. Red–yellow, positive correlation; green–blue, negative correlation. **Ad** | Correlograms from the epoch of ongoing activity just before stimulus appearance (d1) and from an epoch after the door press (d2). The high-amplitude zero peak shows that synchrony occurs before the appearance of the stimulus (d1), presumably reflecting expectancy, and increases during attentive visuomotor processing (d2). Synchrony breaks down completely after the cat has responded to rotation of the pattern by releasing the door⁶³ (data not shown). **Ba,b** | Expectancy-related synchrony in cats trained on a visuomotor GO/NO-GO task^{34,64}. **Ba** | The animal had to track a preparatory stimulus. After a delay, a second stimulus emerged. In the case of a cartoon mouse (GO condition), the cat had to press a lever; in the NO-GO condition, she had to continue to track a small moving rectangle. LFPs were recorded simultaneously from area 7 and the primary visual cortex. **Bb** | Interareal interactions with expected stimuli and novel stimuli, which were occasionally interspersed in the normal sequence of trained stimuli. Cross-correlograms are shown for the alpha (8–12-Hz; blue) and gamma (20–100-Hz; red) frequency ranges. There is a significant correlation in the alpha range during presentation of the expected, but not the novel, stimulus. Synchrony in the gamma range is significant during presentation of both stimuli, but is enhanced for novel stimuli. **Ca–c** | Effects of attention in area V4 of awake monkeys⁵¹. **Ca** | After the appearance of a fixation spot (F), two gratings were presented on a screen after a variable delay. One of the gratings was presented over the receptive field of the recorded neurons (blue outline). Attention was directed to one of the two stimuli. LFPs and unit signals were recorded simultaneously. **Cb** | Spike-triggered averages (STA) of the LFP for trials in which attention was directed to the stimulus inside (red trace) or outside (blue trace) the receptive field. The STAs were computed for a 1-s epoch just before stimulus onset. **Cc** | Power spectra of the STAs for the two conditions. Inset, magnification of the power changes in the gamma range (30–80 Hz). The spatial shift of attention covaries with enhanced gamma power in the delay period, reflecting expectancy. Panels **Ab–d** adapted with permission from REF. 63 © 1997 Macmillan Magazines Ltd; panels **Ba,b** courtesy of P. König; panel **Ca** modified from REF. 51 © 2001 American Association for the Advancement of Science; panels **Cb,c** show unpublished data from the study described in REF. 51, courtesy of P. Fries, J. H. Reynolds, A. E. Rorie and R. Desimone.

If ongoing activity reflects ordered states of internally generated activity (top–down influences in the wider sense proposed in BOX 1) it should show highly specific patterns, and these should reflect the functional architecture of the networks, the traces left by previous stimuli and the features of planned behaviour. Arieli and co-workers^{78–80} were the first to show that, even in the anaesthetized state, ongoing activity is endowed with specific patterning that reflects the functional architecture of the underlying network. Using OPTICAL IMAGING, they showed that ongoing activity in the cat visual cortex is highly coordinated across large assemblies. This coordination is feature specific, as the spontaneous discharges of individual neurons are temporally locked to the activation of other cells with similar orientation preferences⁸⁰. The patterns of coherence in ongoing activity can span several millimeters of cortical surface, indicating that specific long-range interactions are possible even in the absence of visual input. Moreover, these patterns are highly variable and their fluctuations can largely account for the variability of the responses evoked by a subsequent visual stimulus⁷⁹. These data make it likely that ongoing activity contains structured information and therefore has an important role in cortical function⁸⁰.

Specific patterns of coherence in ongoing activity have also been demonstrated by studies that have searched for temporal correlations between distributed neurons using multiple-electrode recordings. It has long been known that states of enhanced arousal and focused attention are, even in the absence of specific stimuli, distinguished by enhanced gamma oscillations^{34,51,63,81–86} that can be coherent across extended frontal and parietal networks^{34,63,64,81,87}, and across thalamocortical loops^{81,84,85}. Behavioural evidence indicates that these patterns are related to states of expectancy about task-relevant events^{34,51,63,81}. The three experiments illustrated in FIG. 1 show coherence in the high frequency range (>20 Hz) during ongoing activity, and relate it to predictions about task-relevant information. As shown in FIG. 1Ac,d, precise synchrony occurs between local field potentials (LFPs) recorded from different areas in the awake cat, even before the appearance of the behaviourally relevant stimulus, probably reflecting the animal's state of expectancy. FIGURE 1Ca–c shows data from the attention study of Fries *et al.*⁵¹. The authors analysed not only how attentional effects modulate visually evoked responses, but also whether they affect the ongoing activity that precedes the appearance of the stimulus at attended or non-attended loci. They found clear evidence for expectancy-related enhancement of gamma-band synchrony (FIG. 1Cc), specifically at the attended location. This spatial specificity shows that the gamma-band activity does not result from global state changes leading to increased arousal.

Studies of temporal correlations in ongoing activity have also provided evidence that emerging patterns of coherence are related to the feature specificity of the recorded neurons. Ongoing synchrony is more pronounced between cells that share the same orientation or directional preference^{30,47,88}. The interactions can

occur in different frequency bands^{34,49,83,84} and with differing precision⁸⁸ (as measured by the peak width of CORRELOGRAMS). These different bands seem to reflect both the spatial scale of the interactions and the similarity of the represented features — precise synchronization at high oscillation frequencies occurs preferentially for cells with similar response properties, and coarser synchronization at low oscillation frequencies reflects long-range coupling between neurons in remote areas^{49,74}. In functional terms, this might reflect the 'width' of contexts for binding and the degree of relatedness in primed object constellations. Alternatively, different frequency bands could mediate top–down and bottom–up interactions, respectively^{34,64,89}.

The fact that synchrony is readily observed in multi-site recordings of ongoing LFP signals (FIG. 1) indicates that substantial coherence must be present in subthreshold membrane potential fluctuations of different neurons. Such field potentials reflect the average transmembrane currents in a volume around the electrode tip, and therefore provide a measure mainly of postsynaptic dendritic responses. Direct evidence for coherence between subthreshold fluctuations of separate neurons has been obtained by Lampl *et al.*⁹⁰, who recorded intracellularly from pairs of visual cortical neurons *in vivo* in the cat. They observed, in nearly all recorded pairs, strong synchronization of the ongoing fluctuations in the cells' membrane potentials. The features of this subthreshold synchrony are very similar to those of synchrony between ongoing spike discharges⁸⁸, both occurring mostly with zero phase lag, and showing a clear dependence on the topographic proximity of receptive fields and the similarity of receptive field types. As we suggest below, coordinated subthreshold excitability changes could be important for specific 'priming' of the local network to particular input constellations, and so implement predictions resulting from top–down processing.

