

A framework for local cortical oscillation patterns

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Oscillations are a pervasive feature of neuronal activity in the cerebral cortex. Here, we propose a framework for understanding local cortical oscillation patterns in cognition: two classes of network interactions underlying two classes of cognitive functions produce different local oscillation patterns. Local excitatory–inhibitory interactions shape neuronal representations of sensory, motor and cognitive variables, and produce local gamma-band oscillations. By contrast, the linkage of such representations by integrative functions such as decision-making is mediated by long-range cortical interactions, which yield more diverse local oscillation patterns often involving the beta range. This framework reconciles different cortical oscillation patterns observed in recent studies and helps to understand the link between cortical oscillations and the fMRI signal. Our framework highlights the notion that cortical oscillations index the specific circuit-level mechanisms of cognition.

Understanding local cortical oscillation patterns in cognition

Groups of neurons in the cerebral cortex are involved in different cognitive functions. These functions are mediated by the different interactions in which a neuronal group engages with other neuronal groups. Many of these interactions are local, confined to small regions of the cortex. Other interactions are long range, spanning even distant cortical and subcortical brain regions. Both classes of interactions often produce local oscillations of neuronal mass activity that can be revealed by spectral analysis (Box 1) [1–3]. The change in the power spectrum of local neuronal activity due to a functional process constitutes the spectral profile of that process (see below).

Local spectral profiles within the neocortex are process-dependent. This is well illustrated in primary visual cortex (V1), for which the spectral profiles of different functions have been particularly well characterized [2]. Visual stimulation enhances oscillations in the gamma frequency band and suppresses lower-frequency (in particular alpha) activity (Figure 1a). This spectral profile differs markedly from that for visual awareness during bistable perceptual suppression phenomena. Within V1, awareness of a salient stimulus during binocular rivalry or flash suppression

seems not reflected in the gamma band, but only in low-frequency (<30 Hz) activity (Figure 1b) [4–6].

Here, we propose that the different spectral profiles observed within a single region of the neocortex result from the different network interactions this region engages in during different cognitive functions. We suggest that two largely overlapping dimensions provide useful heuristics for understanding and predicting local spectral profiles: encoding versus integrative functions and local versus long-range interactions. Encoding functions (such as the encoding of sensory features or motor plans) primarily involve local cortical network interactions. Integrative functions (such as perceptual inference and decision-making) involve long-range interactions among distant brain regions. These different classes of network interactions give rise to different local cortical oscillation patterns: gamma-band oscillations (local encoding) and more diverse oscillations often involving the beta range (integrative functions).

Glossary

Electrophysiological mass activity: generic term for measures of neuronal population activity at different spatial scales such as the local field potential (LFP), intracranial and extracranial electroencephalography (EEG) and magnetoencephalography (MEG).

Local field potential (LFP): low-frequency component (<250 Hz) of the extracellular electrophysiological signal. The LFP reflects summed dendrosomatic currents surrounding the electrode tip (approx. <1 mm) averaged over several hundreds of neurons. The LFP reflects predominantly synchronized synaptic events.

EEG–MEG: electric potentials and magnetic fields produced by the spatial superposition of LFPs measured by means of scalp electrodes or magnetic field sensors. The EEG and MEG predominantly reflect synchronized synaptic events in the dendrites of pyramidal neurons perpendicular to the cortical surface.

Frequency bands: LFP, EEG, and MEG signals are often decomposed into delta (~2–4 Hz), theta (~4–8 Hz), alpha (~8–12 Hz), beta (~12–30 Hz) and gamma bands (~30–100 Hz). These bands are derived from clinical EEG conventions. There are considerable inconsistencies in the exact ranges of these bands across studies. In addition to oscillations, cortical mass activity often exhibits broadband modulations that reflect the average level of synaptic neuronal activity rather than oscillations [14,41].

Perceptual suppression: salient visual stimuli can be suppressed from visual awareness due to bistable perceptual processes [79]. In binocular rivalry, two dissimilar patterns presented to the two eyes are perceived in alternation, with one being suppressed from awareness at any given time. In generalized flash suppression, a salient target presented to one eye disappears from awareness on the onset of a moving surround.

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Box 1. Why use spectral analysis in cognitive neurophysiology?

Spectral analysis is ideally suited for linking electrophysiological mass activity to cognition. Task-related cortical activity typically contains sustained modulations that are induced by, but not phase-locked to, external events such as the stimulus onset or the subject's motor response [2,39,80]. These non-phase-locked activity components cancel out in time domain averages (i.e. event-related fields) but not in averages of the spectral power. The figure illustrates this with a simple example: human MEG responses to visual stimulation (Figure 1). Integrative functions such as perceptual inference, top-down attention and decision-making are typically prominently reflected in the sustained non-phase-locked activity components. This is because these processes are relatively slow (evolving over hundreds of milliseconds) and result from intrinsic network interactions within the brain, rather than from external drive. Furthermore, by decomposing neuronal activity into its frequency components, spectral analysis sheds light on the network interactions mediating these processes (see the main text).

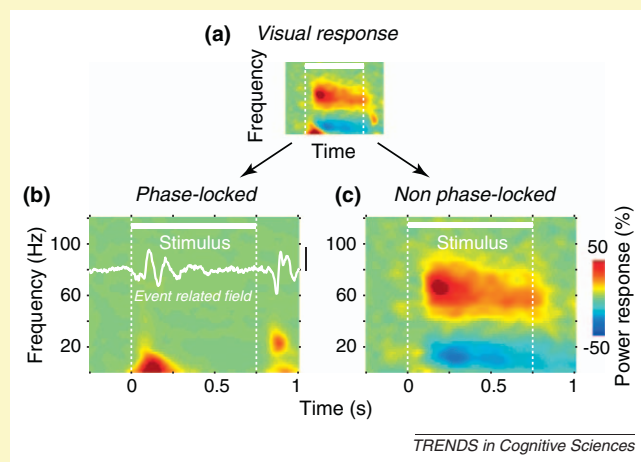


Figure 1. Dissociation of neuronal response components phase-locked and non-phase-locked to external events. (a) Time–frequency representation of a human MEG response to a visual stimulus (same data as in Figure 1a). (b) The phase-locked signal components correspond to the event-related field (ERF; white line overlaid on the time–frequency image; scale bar, 4 pT) and were calculated by averaging the MEG signal across trials in the time domain. These phase-locked components only capture the transient responses phase-locked to stimulus onset and offset. (c) By contrast, the non-phase-locked components capture the two sustained response components induced by the stimulus: a power reduction in the alpha and beta bands (10–30 Hz) and power enhancement in the gamma band (40–90 Hz). The non-phase-locked response was isolated by subtracting the time-domain average from each trial before transforming the data into the frequency domain (adapted with permission from [2]).

