

Spectral fingerprints of large-scale neuronal interactions

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Abstract | Cognition results from interactions among functionally specialized but widely distributed brain regions; however, neuroscience has so far largely focused on characterizing the function of individual brain regions and neurons therein. Here we discuss recent studies that have instead investigated the interactions between brain regions during cognitive processes by assessing correlations between neuronal oscillations in different regions of the primate cerebral cortex. These studies have opened a new window onto the large-scale circuit mechanisms underlying sensorimotor decision-making and top-down attention. We propose that frequency-specific neuronal correlations in large-scale cortical networks may be ‘fingerprints’ of canonical neuronal computations underlying cognitive processes.

Spectral analysis

A general term for analysis techniques (for example, Fourier transform or wavelet transform) that decompose time domain signals into their different frequency components.

Multi-microelectrode recordings

Simultaneous recordings of single- or multi-unit activity from multiple electrodes implanted in the brain.

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Cognitive processing is highly selective, integrative and flexible. This is achieved through the transient formation of large ‘coalitions of neurons’¹, which are widely distributed across many brain areas, exchange signals in a specific manner and compete with each other. Just as in politics, one coalition typically rules until it is overturned by another. In the brain, the winning coalition governs a percept, thought or action. Thus, understanding the neuronal basis of cognition requires an understanding of how transient coalitions of neurons form, compete and dissolve.

Around 30 years ago, it was suggested that the synchronization of oscillatory neuronal activity might have a key role in the integration of sensory signals during perceptual organization^{2,3}. Several investigations into the visual system provided evidence for^{4–9} and against^{10–12} this hypothesis. One decade ago, three influential Reviews in this journal further highlighted the functional significance of neuronal oscillations for the large-scale neuronal interactions underlying cognition^{13–15}. Since then, several groups have begun to unravel these interactions and their dynamics, aided by the development of powerful new measurement and analysis tools.

Here, we discuss recent studies characterizing the interactions between distant regions of the primate cerebral cortex through the study of correlated oscillations. We use sensorimotor decision-making and top-down visual attention as showcases. Although most other cognitive processes (for example, multisensory integration^{16–19}) also involve large-scale interactions, we focus on decision-making and attention for two reasons. First, both processes critically depend on the

interaction between neuronal populations located in widely separated cortical areas. Second, both have been the focus of several recent studies linking interactions between brain areas to cognition. These studies showed that large-scale cortical interactions typically involve frequency-specific, correlated neuronal oscillations. The detailed analyses of such frequency-specific interactions indicate tight mechanistic links between processes that may seem different at the behavioural level of analysis. They have also been able to dissociate between seemingly analogous processes. These insights could hardly have emerged from analysing only local neuronal activity patterns. Thus, the evidence discussed in this Review suggests that frequency-specific correlated oscillations in distributed cortical networks may provide indices, or ‘fingerprints’, of the network interactions that underlie cognitive processes. We propose that these fingerprints may index canonical neuronal computations underlying cognition, which are commonly inferred, but not directly accessed.

A window onto cortical interactions

We focus on electrophysiological studies that have characterized frequency-specific neuronal dynamics by means of spectral analysis of non-invasive electroencephalography (EEG), magnetoencephalography (MEG) or invasive multi-microelectrode recordings. Frequency-specific cortical population signals — which are often narrow band and as such reflect neuronal oscillations — are markers of the underlying neuronal network interactions^{2,13,14,20–25}. Thus, measures of the association between brain areas based on such frequency-specific signals

Blood oxygen level-dependent functional MRI

(BOLD fMRI). Brain imaging technique that measures the haemodynamic response to neural activity based on changes in blood oxygenation.

Sensor level

The level of the sensors, which record neuronal mass activity (for example, electroencephalography electrodes or magnetoencephalography sensors). Each sensor-level signal constitutes a linear mixture of the signals generated by many neuronal sources.

Source reconstruction

Estimation of the sources of neuronal activity that underlie the electromagnetic signals measured at distant electroencephalography or magnetoencephalography sensors.

Effective connectivity

The influence one neuronal system exerts on another; in many studies it is measured by quantifying Granger causality.

(FIG. 1) are likely to provide more detailed information than corresponding measures based on broadband electrophysiological signals or the blood oxygen level-dependent functional MRI (BOLD fMRI) signal.

The coupling between neuronal oscillations in different brain regions has been commonly assessed in terms of either the correlation of their relative phase ('phase coherence') or, on a slower timescale, the correlation of their amplitude envelopes (here referred to as 'amplitude correlation') (FIG. 1). Inter-areal interactions can also be assessed by determining correlations between BOLD fMRI signals measured in different brain regions²⁶. The link between measures of cortical interactions based on frequency-specific electrophysiological signals and measures of cortical interactions based on the BOLD fMRI signal is discussed in BOX 1. It is important to be aware that the relationships between interaction measures based on electrophysiology and fMRI are far from simple, and that these measures may reflect different neuronal circuit mechanisms. Furthermore, attempts to study cortical large-scale interactions face several serious methodological challenges (BOX 2). For EEG and MEG, field spread (BOX 2) severely limits the use of correlational measures at the sensor level. Thus, we focus on EEG and MEG studies that used source reconstruction techniques to assess either amplitude correlation or phase coherence between neuronal oscillations in different cortical regions. In the following paragraphs, we briefly discuss the neurophysiological basis and significance of both measures.