Predictive power of synchrony

Our hypothesis is that top–down factors can lead to states of 'expectancy' or 'anticipation' that can be expressed in the temporal structure of activity patterns before the appearance of stimuli. To validate this idea, it must be shown that ongoing activity has predictive power, and that some of its features are correlated with subsequent perceptual decisions or behavioural events. The predictive nature of self-generated fluctuations of neuronal excitability levels has been demonstrated in both functional imaging and microelectrode studies. During states of attentive expectation, baseline firing rates in monkey extrastriate areas V2 and V4 increase when attention is directed inside the receptive field of the recorded neurons⁹¹. Such shifts in ongoing firing levels might reflect top–down signals that create a bias in favour of stimuli that will appear at the attended location. Functional imaging in humans has provided evidence for stimulus-independent increases in activity during attentional expectation, which have also been interpreted as expressing top–down influences^{32,92}. Similar conclusions can be drawn from studies of delay-period activity during

OPTICAL IMAGING

Recording of neural activity by measuring the optical properties of brain tissue, using either voltage-sensitive dyes or intrinsic signals related to the oxygen saturation of haemoglobin.

CORRELOGRAM

A histogram describing the time relation between two signals, in which a centre peak indicates synchrony and side peaks reflect oscillations.

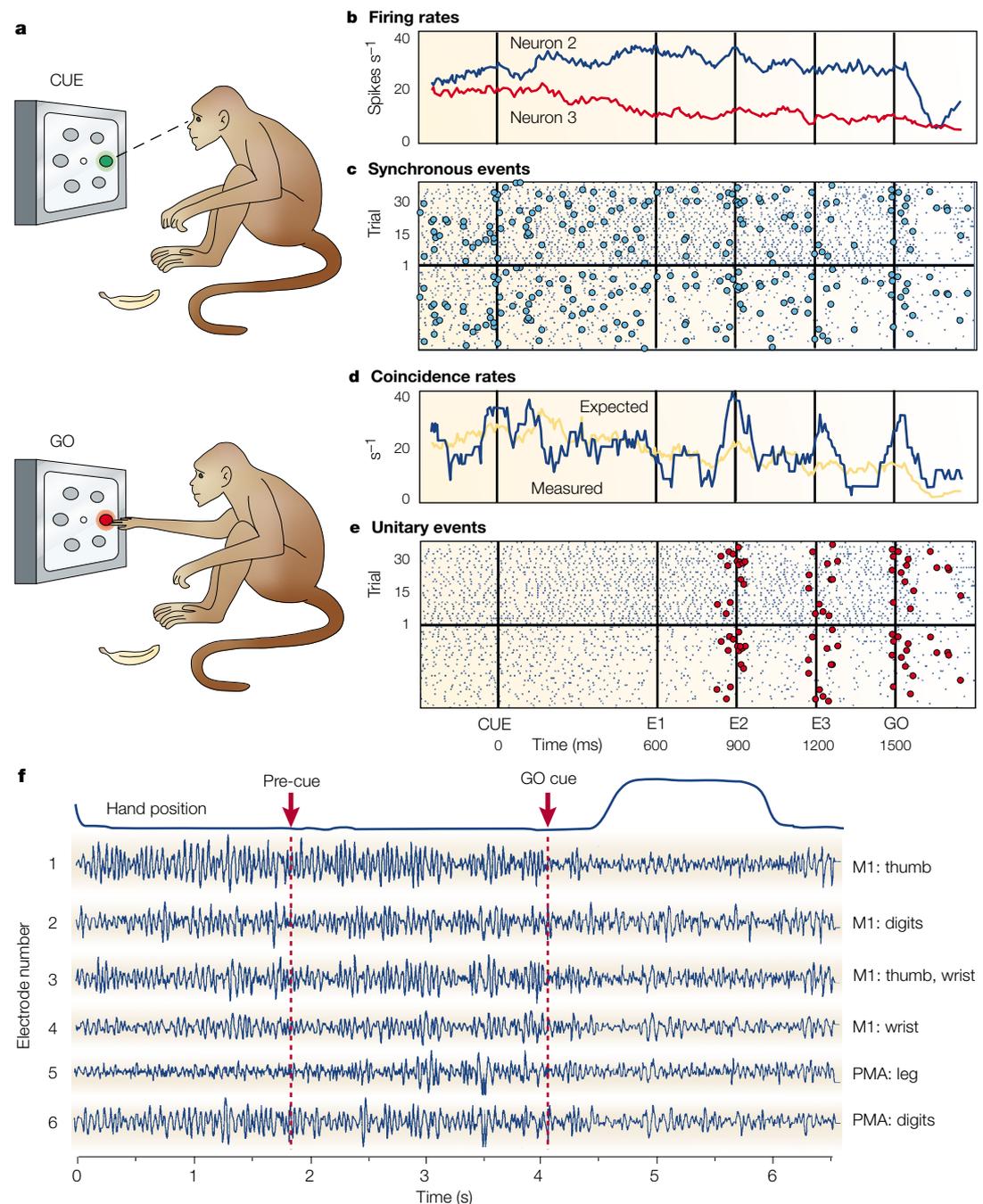


Figure 2 | Synchronization during movement preparation in the monkey. **a** Macaque monkeys were trained to a delayed pointing task³¹. They had to touch a target on a video screen. Target position was indicated by a preparatory CUE (green circle). Before responding, the monkey had to wait until a GO signal occurred at the same location (red circle) after variable delays of 600, 900, 1200 or 1500 ms. **b–e** | Synchronous firing of two simultaneously recorded neurons from primary motor cortex during trials with the longest preparatory period (1500 ms). The monkey could expect the response signal (GO) at three successive times (E1, E2, and E3) before it appeared. **b** | Spike discharge rate for the two neurons. **c** | Raster displays of the discharges (top, neuron 2; bottom, neuron 3) with superimposed labels for spike coincidences (blue dots, precision window of 5 ms). **d** | Measured and expected coincidence rates. The measured coincidence rate (blue curve) was derived by sliding a window of 100 ms in steps of 5 ms over the synchronous events. The expected coincidence rate (yellow curve) was calculated from the product of the individual firing rates. **e** | Analysis of ‘unitary events’. For each time window, the statistical significance for a difference between measured and expected coincidence rates was calculated³¹. Epochs containing significant excess coincidences are marked as unitary events (red dots), which are clustered around the expected occurrence times of the GO signal. **f** | Local field potential (LFP) synchrony in primary motor and premotor cortex during movement preparation¹⁰². Monkeys were trained to perform wrist- or finger-flexion movements during a delay task. A pre-cue informed the animal about the extent of movement required, which had to be executed after a GO cue. The six black traces show simultaneous LFP recordings from sites in primary motor cortex (M1) and premotor area (PMA). Stimulation at each of the recording sites led to evoked movements as indicated. At all sites, high-frequency oscillations are apparent before and during movement preparation, which diminish in amplitude during movement execution. Note the diversity of oscillations in the various records, from relatively brief bursts (for example, electrode 5) to sustained oscillations (for example, electrode 1). The LFP fluctuations are synchronized across all recording sites. Panels **b–e** adapted with permission from REF. 31 © 1997 American Association for the Advancement of Science; panel **f** modified with permission from REF. 102 © 1993 National Academy of Science USA.