It has previously been proposed that long-range oscillatory cortical interactions might be expressed in lower-frequency bands than local interactions [7,8], but this notion has not been linked to the different classes of functional processes we propose here. Our framework offers a coherent scheme for explaining several seemingly contradictory findings from two lines of recent research: studies of visual and visuomotor processing and studies of the link between cortical electrophysiology and fMRI. The framework also generates several new predictions that can be tested in future experiments.

Spectral profiles of functional processes

We use the term spectral profile to denote the change in the cortical power spectrum due to a functional process. Thus, construction of this profile requires contrasting power

spectra between experimental conditions that differ in the process of interest. A spectral profile might depict the difference between two conditions (e.g. stimulation vs. baseline or attended vs. unattended) or the correlation with a parametric experimental variable (e.g. stimulus contrast or attentional load). Indeed, such contrasts are commonly used to delineate the frequency bands involved in a functional process (Figures 1 and 2).

Although these processes are typically dynamic, we omit the time dimension here for simplicity. The underlying assumption is that the spectral profile of a process does not change while the process is active. This assumption is supported by the sustained spectral profiles of sustained cognitive processes (Figures 1 and 2). In other words, we treat spectral profiles as static snapshots of functional processes (insets in Figures 1 and 2). Furthermore, the above definition and our current framework focus on the local activity within a single cortical region. In an analogous fashion, spectral profiles could be defined for the coherence between different brain regions.

A key component of a spectral profile is that functionally relevant frequency ranges are defined in a data-driven fashion. This stands in contrast to the notion of classical frequency bands, defined *a priori* according to clinical EEG conventions. The classical frequency bands often do not capture the true oscillatory dynamics underlying specific functions. Process-related effects can span multiple classical bands (e.g. from theta to beta during perceptual suppression [5,6]) and different processes can occur in different sub-bands of the classical bands (e.g. in distinct gamma sub-bands for attention and target detection [9]).

Spectral profiles of local encoding

A large body of evidence suggests that gamma-band oscillations are a generic signature of local encoding in the cortex [2,9–30]. This point is well illustrated by modulations of local oscillatory activity associated with visual stimulation and motor planning (Figure 2a,c). In visual cortex, the intensity of simple visual features (e.g. the luminance contrast of gratings or the motion coherence of dynamic random dot patterns) modulates local gamma-band activity (Figure 2a) [10–15]. At finer spatial scales assessed using LFP recordings, gamma-band activity is also modulated by the identity of these features (e.g. grating orientation or motion direction) [16–18].

This gamma-band signature of local encoding is not confined to visual cortex. For example, in parietal cortex, plans to make motor movements (e.g. a saccade or a reach) are also reflected in enhanced gamma-band activity (Figure 2c) [19–22]. Likewise, in premotor and primary motor cortex, gamma-band activity increases during encoding of hand movement plans [23–25].

Converging evidence suggests that local gamma-band oscillations directly reflect the circuit-level mechanisms mediating local encoding functions. Intracellular [28,31] and extracellular [15,27,32] recordings, optogenetic manipulations [33,34] and biophysical models [8,35,36] suggest that gamma-band oscillations emerge from local excitatory–inhibitory interactions. Within each oscillatory cycle, excitatory neurons drive GABAergic interneurons, which in turn synchronously suppress local excitation.

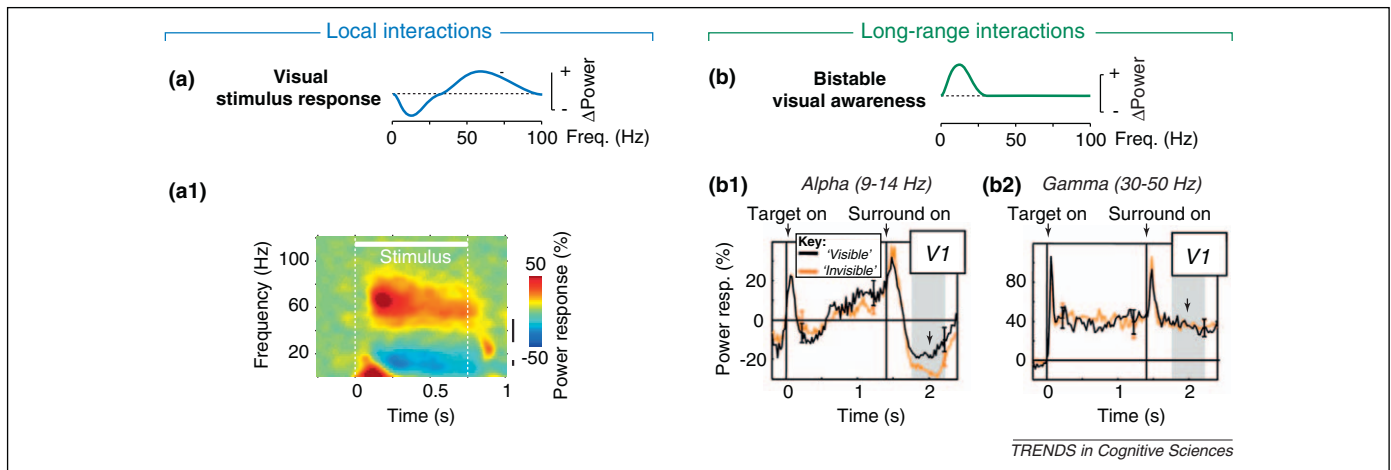


Figure 1. Distinct spectral profiles of visual stimulus processing and bistable visual awareness in primary visual cortex. **(a)** Spectral profile of stimulus responses in human visual cortex measured with MEG (adapted with permission from [2]). **(a1)** Time–frequency representation of the MEG response to a full-contrast drifting sine-wave grating measured at one sensor overlying visual cortex. The stimulus response comprises a tonic power suppression in the alpha and beta bands (10–30 Hz) and sustained enhancement in the gamma band (40–90 Hz). **(b)** Spectral profile of bistable visual awareness during generalized flash suppression in V1 (adapted with permission from [6]). Time courses of band-limited power responses to a monocular visual target followed by a binocular surround pattern. The perceptual target suppression (compare visible and invisible) is reflected in the low-frequency **(b1)** but not in the gamma-band LFP **(b2)**. All responses are expressed as the percentage power change relative to the pre-stimulus baseline.

Inhibitory interneurons also play an integral part in shaping the structure of neuronal representations in local cortical microcircuits [37,38]. Indeed, the same inhibitory interactions that shape local neuronal representations also seem to contribute to the generation of local gamma-band oscillations [27].