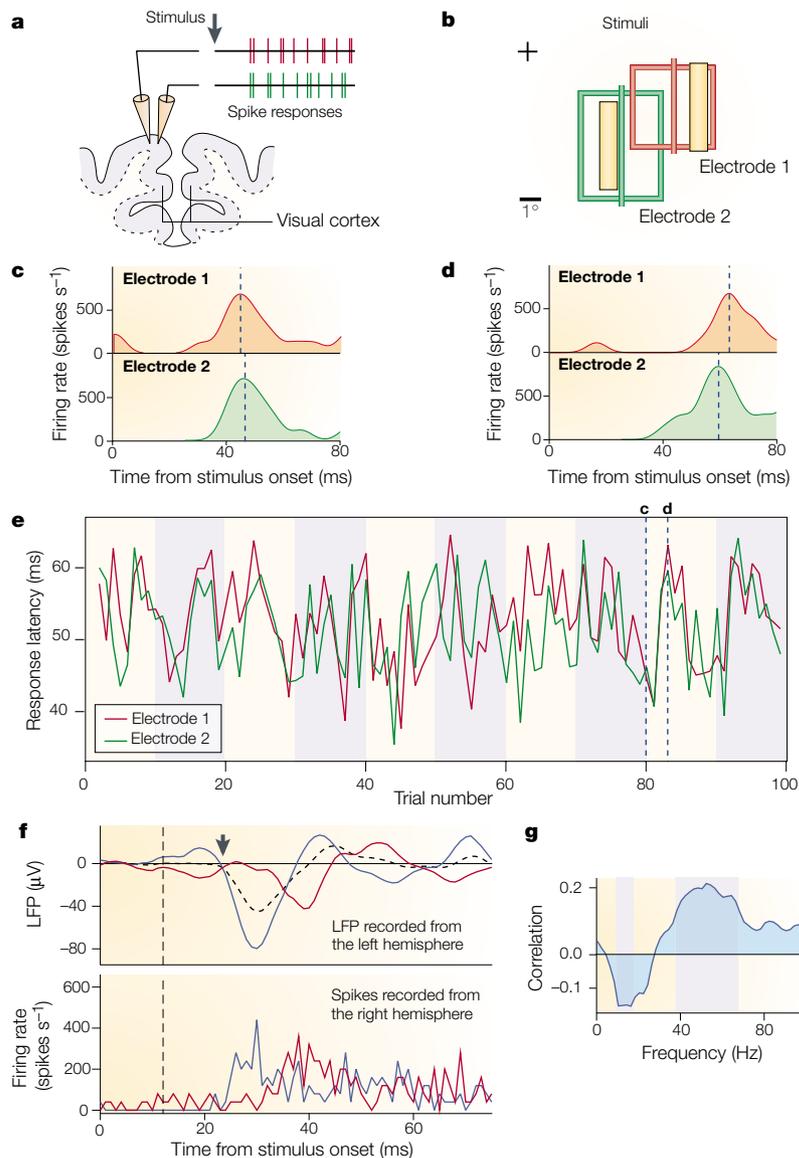


Figure 3 | Predictive power of ongoing oscillations. **a** | Unit activity was recorded simultaneously from multiple sites in primary visual cortex of anaesthetized cats⁴⁷. **b** | Light bars of optimal orientation (yellow) were flashed into the cells' receptive fields (red and green outlines). **c, d** | Spike density functions were computed for all trials by gaussian convolution of the spikes. Response latencies were determined by taking the peak of the spike density function (dashed blue lines). The panels illustrate two trials with short (**c**) and long (**d**) response latencies. **e** | Covariation of latencies for the same neurons across 100 successive trials (abscissa). The dashed vertical lines indicate the trials shown in **c** and **d**. **f** | To test the predictive nature of local field potential (LFP) signals, response latencies were compared for LFP and unit recordings from the left and right hemisphere, respectively. The top panel shows averaged LFPs (25 trials), the trajectories of which fall (blue) or rise (red) in the interval preceding response onset. Response onset (arrow) was determined from the grand average of all LFPs (dashed black curve), which corresponds to the visually evoked potential. About 10 ms before response onset (dashed vertical line), the two groups of LFPs start to differ significantly. The bottom panel displays averaged unit responses of neurons that were, simultaneously with the LFP, recorded from a site in the right hemisphere. Traces show averages of firing rates calculated separately for the two groups of trials with falling and rising LFPs. Responses preceded by negative-going LFPs have short latencies (blue), whereas unit responses preceded by positive-going LFPs have long latencies (red). **g** | Bin-wise (2 Hz per bin) correlation between the cross-spectra of the ongoing LFPs (in the 1-s epoch just preceding the light response) and the covariation of unit latencies for 392 pairs of recording sites. Grey shading indicates regions with significance at the 1% level. Positive correlation coefficients for the gamma range (40–70 Hz) indicate that LFP synchrony in this frequency range predicts a strong latency covariation among recorded cells. Conversely, high alpha synchrony predicts weak latency correlation between the units. Panels **c–g** modified with permission from REF. 47 © 2001 Macmillan Magazines Ltd.

working memory tasks. Many studies have shown that sustained activity during delayed response tasks can encode, in a spatially selective and feature-selective manner, expected target stimuli (for review, see REFS 37,39,93). Neurons that produce such sustained activity have been found in many association areas, including prefrontal, posterior parietal and inferotemporal cortex, and also in subcortical structures⁹⁴. Similar predictive changes in neuronal activation levels have also been found during periods of reward expectation^{29,35,94}.

Another well-studied phenomenon that is relevant in this context is motor preparation — the activation of motor and premotor structures that precedes the execution of specific movements^{95–98}. Changes in activity levels during such preparatory states are thought to reflect specific processes, such as response selection, specification of movement parameters and the coordination of relevant neural populations. Activity in preparatory periods has been shown to predict, for instance, the direction, latency and speed of subsequent movements^{95,97,99,100}. The processes of motor preparation and the top-down-controlled aspects of sensory processing ('sensory preparation') could be similar in terms of their dynamic organization, as both involve internally generated states of prediction, or anticipation, and both are related, at least partly, to common sources of modulation, such as the prefrontal cortex^{26,27,37}.

Recent studies provide evidence that not only changes in discharge rate, but also changes in neural synchrony, can be predictive in nature. Motor and premotor neurons engage in synchronous firing during preparatory delay periods^{31,101–104}. Riehle *et al.*^{31,101} showed that, in a delayed reaching task (FIG. 2a), synchrony occurred particularly at those times when the monkey was expecting a GO signal to appear on the screen (FIG. 2b–e). Interestingly, in those trials in which the GO signal appeared after prolonged periods of expectation, the number of significantly synchronized events increased over the delay period³¹ (FIG. 2e), and spike synchrony became more precise as the GO cue approached¹⁰¹. This indicates a relationship between growing stimulus expectancy and the synchronization of network activity. Moreover, the level of synchrony clearly predicted both the performance and the reaction times of the animal. In most of the cells recorded, the expectation-related changes in synchrony were not accompanied by similar modulations of firing rates.

The enhanced synchrony of preparatory activity often goes along with oscillatory patterning^{102–104}. So, motor cortical neurons can engage in high-frequency (beta and gamma) oscillations that are particularly strong and well synchronized during the expectation of GO signals, and that become weaker and less well synchronized across recording sites during subsequent movement execution (FIG. 2f). Moreover, preparatory neural signals are coherent over considerable distances in the motor cortex, compatible with the idea that top-down processing during planning and response selection requires states of large-scale integration^{18,43,49,105}. This is also supported by a recent study by Bressler *et al.*⁸⁷, who investigated coherence among prefrontal recording sites in monkeys performing

a visuospatial pattern discrimination task. During anticipation of the visual stimulus, prefrontal sites selectively participated in a large-scale network that synchronized in the beta frequency range. The degree of synchrony between the recording sites was highly correlated with

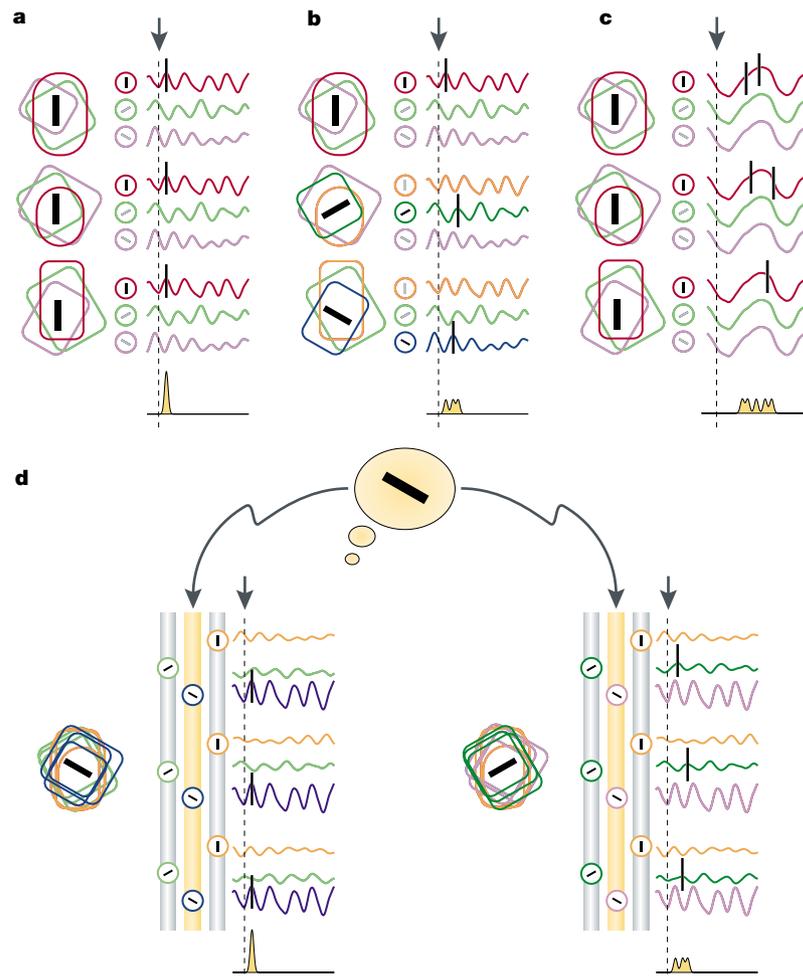


Figure 4 | Subthreshold oscillations can control spike synchrony in a feature-specific way. Hypothetical model summarizing the experimental data illustrated in FIG. 3. **a** | Three groups of neurons (red, green and blue) are considered with different orientation preferences (bars) and receptive fields at three different locations in the visual field. It is assumed that local field potentials reflecting membrane potential fluctuations (right) oscillate in the gamma range and are coherent for neurons with the same, but incoherent for neurons with different, orientation preference. A stimulus array of three vertical bars (black bars over the receptive fields) drives neurons selective for vertical orientations (time of EPSP arrival indicated by arrow and dashed line). Response onsets are shifted coherently due to correlated membrane potential fluctuations, leading to a well-synchronized population response, as indicated by the sharp spike density function (bottom). **b** | Conventions as in **a**, but stimulation with bars of different orientations. As the membrane potentials of the activated neurons fluctuate incoherently, response onsets are not synchronized, and the population response is temporally dispersed (bottom). **c** | If the ongoing oscillations with low frequency are coherent across all neuronal groups, the collinear stimulus configuration (cf. **a**) does not lead to first-spike synchrony. Due to their low frequency, the membrane potential oscillations have no latency-shifting effect. Neurons fire more spikes than with gamma-dominated ongoing oscillations, but latencies are longer, and responses are spread out in time. **d** | We propose that top-down influences can enhance the coherence of ongoing oscillations selectively for subsets of neurons in the network. Neurons participating in coherently oscillating assemblies before stimulus onset will, when stimulated, show well-synchronized responses that are transmitted faster and more reliably than non-synchronized responses. So, stimuli that meet the 'expectancies' expressed by coherent states of the network generate more salient responses (left) than non-attended or unexpected stimuli (right). Panels **a–c** modified with permission from REF. 47 © Macmillan Magazines Ltd.

the animal's response times, and with the amplitude and latency of visual evoked potentials.

Data obtained in the visual cortex indicate that ongoing oscillations also contribute to sensory processing by biasing the coherence of stimulus-induced neuronal discharges⁴⁷. As illustrated in FIG. 3a–e, pairs of neurons can show correlated fluctuations in response latency in response to the repeated presentation of flashed stimuli within their receptive fields. These latency — or first-spike — correlations can occur both within and across the hemispheres, and are stronger for cells with overlapping receptive fields and similar orientation preferences. Moreover, first-spike synchrony depends on the dynamics of the ongoing activity, occurring only when the network shows coherent gamma oscillations in the epoch that precedes the response. The phase of these gamma oscillations at response onset predicts the absolute latency of the neuronal spike response (FIG. 3f). Low-frequency oscillations, by contrast, go along with a decrease in the strength of first-spike synchronization (FIG. 3g) and a prolongation of the absolute response latencies⁴⁷. As shown by EEG studies, these latency variations correlate with behaviour — high-frequency rhythms in ongoing EEG are associated with a shortening of reaction times¹⁰⁶, whereas behavioural responses are delayed if the preceding EEG is dominated by low frequencies¹⁰⁷.

These data indicate that coherent and selective membrane potential oscillations are important in sensory processing. Such membrane potential fluctuations define 'windows of depolarization' during which arriving inputs are more effective than during hyperpolarized states^{108,109}. This leads not only to the phase-specific gating of transmission, but also to a shifting of spike latencies, and therefore to effective modulation of temporal relations between neuronal discharges (FIG. 4a–c). Such a mechanism could have several advantages. First, column-specific patterns of coherent subthreshold oscillations could provide templates for the 'filtering' of incoming patterns. Second, such a mechanism allows a rapid build-up of assemblies of synchronized neurons, leading to enhanced processing speed and reliability. Third, ongoing oscillations could allow the subliminal priming of stimuli. If latency shifting can be controlled by top-down influences, then the saliency of neuronal responses coding for an expected stimulus could be enhanced efficiently (FIG. 4d). Other populations that do not code for the expected stimulus would not be primed, and would therefore have longer latencies and be less well synchronized. So, the saliency of these signals in the network would be lower, because they are not as easily recognized and processed by other centres as highly coincident signals^{44–46,110}. Together, the data indicate that ongoing neural synchrony and oscillatory patterning can have a predictive function in sensorimotor networks. In the case of motor preparation, they seem to reflect the dynamic organization of distributed populations of motor and premotor neurons. On the sensory side, the establishment of selective temporal relations before stimulus onset could lead to the priming of particular stimulus constellations, to which the organism will then respond faster and with high reliability.