The enhancement of gamma-band activity with visual stimulation and motor planning is frequently associated with suppression of low-frequency activity (Figure 1a) [14,16–18,23–26,39]. Several lines of evidence suggest that this low-frequency suppression does not directly reflect the circuit mechanisms of local encoding. First, this suppression is often anatomically less confined to the activated neuronal population [25,26,40,41] than the corresponding gamma-band enhancement. Second, it is less consistently modulated by specific stimulus [14,16–18] or motor parameters [25,26,40,41]. Third, low-frequency suppression reflects reduction of an ongoing oscillation rather than activation of an oscillation. For these reasons, our current account of local encoding focuses on gamma-band oscillations (spectral profiles in Figures 2 and 3). However, low-frequency suppression could be readily incorporated into this account if future evidence linked this suppression as closely to the mechanisms of local encoding as gamma-band enhancement.

Spectral profiles of integrative functions

An increasing body of evidence suggests that within the same cortical regions, the spectral profiles of integrative cognitive functions differ markedly from the spectral profiles of local encoding discussed above. In particular, several recent studies have pointed to the involvement of beta oscillations in integrative cognitive functions. To highlight the contrast between local encoding and integrative functions, we focus on the same cortical regions as those discussed in the previous section: visual and parietal cortex.

In primary visual cortex, top-down attention has a different spectral profile from the local encoding of sensory

features (compare Figure 2a and b). Several studies have shown that the effect of attention is to enhance gamma-band activity in extrastriate visual cortex, just like bottom-up visual stimulation (see also Limitations below) [9,30,42–46]. However, the spectral profile of attention depends on the visual cortical area, and in V1 the profile of attention differs sharply from that of visual stimulation [42,44]. In human V1, attention selectively enhances beta-band activity during stimulation and suppresses gamma-band activity before stimulus onset (Figure 2c) [44].

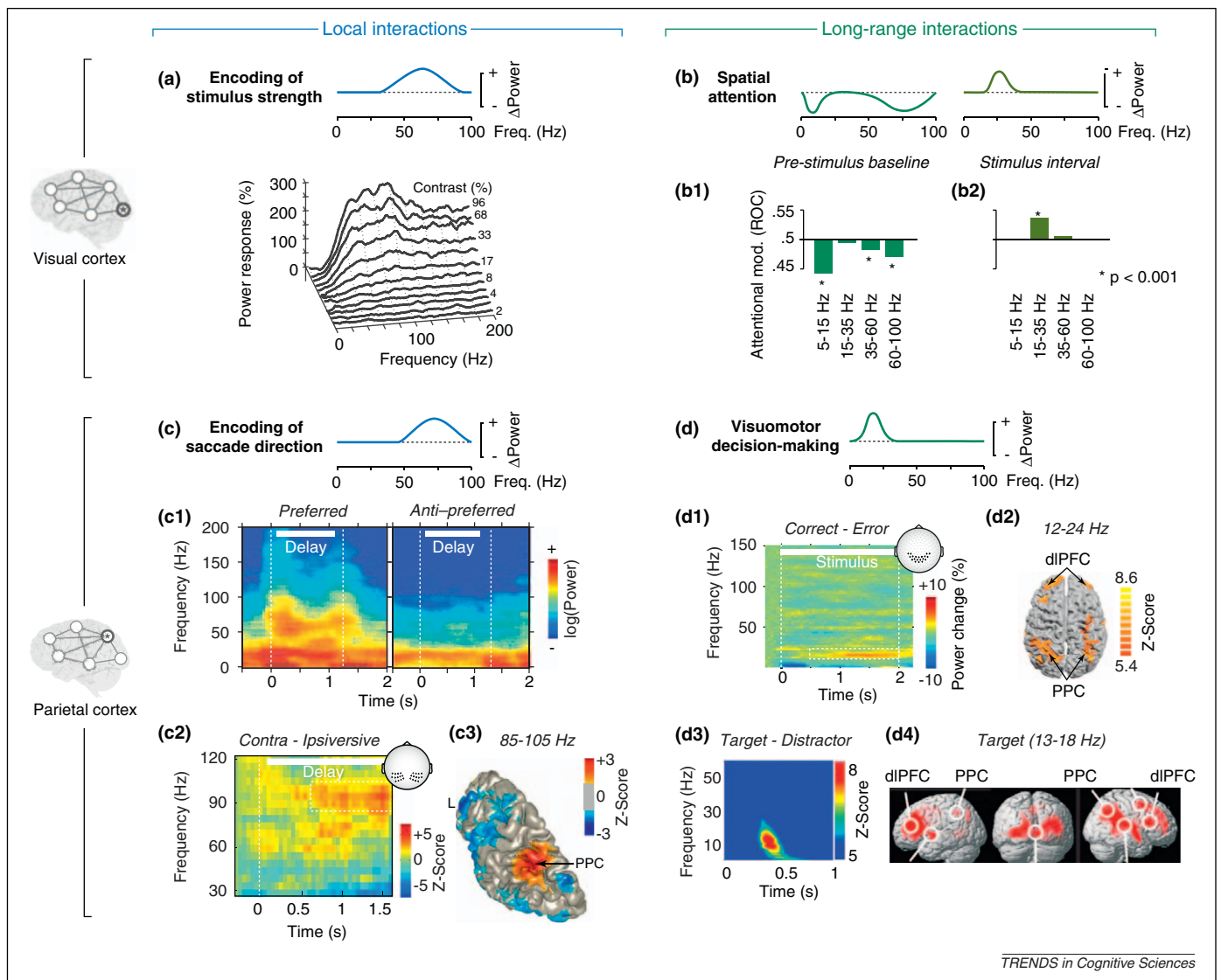
In posterior parietal cortex, decision-making has a different spectral profile from that of motor planning (compare Figure 2c and d). Visuomotor decision processes are reflected in beta-band (~10–25 Hz) oscillations in parietal cortex (Figure 2d) [47–50]. For example, during a search for weak visual motion signals in dynamic noise, parietal beta-band oscillations predict the accuracy of the upcoming perceptual choice [47]. Likewise, during the attentional blink phenomenon, parietal beta-band oscillations increase with the occurrence of target letters in a rapid visual stream [48].

Decision-related beta-band oscillations typically occur in a wider network including frontal cortex (Figure 2d) [47,48]. They have been interpreted as a signature of large-scale reverberation that mediates persistent activity during sensory evidence accumulation for the decision [47,51–53]. Indeed, beta-band oscillations in prefrontal [54,55] and inferotemporal [56,57] cortex reflect persistent activity during visual short-term memory.

The evidence discussed in the last two sections highlights the fact that neuronal activity within the same cortical region often exhibits distinct spectral profiles for local encoding and integrative functions.