Outlook: synchrony and top-down processing

The data reviewed indicate that top-down processing is, in many instances, associated with modulation of the temporal structure of both ongoing and stimulus-evoked activity. In a wider sense, top-down influences can be defined as intrinsic sources of contextual modulation of neural processing. Obviously, top-down factors include the activity of systems involved in goal definition, action planning, working memory and selective attention^{12,25–27,29,37,39,57}. These seem to be implemented by large-scale assemblies that comprise neuronal populations in widespread networks of frontal, parietal and limbic areas. Top-down interactions could then be mediated by the entraining effect that such assemblies carrying high-level representations might exert on assemblies involved in the processing of specific new information. Moreover, long-term memory is an important source of top-down processing. In our view, this includes not only declarative memories, but also the procedural knowledge stored in the functional architecture of sensorimotor networks. Network architecture could constitute an ‘implicit’ source of top-down influences as, for instance, the topology of lateral connections within cortical areas is known to embody stored predictions that have been acquired both during evolution and through experience-dependent learning, and have proven to be of adaptive value^{16,21,22,36,42,111}. Furthermore, we should consider the activity of arousal systems that have important gating functions in thalamocortical processing^{83–86}. Finally, sensorimotor context also provides an important top-down source of contextual modulation. Motor control requires internal forward models that lead to predictions (expressed as ‘corollary discharges’) about the sensory consequences of motor commands, and there is clear evidence that such predictions have an enormous impact on the interpretation of bottom-up inputs^{112,113}.

Temporal binding mechanisms (BOX 2) might have a key role in top-down processing. As top-down influences do not arise from small, localized groups of ‘command neurons’, but from highly distributed populations that store high-level contents, the organization of such influences into meaningful patterns clearly requires binding functions. If top-down processing presupposes the activation of widespread networks, mechanisms are required that coordinate the interactions of neuronal populations across areas. Moreover, fundamental superposition problems⁴⁰ need to be solved that arise from the very nature of distributed assembly coding, and which therefore reiterate in the case of top-down processing. As assemblies can partly share the same neurons, responses must be specifically tagged as belonging to one particular assembly to avoid ambiguities in representational states. As discussed elsewhere^{16,17,41–43}, temporal binding could provide a convenient and physiologically plausible solution to these problems. Another important aspect is that the temporal patterning of activity patterns could be ideally suited to achieve matching of top-down predictions with bottom-up inputs, as implied by Grossberg’s adaptive resonance theory^{22,36}. If top-down effects

induce a particular pattern of subthreshold fluctuations in dendrites of the target population, these could be ‘compared’ with temporal patterns arising from peripheral input by virtue of the fact that phase-shifted fluctuations will cancel each other, whereas in-phase signals will summate and amplify in a highly nonlinear way, leading to a salient postsynaptic signal (FIG. 4). So, temporal patterning could provide a straightforward implementation of the mechanisms of ‘quenching’ and amplification predicted by the Grossberg model^{22,36}.

On the basis of these considerations and the evidence reviewed earlier, we suggest a broadening of the idea of ‘top-down’ to include what we have termed the ‘dynamicist’ view (BOX 1) — the idea that large-scale dynamics^{18,34,49,105}, expressing contextual influences and knowledge stored in the system, can influence local processing^{105,111}. In this sense, top-down processing would not be confined to feedback in a processing hierarchy, but, rather, would involve a wide variety of brain signals that convey information related to previous experience. The view that emerges from the available evidence can be summarized as follows. Temporal patterning can be important for all steps of top-down processing (the creation and distribution of top-down signals, as well as their dynamic resonance, or matching, with bottom-up inputs). Incoming afferent signals induce some patterning of activity in cortical areas that arises from local computations operating on the input. These local patterns, however, are constantly subject to modulation by specific synchronizing and desynchronizing influences that impinge on the respective region through long-range interactions, both from other cell populations in the same area and from assemblies that are activated in other areas. These modulatory influences carry predictions — expressed as temporal patterns across the long-range inputs — about specific feature constellations. The various influences compete for stable, resonant states of the involved cell populations that would express a successful match of the input to the predicted constellation. Such a successful match will result in the amplification of a specific pattern of synchronized neural discharges, which, in turn, will be broadcast as a salient signal to other neuronal populations and support the stabilization of large-scale patterns of temporal coherence. As discussed above, the modulatory effects, or priming of assemblies, can arise from intrinsic interactions in the absence of stimuli and, hence, be expressed in ongoing activity. It should also be noted that our model does not imply that particular ‘interface’ areas would be dedicated to the matching process. Where the match is computed should depend on the context of the task or behavioural situation, and on the nature of the stimuli. Any area could, in principle, modulate any other area to which it is connected. The process of reentry^{12,54,55} is ‘democratic’ in the sense that ‘majority votes’ count, but superiority in an anatomical hierarchy might not. So, synchronizing influences from a large number of areas that exploit different binding criteria could compete, and the binding solution that is compatible with maximal resonance could win.

In conclusion, the model proposed here attempts to integrate the evidence for self-generated temporal dynamics in neuronal networks, with the view of the active and adaptive brain that has emerged during recent years. This dynamicist model yields several suggestions for future research: experiments on awake brains engaged in sensorimotor contexts should provide evidence that top-down processing is reflected in large-scale coherence across areas or subsystems, and that such

patterns of large-scale integration can covary with specific predictions about forthcoming stimuli. Moreover, it would be of interest to study phase coupling between oscillations in different frequency bands during epochs of cross-systems interactions, reflecting, for instance, neocortical-hippocampal binding¹¹⁴. Finally, attempts could be made to interfere with predictions that are important for perception or action by manipulating the spatiotemporal patterning of ongoing activity.