Our framework

The schematic shown in Figure 3 illustrates our framework for understanding local spectral profiles measured in the neocortex during cognitive tasks. A cortical region (nodes



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Figure 2. Process-dependent spectral profiles in the cerebral cortex. (a) Luminance contrast modulates gamma-band LFP activity (~ 40 – 100 Hz) in macaque primary visual cortex (adapted with permission from [11]). The graph shows contrast-dependent modulations of spectral power during stimulation relative to the pre-stimulus baseline. (b) Spectral profiles of spatial attention in human primary visual cortex during pre-stimulus baseline (b1) and stimulation (b2) of a motion discrimination task (adapted with permission from [44]). ROC indices greater and less than 0.5 correspond to attentional enhancements and suppressions, respectively. (c) Saccade plans are encoded in parietal gamma-band activity (adapted from [19,22]). (c1) Time–frequency representation of LFP activity in macaque LIP during a delayed saccade task. The gamma-band LFP (~ 40 – 130 Hz) is selective for the prepared saccade. (c2) Time–frequency representation of saccade-selective (contraversal vs ipsiversal) parietal MEG activity in humans during the same delayed saccade task. Again, delay activity in the gamma band (~ 60 – 100 Hz) is selective for planned saccades. (c3) Saccade-selective activity is expressed in posterior parietal cortex (PPC). (d) Low beta-band (~ 12 – 25 Hz) MEG activity in human parietal cortex reflects perceptual decision processes (adapted from [47,48]). (d1) Time–frequency representation of performance-predictive parietal activity. Subjects searched for a weak visual motion signal embedded in noise. Low beta-band activity predicts correct detection decisions (hits and correct rejections). (d2) Performance-predictive beta-band activity peaks in PPC and dorsolateral prefrontal cortex (dlPFC). (d3) Time–frequency representation of target-related (target vs. distractor stimuli) MEG activity during a rapid serial visual presentation producing the attentional blink. Target-related activity occurs in the same low-beta range as in d1 and d2. (d4) Target-related beta-band activity is also expressed in PPC and dlPFC. Insets in all panels display coarse schematics of the corresponding spectral profiles.

marked by asterisks) can engage in two classes of recurrent network interactions (colored arrows): local and long-range interactions. These two classes of network interactions mediate two classes of cognitive functions (top row). Local interactions encode information (sensory, motor or cognitive variables) within local neuronal populations. Long-range interactions mediate integrative cognitive functions (e.g. top-down control and decision-making) that link these local neuronal populations. These two classes of network interactions also produce different local cortical oscillations (bottom row). Local circuit interactions during encoding produce gamma-band oscillations (often accompanied by less specific low-frequency suppression).

Long-range interactions frequently produce local beta-band oscillations, but the spectral profiles of these interactions exhibit considerable variability (see Prospects and conclusions).

Importantly, during cognitive processing, a cortical region typically simultaneously engages in both classes of network interactions. Thus, the associated spectral profiles can co-exist within a region at the same time and can be dissociated via different experimental contrasts.

Scope

The present framework focuses on changes in the power spectrum of local population activity that result from

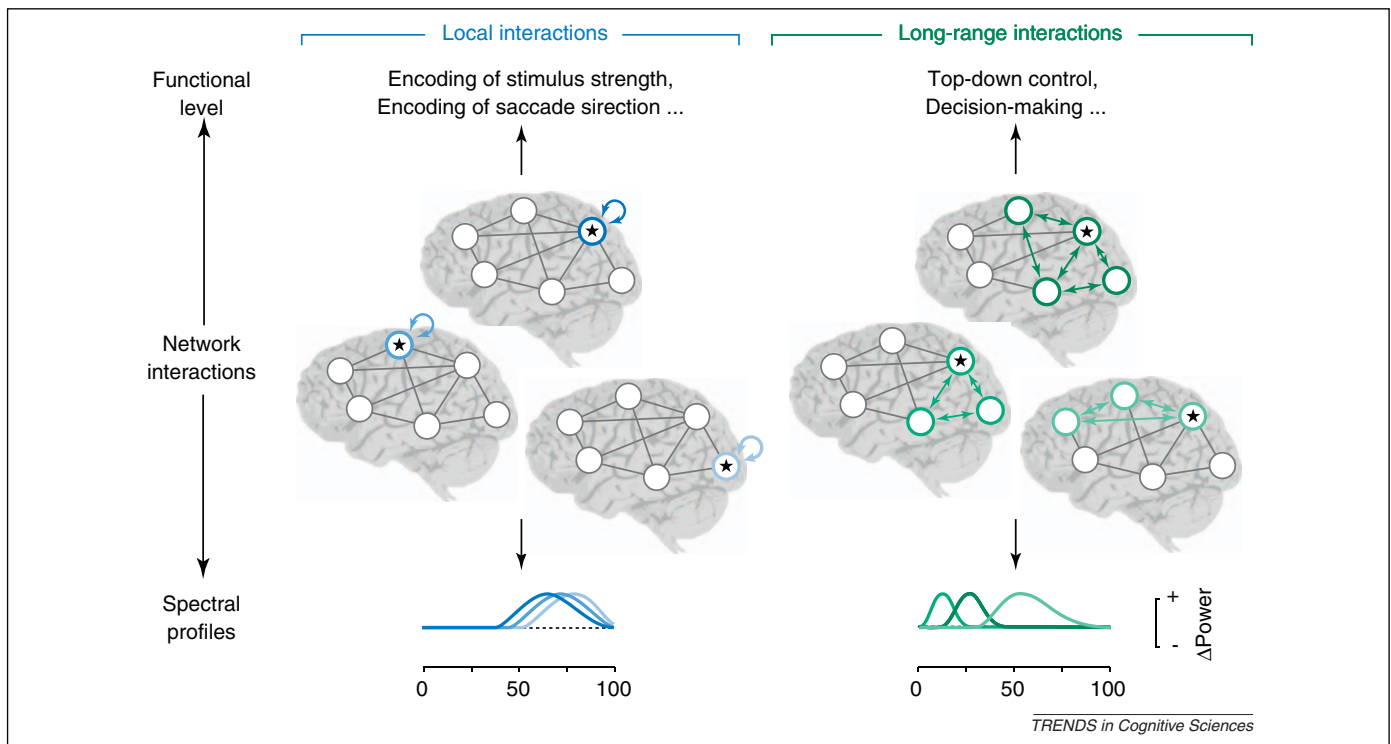


Figure 3. Network interactions shaping spectral profiles of cognitive functions. Local neuronal populations in the cortex engage in two classes of network interactions (local and long-range) during local encoding and integrative functions, so their local activity exhibits different spectral profiles. Middle row: six different hypothetical local and long-range processes. Each circle represents a local neuronal group constituting a large-scale network node. Lines and loops represent long-range and locally recurrent connections, respectively. Top row: network interactions that mediate the corresponding cognitive functions. Bottom row: schematics of the spectral profiles expressed in the local network node indicated by the asterisk. Whereas local encoding functions exhibit similar gamma-band modulations, long-range integrative functions exhibit more diverse spectral profiles, in particular in the beta range.

modulations of locally synchronized oscillations [1,3,14, 30,58] (but see [41]). Long-range interactions are more directly assessed in terms of the coherence between cortical regions [44,45,49,50,59,60]. It is an open question how the patterns of inter-regional coherence are related to local oscillation patterns. It might be expected that frequency-specific communication between network nodes should lead to local power effects in the corresponding frequency bands. However, recent evidence suggests that, at least under some conditions, there is no simple mapping between modulations of local power and inter-regional coherence [44,49,50,61].

Furthermore, our framework focuses on network interactions within the neocortex. A large body of evidence links theta-band oscillations to neuronal coding and computation in the hippocampus [62] and to long-range interactions between the hippocampus and the neocortex [63,64]. Different principles from those illustrated in Figure 3 might apply to local interactions within the hippocampus and its interactions with the neocortex.

Explanatory power

Our framework offers a simple coherent explanation for why different experimental manipulations yield different, and sometimes even opposite, spectral profiles. Specifically, the framework explains prominent dissociations between the local spectral profiles of encoding and integrative processes that have recently been observed in primate visual and parietal cortex (Figures 1 and 2). It is likely that the dissociations between encoding and integrative functions can be generalized across the cere-

bral cortex. The framework links spectral profiles and corresponding cognitive functions via the underlying neuronal interactions (Figure 3).

The framework also accounts for recent puzzling findings concerning the link between local oscillatory activity and the BOLD-fMRI signal in visual cortex (Box 2). It explains why, on the one hand, the BOLD signal is consistently correlated with local gamma-band oscillations, but on the other hand there is no stereotypical mapping between the BOLD signal and low-frequency oscillations. This mapping varies with the functional process targeted by the experimental manipulation at hand.

Experimental predictions

Our framework suggests a number of testable predictions. First, it should be possible to generalize the principles shown schematically in Figure 3 to other cortical regions, namely other sensory, motor and association cortices. Testing of this prediction will require analogous systematic manipulations of both local encoding and integrative functions, as in studies of visual and visuo-motor processing (Figures 1 and 2). It is straightforward to manipulate physical stimulus or motor variables to study local encoding functions in sensory and motor cortex. It is more challenging to define and manipulate the variables encoded in associative regions such as prefrontal cortex. Categories and task rules [65], as well as subjective action values [66–68], are suitable variables for future studies on the role of neuronal oscillations in the local encoding functions of association cortices.

Second, the framework predicts that when a cortical region is encoding information but does not participate in

Box 2. Process-dependent coupling between neuronal oscillations and the BOLD-fMRI signal

Our framework explains seemingly contradictory findings concerning the link between the BOLD signal and electrophysiological activity. It has become common practice to characterize the coupling between BOLD and electrophysiological activity as a function of the frequency of the latter. However, in particular for lower-frequency ranges, there is no fixed mapping between oscillatory activity and BOLD. Consider processes yielding the diverse spectral profiles discussed in the main text: stimulus encoding, release from perceptual suppression, and spatial attention in visual cortex; and saccade planning and visual decision-making in parietal cortex. Some of the corresponding spectral profiles even exhibit opposite signs within lower (alpha or beta) frequency bands (Figure 2). However, they all produce BOLD increases [2]. Thus, the coupling between band-limited activity and BOLD is process-dependent [5,81].

Our account of the process dependence of local spectral profiles also offers a useful heuristic for understanding the process dependence of the link between electrophysiology and BOLD (Figure 1). Recurrent network interactions produce local cortical oscillations. It is likely that these interactions also drive local metabolic demand and thus enhance the BOLD signal. Local gamma-band oscillations reliably index local excitatory-inhibitory interactions (see the main text) and consequently reliably predict local BOLD increases [10,12,13,29,78,79,82,83]. The activation of local cortical regions is typically also associated with low-frequency suppression, yielding a negative correlation with BOLD [29]. By contrast, the long-range interactions mediating the above integrative functions typically enhance oscillations in overlapping lower-frequency ranges, yielding a positive correlation with BOLD. Thus, low-frequency modulations

and BOLD correlate positively for integrative functions and correlate negatively for local encoding functions.

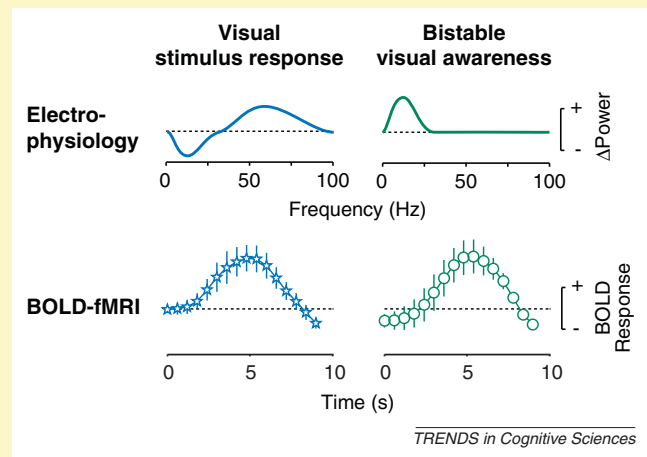


Figure 1. Schematic illustration of the process dependence of the link between spectral profiles and BOLD-fMRI responses. In V1, stimulus responses and release from bistable perceptual suppression of salient stimuli are associated with distinct spectral profiles that involve opposite modulations in the alpha and beta frequency ranges. By contrast, BOLD-fMRI modulations in human V1 during bistable perceptual suppression are virtually indistinguishable for responses to physical stimulus onsets and to spontaneous stimulus reappearance after perceptual suppression. The top panel is reproduced from Figure 1 of the main text. The bottom panel is adapted with permission from [84].

an integrative process, gamma-band oscillations will occur but the profiles of long-range interactions will be absent. This could be tested by presenting stimuli consisting of features or modalities encoded in different sensory regions and by asking subjects to only ‘use’ one of these features or modalities for a perceptual decision. This prediction could also be tested in experiments in which sensory cortex is encoding stimulus information while the subject’s attention is diverted from this stimulus, making it unavailable for behavioral report [69,70]. Finally, it could be tested causally by inactivating key regions controlling interactions within a large-scale cortical network, thereby isolating sensory regions from such top-down influences. Sensory stimulation of such isolated sensory regions should still induce local gamma-band oscillations, but not the spectral profiles of integrative functions.