1. Varela, F. J., Thompson, E. & Rosch, E. *The Embodied Mind* (MIT Press, Cambridge, Massachusetts, 1991).
2. Ullman, S. in *Representations of Vision* (ed. Gorea, A.) 305–317 (Cambridge Univ. Press, Cambridge, UK, 1991).
3. Churchland, P. S., Ramachandran, V. S. & Sejnowski, T. J. in *Large-Scale Neuronal Theories of the Brain* (eds Koch, C. & Davis, J. L.) 23–60 (MIT Press, Cambridge, Massachusetts, 1994).
4. Aloimonos, Y. & Rosenfeld, A. Computer vision. *Science* **253**, 1249–1254 (1991).
5. Hubel, D. H. & Wiesel, T. N. Receptive fields and functional architecture in two nonstriate visual areas (18 and 19) of the cat. *J. Neurophysiol.* **28**, 229–289 (1965).
6. Marr, D. *Vision* (Freeman, San Francisco, 1982).
7. Biederman, I. Recognition-by-components: a theory of human image understanding. *Psychol. Rev.* **94**, 115–147 (1987).
8. Thorpe, S., Fize, D. & Marlot, C. Speed of processing in the human visual system. *Nature* **381**, 520–522 (1996).
9. Livingstone, M. & Hubel, D. Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science* **240**, 740–749 (1988).
10. DeYoe, E. A. & Van Essen, D. C. Concurrent processing streams in monkey visual cortex. *Trends Neurosci.* **11**, 219–226 (1988).
11. Barlow, H. B. Single units and sensation: a neuron doctrine for perceptual psychology? *Perception* **1**, 371–394 (1972).
12. Edelman, G. M. *The Remembered Present* (Basic Books, New York, 1989).
13. Clark, A. An embodied cognitive science? *Trends Cogn. Sci.* **3**, 345–351 (1999).
14. Port, R. F. & Van Gelder, T. (eds) *Mind as Motion* (MIT Press, Cambridge, Massachusetts, 1995).
15. Beer, R. D. Dynamical approaches to cognitive science. *Trends Cogn. Sci.* **4**, 91–99 (2000).
16. Singer, W. & Gray, C. M. Visual feature integration and the temporal correlation hypothesis. *Annu. Rev. Neurosci.* **18**, 555–586 (1995).
17. Engel, A. K. & Singer, W. Temporal binding and the neural correlates of sensory awareness. *Trends Cogn. Sci.* **5**, 16–25 (2001).
18. Varela, F., Lachaux, J.-P., Rodriguez, E. & Martinerie, J. The brainweb: phase synchronization and large-scale integration. *Nature Rev. Neurosci.* **2**, 229–239 (2001).
19. Markman, A. B. & Dietrich, E. Extending the classical view of representation. *Trends Cogn. Sci.* **4**, 470–475 (2000).
20. Rumelhart, D. E., McClelland, J. L. & the PDP Research Group (eds) *Parallel Distributed Processing* Vol. 1 (MIT Press, Cambridge, Massachusetts, 1986).
21. Hebb, D. O. *The Organization of Behavior* (Wiley, New York, 1949).
22. Grossberg, S. The link between brain learning, attention, and consciousness. *Conscious. Cogn.* **8**, 1–44 (1999).
23. Mumford, D. On the computational architecture of the neocortex. *Biol. Cybern.* **66**, 241–251 (1992).
24. Ullman, S. Sequence seeking and counter streams: a computational model for bidirectional information flow in the visual cortex. *Cereb. Cortex* **5**, 1–11 (1995).
25. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* **18**, 193–222 (1995).
26. Miller, E. K. & Cohen, J. D. An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* **24**, 167–202 (2001).
27. Schall, J. D. Neural basis of deciding, choosing and acting. *Nature Rev. Neurosci.* **2**, 33–42 (2001).
28. König, P. & Luksch, H. Active sensing — closing multiple loops. *Z. Naturforsch. [C]* **53**, 542–549 (1998).
29. Schultz, W. Multiple reward signals in the brain. *Nature Rev. Neurosci.* **1**, 199–207 (2000).
30. De Oliveira, S. C., Thiele, A. & Hoffmann, K. P. Synchronization of neuronal activity during stimulus expectation in a direction discrimination task. *J. Neurosci.* **17**, 9248–9260 (1997).
31. Riehle, A., Gruen, S., Diesmann, M. & Aertsen, A. Spike synchronization and rate modulation differentially involved in motor cortical function. *Science* **278**, 1950–1953 (1997).
- A study describing synchrony among motor neurons during anticipation of a GO cue. Temporal correlation is enhanced at time points when the animal expects the cue to appear.**
32. Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R. & Ungerleider, L. G. Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron* **22**, 751–761 (1999).
33. Shulman, G. L. et al. Areas involved in encoding and applying directional expectations to moving objects. *J. Neurosci.* **19**, 9480–9496 (1999).
34. Von Stein, A., Chiang, C. & König, P. Top-down processing mediated by interareal synchronization. *Proc. Natl Acad. Sci. USA* **97**, 14748–14753 (2000).
- The paper describes synchrony between visual areas in awake cats during a GO/NO-GO task. Depending on the behavioural significance of the stimulus, interareal interactions occur in different frequency bands. Phase relations are compatible with top-down processing.**
35. Breiter, H. C., Aharon, I., Kahneman, D., Dale, A. & Shizgal, P. Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron* **30**, 619–639 (2001).
36. Grossberg, S. How does the brain build a cognitive code? *Psychol. Rev.* **87**, 1–51 (1980).
37. Fuster, J. M. *The Prefrontal Cortex* (Raven, New York, 1989).
38. Frith, C. & Dolan, R. J. Brain mechanisms associated with top-down processes in perception. *Phil. Trans. R. Soc. Lond. B* **352**, 1221–1230 (1997).
39. Miller, E. K. The prefrontal cortex and cognitive control. *Nature Rev. Neurosci.* **1**, 59–65 (2000).
40. Von der Malsburg, C. in *Models of Neural Networks II* (eds Domany, E., Van Hemmen, J. L. & Schulten, K.) 95–119 (Springer, Berlin, 1994).