Third, the framework predicts a local process-dependent cross-frequency coupling [71,72] between the local gamma band and lower-frequency ranges. This cross-frequency coupling should only occur whenever a cortical region is involved in an integrative process. For example, during sensory-motor decisions [51], gamma-band oscillations in cortical regions encoding the sensory evidence for the decision [9,14] and the resulting motor plan [24] should be coupled to lower-frequency oscillations reflecting the decision process [73]. This cross-frequency coupling should disappear if the same stimuli and motor plans are encoded but not linked to one another by a sensory-motor integration process.

Fourth, the framework can guide future studies testing the hypothesis that coupling between the frequency bands of local cortical activity and the BOLD-fMRI signal [12] depends on the process at hand. Such process dependence is strongly suggested by a comparison between studies

(Box 2). However, apart from one notable exception [5], this has not yet been directly demonstrated within a single experiment. Our framework suggests that manipulation of both local encoding and integrative functions within a single experiment will establish maximum process dependence in the associated local spectral profiles. This provides an ideal opportunity for assessing the process dependence of the association of these spectral profiles with the local BOLD signal.

Limitations

Several studies have shown that top-down attention, an important integrative function, is associated with modulations of local gamma-band oscillations in visual cortex [9,43–46]. How does this fit into the current framework? Top-down attention is mediated by long-range feedback interactions between higher-order control regions and sensory cortices [44,45,74,75]. The effect of these feedback interactions is modulation of the local encoding in sensory cortex [76], which is mediated by the local network interactions [77,78]. Therefore, the attentional modulation of gamma-band activity in visual cortex is consistent with the notion that gamma-band activity reflects local circuit interactions, but it complicates the simple distinction between classes of functions we propose.

This points to a more general challenge: local cortical representations are always shaped by the integrative processes that link these representations. For example, the cortical representations of motor plans during sensory-motor decisions [51] are the result of an integrative process that maps the sensory input onto an action [24,51]. Thus, a challenge for future studies of cortical oscillations will be to determine the experimental contrasts that most clearly dissociate local encoding and integrative functions.

Box 3. Neuromodulation and the spectral profiles of integrative cognitive functions

The cortex receives massive and diffuse projections from several small nuclei located in the brainstem and basal forebrain. These ascending projections carry neuromodulatory transmitters such as acetylcholine, dopamine, norepinephrine, serotonin and histamine. Several lines of evidence suggest that these neuromodulators are important factors in shaping the spectral profiles of integrative cognitive functions. First, it is becoming increasingly clear that these systems are not merely slow and nonspecific regulators of the coarse behavioral state. Instead, they play specific roles in cognitive functions such as attention and decision-making, partly mediated by temporally specific phasic activation during cognitive acts [85–88]. Second, neuromodulators seem to strongly modulate local cortical oscillation patterns [85,89,90]. Third, neuromodulators seem to profoundly shape local and long-range cortical interactions. For example, evidence suggests that acetylcholine contributes to selective attention effects in visual cortex [87] and that phasic norepinephrine facilitates sensory-motor decision processes [86].

Prospects and conclusions

The integrative functions discussed above are associated with low-frequency oscillations predominantly in the beta-band, but increasing evidence suggests that integrative functions involve far more diverse frequency ranges than the local encoding functions (Figure 3) [6,44,45,49,50,59–61]. For example, as discussed above, bistable perceptual suppression in V1 is linked to broad low-frequency modulations spanning theta, alpha and beta bands (Figure 1) [6], whereas sensory–motor decision processes in prefrontal and parietal cortex are associated with more narrow-band modulations in the low beta range (Figure 2) [47,48]. Thus, there does not seem to be a simple stereotypical mapping between long-range interactions and local oscillations in a single frequency range.

Previous accounts suggested that conduction delays constrain oscillatory long-range interactions to frequencies below the gamma-band [7,8]. However, the variability in the exact frequency ranges across recent studies, and in particular the observation of long-range gamma coupling [44,45,50,60], suggests that other factors beyond conduction delays might govern the spectral profiles of integrative functions. Such other factors might include the number of interacting cortical regions and modulatory neurotransmitters released from ascending subcortical systems (Box 3). Future studies should identify the principles underlying the diverse spectral profiles of cortical long-range interactions (Box 4).

Our framework does not attribute any direct functional role to the neuronal oscillations shaping spectral profiles (Figure 3). Rather, it highlights the notion that these oscillations index the network interactions underlying cognitive functions. This suggests a novel perspective on cortical oscillations, namely as ‘fingerprints’ of the circuit-level mechanisms of cognition. Local gamma-band oscillations provide a showcase for this notion: local gamma-band oscillations during a cognitive process index a specific excitatory–inhibitory circuit interaction in the local cortical network. Future studies that unravel the detailed circuit mechanisms of cortical long-range interactions will show if the associated spectral profiles are specific enough to serve as fingerprints of these mechanisms.

Box 4. Outstanding questions

- Can the framework (Figure 3) be generalized throughout the cortex and cognitive functions? If not, is there anything special about the cortical regions or functions that are exceptions?
- What are the principles underlying the spectral profiles of long-range interactions? Why are these spectral profiles so diverse? In particular, under what conditions do long-range interactions occur in the gamma band?
- How does oscillatory synchronization between regions relate to modulations of oscillation patterns within a region?
- How do neuromodulators shape the spectral profiles of integrative processes (Box 3)?