41. Engel, A. K., König, P., Kreiter, A. K., Schillen T. B. & Singer, W. Temporal coding in the visual cortex: new vistas on integration in the nervous system. *Trends Neurosci.* **15**, 218–226 (1992).
42. Singer, W. Neuronal synchrony: a versatile code for the definition of relations? *Neuron* **24**, 49–65 (1999).
43. Roelfsema, P. R., Engel, A. K., König, P. & Singer, W. The role of neuronal synchronization in response selection: a biologically plausible theory of structured representation in the visual cortex. *J. Cogn. Neurosci.* **8**, 603–625 (1996).
- A model is presented of how synchrony could be relevant for dynamic response selection during sensorimotor processing.**
44. Abeles, M. Role of the cortical neuron: integrator or coincidence detector? *Isr. J. Med. Sci.* **18**, 83–92 (1982).
45. König, P., Engel, A. K. & Singer, W. Integrator or coincidence detector? The role of the cortical neuron revisited. *Trends Neurosci.* **19**, 130–137 (1996).
46. Alonso, J. M., Usrey, W. M. & Reid, R. C. Precisely correlated firing in cells of the lateral geniculate nucleus. *Nature* **383**, 815–819 (1996).
47. Fries, P., Neuenschwander, S., Engel, A. K., Goebel, R. & Singer, W. Rapid feature selective neuronal synchronization through correlated latency shifting. *Nature Neurosci.* **4**, 194–200 (2001).
- Study of first-spike synchrony observed between spatially separate neurons in cat visual cortex. Temporal patterning of ongoing activity in the epoch preceding the stimulus is shown to predict the latency correlation induced by stimulation.**
48. Tallon-Baudry, C. & Bertrand, O. Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn. Sci.* **3**, 151–162 (1999).
49. Von Stein, A. & Sarnthein, J. Different frequencies for different scales of cortical integration: from local gamma to long-range alpha/theta synchronization. *Int. J. Psychophysiol.* **38**, 301–313 (2001).
50. Fries, P., Roelfsema, P. R., Engel, A. K., König, P. & Singer, W. Synchronization of oscillatory responses in visual cortex correlates with perception in interocular rivalry. *Proc. Natl Acad. Sci. USA* **94**, 12699–12704 (1997).
51. Fries, P., Reynolds, J. H., Rorie, A. E. & Desimone, R. Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* **291**, 1560–1563 (2001).
- This paper shows that in monkey V4, attention enhances the coupling between spikes and field potentials, reflecting a coherent local population, in a spatially selective manner. This effect occurs in ongoing activity during stimulus expectation.**
52. Damasio, A. R. The brain binds entities and events by multiregional activation from convergence zones. *Neural Comput.* **1**, 123–132 (1989).
53. Damasio, A. R. Synchronous activation in multiple cortical regions: a mechanism for recall. *Semin. Neurosci.* **2**, 287–296 (1990).
54. Tononi, G., Sporns, O. & Edelman, G. M. Reentry and the problem of integrating multiple cortical areas: simulation of dynamic integration in the visual system. *Cereb. Cortex* **2**, 310–335 (1992).
55. Lumer, E. D., Edelman, G. M. & Tononi, G. Neural dynamics in a model of the thalamocortical system. I. Layers, loops and the emergence of fast synchronous rhythms. *Cereb. Cortex* **7**, 207–227 (1997).
56. Koechlin, E., Anton, J. L. & Burnod, Y. Dynamical computational processing of local cortical networks for visual and motor processing: a bayesian framework. *J. Physiol. (Paris)* **90**, 257–262 (1996).
57. Kastner, S. & Ungerleider, L. G. Mechanisms of visual attention in the human cortex. *Annu. Rev. Neurosci.* **23**, 315–341 (2000).
58. Treue, S. Neural correlates of attention in primate visual cortex. *Trends Neurosci.* **24**, 295–300 (2001).
59. Büchel, C. & Friston, K. J. Modulation of connectivity in visual pathways by attention: cortical interactions evaluated with structural equation modelling and fMRI. *Cereb. Cortex* **7**, 768–778 (1997).
60. Rowe, J. et al. Attention to action in Parkinson's disease: impaired effective connectivity among frontal cortical regions. *Brain* (in the press).
61. Haenny, P., Maunsell, J. H. R. & Schiller, P. H. State dependent activity in monkey visual cortex. II. Retinal and extraretinal factors in V4. *Exp. Brain Res.* **69**, 245–259 (1988).
62. Steinmetz, P. N. et al. Attention modulates synchronized neuronal firing in primate somatosensory cortex. *Nature* **404**, 187–190 (2000).
- Among the first studies to show, at the cellular level, that attention modulates synchrony in neuronal assemblies.**
63. Roelfsema, P. R., Engel, A. K., König, P. & Singer, W. Visuomotor integration is associated with zero-lag synchronization among cortical areas. *Nature* **385**, 157–161 (1997).
64. Bernasconi, C., Von Stein, A., Chiang, C. & König, P. Bidirectional interactions between visual areas in the awake behaving cat. *Neuroreport* **11**, 1–4 (2000).
65. Tiitinen, H. et al. Selective attention enhances the auditory 40-Hz transient response in humans. *Nature* **364**, 59–60 (1993).
66. Tallon-Baudry, C., Bertrand, O., Peronnet, F. & Pernier, J. Oscillatory γ -band (30–70 Hz) activity induced by a visual search task in humans. *J. Neurosci.* **17**, 722–734 (1997).
- The authors were among the first to show that induced (non-phase-locked) gamma-band oscillations can specifically reflect top-down processing in humans.**
67. Gruber, T., Müller, M. M., Keil, A. & Elbert, T. Selective visual-spatial attention alters induced gamma band

- responses in the human EEG. *Clin. Neurophysiol.* **110**, 2074–2085 (1999).
68. Müller, M. M., Gruber, T. & Keil, A. Modulation of induced gamma band activity in the human EEG by attention and visual information processing. *Int. J. Psychophysiol.* **38**, 283–299 (2001).
69. Rodriguez, E. *et al.* Perception's shadow: long-distance synchronization of human brain activity. *Nature* **397**, 430–433 (1999).
- This and the next paper represent pioneering studies in which phase synchrony among EEG signals was analysed separately from changes in spectral power.**
70. Milner, W. H. R., Braun, C., Arnold, M., Witte, H. & Taub E. Coherence of gamma-band EEG activity as a basis for associative learning. *Nature* **397**, 434–436 (1999).
71. Pulvermüller, F., Lutzenberger, W., Preissl, H. & Birbaumer, N. Spectral responses in the gamma-band: physiological signs of higher cognitive processes? *Neuroreport* **6**, 2059–2064 (1995).
72. Müller, M. M., Keil, A., Gruber, T. & Elbert, T. Processing of affective picture modulates right-hemispheric gamma band EEG activity. *Clin. Neurophysiol.* **110**, 1913–1920 (1999).
73. Karakas, S., Basar-Eroglu, C., Özsemit, C., Kafadar, H. & Erzen, Ö. U. Gamma response of the brain: a multifunctional oscillation that represents bottom-up with top-down processing. *Int. J. Psychophysiol.* **39**, 137–150 (2001).
74. Sarnthein, J., Rappelsberger, P., Shaw, G. L. & Von Stein, A. Synchronization between prefrontal and posterior association cortex during working memory tasks in humans. *Proc. Natl Acad. Sci. USA* **95**, 7092–7096 (1998).
75. Goebel, R., Khorram-Sefat, D., Muckli, L., Hacker, H. & Singer, W. The constructive nature of vision: direct evidence from functional magnetic resonance imaging studies of apparent motion and motion imagery. *Eur. J. Neurosci.* **10**, 1563–1573 (1998).
76. Dierks, T. *et al.* Activation of Heschl's gyrus during auditory hallucinations. *Neuron* **22**, 615–621 (1999).
77. Shadlen, M. & Newsome, W. T. Noise, neural codes and cortical organization. *Curr. Opin. Neurobiol.* **4**, 569–579 (1994).
78. Arieli, A., Shoham, D., Hildesheim, R. & Grinvald, A. Coherent spatiotemporal patterns of ongoing activity revealed by real-time optical imaging coupled with single-unit recording in the cat visual cortex. *J. Neurophysiol.* **73**, 2072–2093 (1995).
79. Arieli, A., Sterkin, A., Grinvald, A. & Aertsen, A. Dynamics of ongoing activity: explanation of the large variability in evoked cortical responses. *Science* **273**, 1868–1871 (1996).
80. Tsodyks, M., Kenet, T., Grinvald, A. & Arieli, A. Linking spontaneous activity of single cortical neurons and the underlying functional architecture. *Science* **286**, 1943–1946 (1999).
- A very important paper showing that patterning of ongoing activity is related to the functional architecture of the cortical network.**
81. Bouyer, J. J., Montaron, M. F. & Rougeul, A. Fast frontoparietal rhythms during combined focused attentive behaviour and immobility in the cat: cortical and thalamic localizations. *Electroencephalogr. Clin. Neurophysiol.* **51**, 244–252 (1981).
82. Sheer, D. E. in *Springer Series in Brain Dynamics 2* (eds Basar, E. & Bullock, T. M.) 339–374 (Springer, Berlin, 1989).
83. Steriade, M., Amzica, F. & Contreras, D. Synchronization of fast (30–40 Hz) spontaneous cortical rhythms during brain activation. *J. Neurosci.* **16**, 392–417 (1996).
84. Steriade, M., Contreras, D., Amzica, F. & Timofeev, I. Synchronization of fast (30–40 Hz) spontaneous oscillations in intrathalamic and thalamocortical networks. *J. Neurosci.* **16**, 2788–2808 (1996).
85. Steriade, M. & Amzica, F. Intracortical and corticothalamic coherency of fast spontaneous oscillations. *Proc. Natl Acad. Sci. USA* **93**, 2533–2538 (1996).
86. Munk, M. H. J., Roelfsema, P. R., König, P., Engel, A. K. & Singer, W. Role of reticular activation in the modulation of intracortical synchronization. *Science* **272**, 271–274 (1996).
87. Bressler, S. L., Liang, H. & Ding, M. Top-down influence on early visual processing by an anticipatory large-scale network in macaque prefrontal cortex. *Soc. Neurosci. Abstr.* **27**, 533.1 (2001).
88. Nelson, J. I., Salin, P. A., Munk, M. H. J., Arzi, M. & Bullier, J. Spatial and temporal coherence in cortico-cortical connections: a cross-correlation study in areas 17 and 18 in the cat. *Vis. Neurosci.* **9**, 21–37 (1992).
89. Siegel, M., Kording, K. & König, P. Integrating top-down and bottom-up sensory processing by somato-dendritic interactions. *J. Comput. Neurosci.* **8**, 161–173 (2000).
- A computational model that relates top-down processing to neural synchrony. It is suggested that neuronal bursting behaviour can implement the matching of bottom-up and top-down influences.**
90. Lampl, I., Reichova, I. & Ferster, D. Synchronous membrane potential fluctuations in neurons of the cat visual cortex. *Neuron* **22**, 361–374 (1999).
91. Luck, S. J., Chelazzi, L., Hillyard, S. A. & Desimone, R. Neural mechanisms of spatial selective attention in areas V1, V2 and V4 of macaque visual cortex. *J. Neurophysiol.* **77**, 24–42 (1997).
92. Ress, D., Backus, B. T. & Heeger, D. J. Activity in primary visual cortex predicts performance in a visual detection task. *Nature Neurosci.* **3**, 940–945 (2000).
93. Wang, X.-J. Synaptic reverberations underlying mnemonic persistent activity. *Trends Neurosci.* **24**, 455–463 (2001).
94. Hikosaka, O., Sakamoto, M. & Usui, S. Functional properties of monkey caudate neurons. III. Activities related to expectation of target and reward. *J. Neurophysiol.* **61**, 814–832 (1989).
95. Riehle, A. & Requin, J. The predictive value for performance speed of preparatory changes in activity of the monkey motor and premotor cortex. *Behav. Brain Res.* **53**, 35–49 (1993).
96. Vaadia, E., Kurata, K. & Wise, S. P. Neuronal activity preceding directional and nondirectional cues in the premotor cortex of rhesus monkeys. *Somatosens. Mot. Res.* **6**, 207–230 (1988).
97. Crammond, D. J. & Kalaska, J. F. Prior information in motor and premotor cortex: activity during the delay period and effect on pre-movement activity. *J. Neurophysiol.* **84**, 986–1005 (2000).
98. Bussaoud, D. Attention versus intention in the primate premotor cortex. *Neuroimage* **14**, S40–45 (2001).
99. Bruce, C. J. & Goldberg, M. E. Primate frontal eye fields. I. Single neurons discharging before saccades. *J. Neurophysiol.* **53**, 603–635 (1985).
100. Dorris, M. C., Pare, M. & Munoz, D. P. Immediate neural plasticity shapes motor performance. *J. Neurosci.* **20**, RC52, 1–5 (2000).
101. Riehle, A., Grammont, F., Diesmann, M. & Grün, S. Dynamical changes and temporal precision of synchronized spiking activity in monkey motor cortex during movement preparation. *J. Physiol. (Paris)* **94**, 569–582 (2000).
102. Sanes, J. N. & Donoghue, J. P. Oscillations in local field potentials of the primate motor cortex during voluntary movement. *Proc. Natl Acad. Sci. USA* **90**, 4470–4474 (1993).
103. Donoghue, J. P., Sanes, J. N., Hatsopoulos, N. G. & Gaal, G. Neural discharge and local field potential oscillations in primate motor cortex during voluntary movements. *J. Neurophysiol.* **79**, 159–173 (1998).
104. MacKay, W. A. & Mendonca, A. J. Field potential oscillatory bursts in parietal cortex before and during reach. *Brain Res.* **704**, 167–174 (1995).
105. Bressler, S. L. & Kelso, J. A. S. Cortical coordination dynamics and cognition. *Trends Cogn. Sci.* **5**, 26–36 (2001).
106. Jokeit, H. & Makeig, S. Different event-related patterns of γ -band power in brain waves of fast- and slow-reacting subjects. *Proc. Natl Acad. Sci. USA* **91**, 6339–6343 (1994).
107. Adler, J. D. & Siffit, J. Alpha EEG and simple reaction time. *Percept. Mot. Skills* **52**, 306 (1981).
108. Lampl, I. & Yarom, Y. Subthreshold oscillations of the membrane potential: a functional synchronizing and timing device. *J. Neurophysiol.* **70**, 2181–2186 (1993).
- This and the subsequent paper are important *in vitro* studies showing that subthreshold oscillations of the membrane potential of a cell lead to latency shifts of inputs and, hence, provide precise temporal windows for creating synchronized patterns in neural activity.**
109. Volgushev, M., Chistiakova, M. & Singer, W. Modification of discharge patterns of neocortical neurons by induced oscillations of the membrane potential. *Neuroscience* **83**, 15–25 (1998).
110. Azouz, R. & Gray, C. M. Dynamic spike threshold reveals a mechanism for synaptic coincidence detection in cortical neurons *in vivo*. *Proc. Natl Acad. Sci. USA* **97**, 8110–8115 (2000).
111. Phillips, W. A. & Singer, W. In search of common foundations for cortical computation. *Behav. Brain Sci.* **20**, 657–722 (1997).
112. Frith, C. D., Blakemore, S.-J. & Wolpert, D. M. Explaining the symptoms of schizophrenia: abnormalities in the awareness of action. *Brain Res. Rev.* **31**, 357–363 (2000).
113. Driver, J. & Frith, C. Shifting baselines in attention research. *Nature Rev. Neurosci.* **1**, 147–148 (2000).
114. Siapas, A. G. & Wilson, M. A. Coordinated interactions between hippocampal ripples and cortical spindles during slow-wave sleep. *Neuron* **21**, 1123–1128 (1998).
115. Palmer, S. E. *Vision Science. Photons to Phenomenology* (MIT Press, Cambridge, Massachusetts, 1999).
116. Han, S., He, X., Yund, W. & Woods, D. L. Attentional selection in the processing of hierarchical patterns: an ERP study. *Biol. Psychol.* **56**, 113–130 (2001).
117. Rock, I. *The Logic of Perception* (MIT Press, Cambridge, Massachusetts, 1983).
118. Henle, M. Some new Gestalt psychologies. *Psychol. Res.* **51**, 81–85 (1989).
119. Haken, H. in *Synergetics of Cognition* (eds Haken, H. & Stadler, M.) 2–31 (Springer, Berlin, 1990).
120. Shepard, R. N. *Mind Sights* (Falgrave, London, 1990).

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