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References

- 1 Nunez, P.L. and Srinivasan, R. (2006) *Electric Fields of the Brain: The Neurophysics of EEG*, Oxford University Press
- 2 Siegel, M. and Donner, T.H. (2010) Linking band-limited cortical population activity to fMRI and behavior. In *Integrating EEG and fMRI: Recording, Analysis, and Application* (Ullsperger, M. and Debener, S., eds), pp. 271–294, Oxford University Press
- 3 Buzsáki, G. (2006) *Rhythms of the Brain*, Oxford University Press
- 4 Gail, A. et al. (2004) Perception-related modulations of local field potential power and coherence in primary visual cortex of awake monkey during binocular rivalry. *Cereb. Cortex* 14, 300–313
- 5 Maier, A. et al. (2008) Divergence of fMRI and neural signals in V1 during perceptual suppression in the awake monkey. *Nat. Neurosci.* 11, 1193–1200
- 6 Wilke, M. et al. (2006) Local field potential reflects perceptual suppression in monkey visual cortex. *Proc. Natl. Acad. Sci. U.S.A.* 103, 17507–17512
- 7 von Stein, A. and Sarnthein, J. (2000) Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization. *Int. J. Psychophysiol.* 38, 301–313
- 8 Kopell, N. et al. (2000) Gamma rhythms and beta rhythms have different synchronization properties. *Proc. Natl. Acad. Sci. U.S.A.* 97, 1867–1872
- 9 Wyart, V. and Tallon-Baudry, C. (2008) Neural dissociation between visual awareness and spatial attention. *J. Neurosci.* 28, 2667–2679
- 10 Hall, S.D. et al. (2005) The missing link: analogous human and primate cortical gamma oscillations. *Neuroimage* 26, 13–17
- 11 Henrie, J.A. and Shapley, R. (2005) LFP power spectra in V1 cortex: the graded effect of stimulus contrast. *J. Neurophysiol.* 94, 479–490
- 12 Logothetis, N.K. et al. (2001) Neurophysiological investigation of the basis of the fMRI signal. *Nature* 412, 150–157
- 13 Niessing, J. et al. (2005) Hemodynamic signals correlate tightly with synchronized gamma oscillations. *Science* 309, 948–951
- 14 Siegel, M. et al. (2007) High-frequency activity in human visual cortex is modulated by visual motion strength. *Cereb. Cortex* 17, 732–741
- 15 Ray, S. and Maunsell, J.H. (2010) Differences in gamma frequencies across visual cortex restrict their possible use in computation. *Neuron* 67, 885–896
- 16 Liu, J. and Newsome, W.T. (2006) Local field potential in cortical area MT: stimulus tuning and behavioral correlations. *J. Neurosci.* 26, 7779–7790
- 17 Siegel, M. and König, P. (2003) A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. *J. Neurosci.* 23, 4251–4260
- 18 Gray, C.M. and Singer, W. (1989) Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. *Proc. Natl. Acad. Sci. U.S.A.* 86, 1698–1702
- 19 Pesaran, B. et al. (2002) Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat. Neurosci.* 5, 805–811

- 20 Scherberger, H. *et al.* (2005) Cortical local field potential encodes movement intentions in the posterior parietal cortex. *Neuron* 46, 347–354
- 21 Van Der Werf, J. *et al.* (2010) Neuronal synchronization in human posterior parietal cortex during reach planning. *J. Neurosci.* 30, 1402–1412
- 22 Van Der Werf, J. *et al.* (2008) Gamma-band activity in human posterior parietal cortex encodes the motor goal during delayed prosaccades and antisaccades. *J. Neurosci.* 28, 8397–8405
- 23 Ball, T. *et al.* (2008) Movement related activity in the high gamma range of the human EEG. *Neuroimage* 41, 302–310
- 24 Donner, T.H. *et al.* (2009) Buildup of choice-predictive activity in human motor cortex during perceptual decision making. *Curr. Biol.* 19, 1581–1585
- 25 Rickert, J. *et al.* (2005) Encoding of movement direction in different frequency ranges of motor cortical local field potentials. *J. Neurosci.* 25, 8815–8824
- 26 Crone, N.E. *et al.* (1998) Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. II. Event-related synchronization in the gamma band. *Brain* 121, 2301–2315
- 27 Gieselmann, M.A. and Thiele, A. (2008) Comparison of spatial integration and surround suppression characteristics in spiking activity and the local field potential in macaque V1. *Eur. J. Neurosci.* 28, 447–459
- 28 Hasenstaub, A. *et al.* (2005) Inhibitory postsynaptic potentials carry synchronized frequency information in active cortical networks. *Neuron* 47, 423–435
- 29 Mukamel, R. *et al.* (2005) Coupling between neuronal firing, field potentials, and fMRI in human auditory cortex. *Science* 309, 951–954
- 30 Taylor, K. *et al.* (2005) Coherent oscillatory activity in monkey area V4 predicts successful allocation of attention. *Cereb. Cortex* 15, 1424–1437
- 31 Atallah, B.V. and Scanziani, M. (2009) Instantaneous modulation of gamma oscillation frequency by balancing excitation with inhibition. *Neuron* 62, 566–577
- 32 Csicsvari, J. *et al.* (2003) Mechanisms of gamma oscillations in the hippocampus of the behaving rat. *Neuron* 37, 311–322
- 33 Cardin, J.A. *et al.* (2009) Driving fast-spiking cells induces gamma rhythm and controls sensory responses. *Nature* 459, 663–667
- 34 Sohal, V.S. *et al.* (2009) Parvalbumin neurons and gamma rhythms enhance cortical circuit performance. *Nature* 459, 698–702
- 35 Bartos, M. *et al.* (2007) Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. *Nat. Rev. Neurosci.* 8, 45–56
- 36 Siegel, M. *et al.* (2000) Integrating top-down and bottom-up sensory processing by somato-dendritic interactions. *J. Comput. Neurosci.* 8, 161–173
- 37 Heeger, D.J. *et al.* (1996) Computational models of cortical visual processing. *Proc. Natl. Acad. Sci. U.S.A.* 93, 623–627
- 38 Shapley, R. *et al.* (2003) Dynamics of orientation selectivity in the primary visual cortex and the importance of cortical inhibition. *Neuron* 38, 689–699
- 39 Pfurtscheller, G. and Lopes da Silva, F.H. (1999) Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol.* 110, 1842–1857
- 40 Crone, N.E. *et al.* (1998) Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. I. Alpha and beta event-related desynchronization. *Brain* 121, 2271–2299
- 41 Miller, K.J. *et al.* (2009) Decoupling the cortical power spectrum reveals real-time representation of individual finger movements in humans. *J. Neurosci.* 29, 3132–3137
- 42 Chalk, M. *et al.* (2010) Attention reduces stimulus-driven gamma frequency oscillations and spike field coherence in V1. *Neuron* 66, 114–125
- 43 Fries, P. *et al.* (2008) The effects of visual stimulation and selective visual attention on rhythmic neuronal synchronization in macaque area V4. *J. Neurosci.* 28, 4823–4835
- 44 Siegel, M. *et al.* (2008) Neuronal synchronization along the dorsal visual pathway reflects the focus of spatial attention. *Neuron* 60, 709–719
- 45 Gregoriou, G.G. *et al.* (2009) High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science* 324, 1207–1210
- 46 Gruber, T. *et al.* (1999) Selective visual-spatial attention alters induced gamma band responses in the human EEG. *Clin. Neurophysiol.* 110, 2074–2085
- 47 Donner, T.H. *et al.* (2007) Population activity in the human dorsal pathway predicts the accuracy of visual motion detection. *J. Neurophysiol.* 98, 345–359
- 48 Gross, J. *et al.* (2004) Modulation of long-range neural synchrony reflects temporal limitations of visual attention in humans. *Proc. Natl. Acad. Sci. U.S.A.* 101, 13050–13055
- 49 Pesaran, B. *et al.* (2008) Free choice activates a decision circuit between frontal and parietal cortex. *Nature* 453, 406–409
- 50 Hipp, J.F. *et al.* (2011) Oscillatory synchronization in large-scale cortical networks predicts perception. *Neuron* 69, 387–396
- 51 Siegel, M. *et al.* (2011) Cortical network dynamics of perceptual decision-making in the human brain. *Front. Hum. Neurosci.* DOI: 10.3389/fnhum.2011.00021
- 52 Wang, X.J. (2008) Decision making in recurrent neuronal circuits. *Neuron* 60, 215–234
- 53 Curtis, C.E. and Lee, D. (2010) Beyond working memory: the role of persistent activity in decision making. *Trends Cogn. Sci.* 14, 216–222
- 54 Siegel, M. *et al.* (2009) Phase-dependent neuronal coding of objects in short-term memory. *Proc. Natl. Acad. Sci. U.S.A.* 106, 21341–21346
- 55 Spitzer, B. *et al.* (2010) Oscillatory correlates of vibrotactile frequency processing in human working memory. *J. Neurosci.* 30, 4496–4502
- 56 Tallon-Baudry, C. *et al.* (2001) Oscillatory synchrony between human extrastriate areas during visual short-term memory maintenance. *J. Neurosci.* 21, RC177
- 57 Tallon-Baudry, C. *et al.* (2004) Oscillatory synchrony in the monkey temporal lobe correlates with performance in a visual short-term memory task. *Cereb. Cortex* 14, 713–720
- 58 Mitzdorf, U. (1987) Properties of the evoked potential generators: current source-density analysis of visually evoked potentials in the cat cortex. *Int. J. Neurosci.* 33, 33–59
- 59 Buschman, T.J. and Miller, E.K. (2007) Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science* 315, 1860–1862
- 60 Axmacher, N. *et al.* (2008) Interactions between medial temporal lobe, prefrontal cortex, and inferior temporal regions during visual working memory: a combined intracranial EEG and functional magnetic resonance imaging study. *J. Neurosci.* 28, 7304–7312
- 61 Cohen, M.X. *et al.* (2009) Nuclei accumbens phase synchrony predicts decision-making reversals following negative feedback. *J. Neurosci.* 29, 7591–7598
- 62 Buzsáki, G. (2005) Theta rhythm of navigation: link between path integration and landmark navigation, episodic and semantic memory. *Hippocampus* 15, 827–840
- 63 Sirota, A. *et al.* (2008) Entrainment of neocortical neurons and gamma oscillations by the hippocampal theta rhythm. *Neuron* 60, 683–697
- 64 Siapas, A.G. *et al.* (2005) Prefrontal phase locking to hippocampal theta oscillations. *Neuron* 46, 141–151
- 65 Miller, E.K. *et al.* (2002) The prefrontal cortex: categories, concepts and cognition. *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 357, 1123–1136
- 66 Kable, J.W. and Glimcher, P.W. (2009) The neurobiology of decision: consensus and controversy. *Neuron* 63, 733–745
- 67 Sugrue, L.P. *et al.* (2005) Choosing the greater of two goods: neural currencies for valuation and decision making. *Nat. Rev. Neurosci.* 6, 363–375
- 68 Wallis, J.D. (2007) Orbitofrontal cortex and its contribution to decision-making. *Annu. Rev. Neurosci.* 30, 31–56
- 69 Koch, C. and Tsuchiya, N. (2007) Attention and consciousness: two distinct brain processes. *Trends Cogn. Sci.* 11, 16–22
- 70 Lee, S.H. *et al.* (2007) Hierarchy of cortical responses underlying binocular rivalry. *Nat. Neurosci.* 10, 1048–1054
- 71 Canolty, R.T. and Knight, R.T. (2010) The functional role of cross-frequency coupling. *Trends Cogn. Sci.* 14, 506–515
- 72 Jensen, O. and Colgin, L.L. (2007) Cross-frequency coupling between neuronal oscillations. *Trends Cogn. Sci.* 11, 267–269
- 73 Handel, B. and Haarmeier, T. (2009) Cross-frequency coupling of brain oscillations indicates the success in visual motion discrimination. *Neuroimage* 45, 1040–1046
- 74 Moore, T. and Armstrong, K.M. (2003) Selective gating of visual signals by microstimulation of frontal cortex. *Nature* 421, 370–373

- 75 Ekstrom, L.B. *et al.* (2008) Bottom-up dependent gating of frontal signals in early visual cortex. *Science* 321, 414–417
- 76 Reynolds, J.H. and Chelazzi, L. (2004) Attentional modulation of visual processing. *Annu. Rev. Neurosci.* 27, 611–647
- 77 Reynolds, J.H. and Heeger, D.J. (2009) The normalization model of attention. *Neuron* 61, 168–185
- 78 Mitchell, J.F. *et al.* (2007) Differential attention-dependent response modulation across cell classes in macaque visual area V4. *Neuron* 55, 131–141
- 79 Kim, C.Y. and Blake, R. (2005) Psychophysical magic: rendering the visible ‘invisible’. *Trends Cogn. Sci.* 9, 381–388
- 80 Tallon-Baudry, C. and Bertrand, O. (1999) Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn. Sci.* 3, 151–162
- 81 Sirotin, Y.B. and Das, A. (2009) Anticipatory haemodynamic signals in sensory cortex not predicted by local neuronal activity. *Nature* 457, 475–479
- 82 Nir, Y. *et al.* (2007) Coupling between neuronal firing rate, gamma LFP, and BOLD fMRI is related to interneuronal correlations. *Curr. Biol.* 17, 1275–1285
- 83 Koch, S.P. *et al.* (2009) Stimulus-induced and state-dependent sustained gamma activity is tightly coupled to the hemodynamic response in humans. *J. Neurosci.* 29, 13962–13970
- 84 Donner, T.H. *et al.* (2008) Opposite neural signatures of motion-induced blindness in human dorsal and ventral visual cortex. *J. Neurosci.* 28, 10298–10310
- 85 Sara, S.J. (2009) The locus coeruleus and noradrenergic modulation of cognition. *Nat. Rev. Neurosci.* 10, 211–223
- 86 Aston-Jones, G. and Cohen, J.D. (2005) An integrative theory of locus coeruleus–norepinephrine function: adaptive gain and optimal performance. *Annu. Rev. Neurosci.* 28, 403–450
- 87 Herrero, J.L. *et al.* (2008) Acetylcholine contributes through muscarinic receptors to attentional modulation in V1. *Nature* 454, 1110–1114
- 88 Yu, A.J. and Dayan, P. (2005) Uncertainty, neuromodulation, and attention. *Neuron* 46, 681–692
- 89 Munk, M.H. *et al.* (1996) Role of reticular activation in the modulation of intracortical synchronization. *Science* 272, 271–274
- 90 Rodriguez, R. *et al.* (2004) Short- and long-term effects of cholinergic modulation on gamma oscillations and response synchronization in the visual cortex. *J. Neurosci.* 24, 10369–10378