Neuronal phase coherence (FIG. 1a) is not just a statistical quantity: it may also have a direct functional role in regulating neuronal communication between brain regions^{14,15,27}. This may be achieved in two ways. First, synchronization of presynaptic spikes within a sending neuronal population in one or several cortical areas may enhance this population's impact on postsynaptic neurons located in a receiving area if neurons in the receiving area act as 'coincidence detectors'^{215,28,29}. Evidence suggests that this is the case: synchronous presynaptic spikes are more effective in driving postsynaptic cortical neurons than non-synchronized inputs³⁰⁻³², in particular in the balanced excitation and inhibition regime that is common in cortical networks^{15,33}. Enhanced functional connectivity through presynaptic synchronization can be potentially assessed by determining either the amplitude correlation (see below) or the phase coherence between sending and receiving cortical regions. Second, the phase alignment of oscillatory signals between sending and receiving neuronal populations located in two cortical areas may itself regulate the effective connectivity between these regions^{27,34}. Sub-threshold membrane potential oscillations induce rhythmic changes in neuronal excitability^{20,35,36}, and presynaptic spikes that are aligned to the excitable phase of such postsynaptic oscillations are more likely to drive spiking activity at the postsynaptic stage^{27,34}.

Amplitude correlation is a measure of the co-modulation of the amplitude envelopes (that is, of the power) of oscillations in two areas³⁷(FIG. 1b). In the primate cerebral cortex, amplitude correlations predominantly occur at low frequencies (<0.1 Hz)³⁸ and seem to be closely linked to slow co-modulations of spontaneous fMRI signal fluctuations in distant cortical regions³⁹ (BOX 1). During cognitive tasks, amplitude correlation is also evident at faster timescales — on a trial-by-trial or within-trial basis — and between different oscillation frequencies. The mechanistic interpretation, and thus the functional significance, of amplitude correlation is less clear than the mechanistic interpretation of phase coherence. One possibility is that amplitude correlations reflect state changes coupled across brain networks that might be driven by neuromodulatory systems and that may be important for coordinating cortical processing on slow timescales^{38,40}. Several studies using amplitude correlation have provided important insights into large-scale interactions even between cortical areas that are only indirectly connected through polysynaptic pathways⁴¹⁻⁴⁴. Thus, amplitude correlation is an informative index of the large-scale cortical interactions that mediate cognition.

In principle, phase coherence and amplitude correlation are independent of one another³⁷. For example, the amplitude envelopes of the oscillatory responses of two regions can co-vary strongly even if their phases are randomly distributed (FIG. 1b). The reverse can be true as well.

New evidence on large-scale interactions

During goal-directed, sensory-guided behaviour, sensory signals are continuously transformed into action plans in a highly flexible fashion. The underlying sensorimotor transformations rely on both feed-forward⁴⁵⁻⁵⁰ and feedback^{42,50-62} interactions between

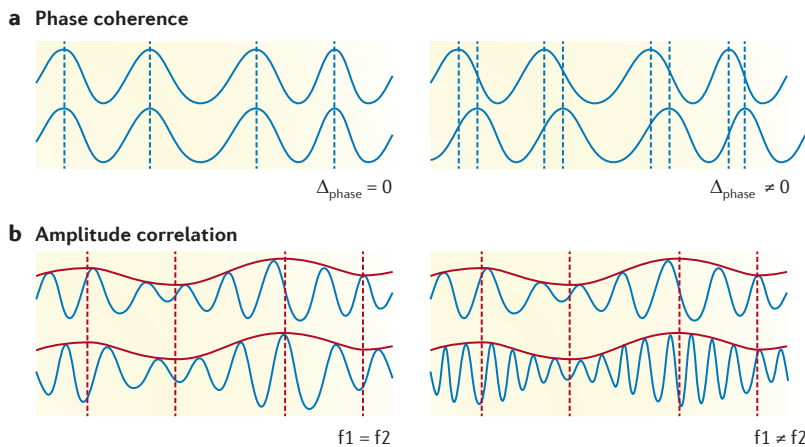


Figure 1 | Phase coherence and amplitude correlation of oscillations. **a** | Phase coherence quantifies the consistency of the relative phase between two simultaneous signals that have the same frequency. The left panel shows an example of two oscillatory signals that are phase coherent with zero phase lag. Signals can also be phase coherent with non-zero phase lag (right panel), that is, they can be phase-shifted relative to each other. **b** | Amplitude correlation is a measure of the correlation of the envelopes (shown in red) of two simultaneous oscillatory signals (amplitude correlation is also often referred to as 'power-to-power correlation' or 'amplitude–amplitude coupling'). Amplitude correlation can be measured between oscillatory signals of the same or different underlying carrier frequencies. Furthermore, amplitudes can be positively correlated or negatively correlated (that is, anti-correlated). The panels show examples of a positive amplitude correlation between two oscillatory signals of the same (left) and different (right) underlying carrier frequencies. Importantly, phase coherence and amplitude correlation are independent of one another. This is exemplified in the left panel of part **b**, in which the amplitudes of the two oscillations are correlated but the underlying oscillations are not phase coherent. *f*, frequency.

Box 1 | Measuring interactions between brain regions: electrophysiology versus functional MRI

The correspondence between the phase coherence of electrophysiological signals at a fine temporal scale and the temporal correlations of sluggish functional MRI (fMRI) signals is unclear. Because of its low temporal resolution, the fMRI signal is not likely to allow for directly measuring the phase coherence between cortical responses, at least in intermediate and high frequency (that is, beta and gamma) ranges. However, evidence has linked the correlations between fMRI signals at distant points in the brain to amplitude correlations of band-limited cortical activity^{38,199,200}. Co-variations between the amplitude envelopes of electrophysiological mass signals are typically as slow as the resting state fluctuations of the fMRI signal, in that they have a $1/f$ spectrum with dominant frequencies around 0.1 Hz and below²⁰¹. It has been speculated that these slow, coherent fluctuations may reflect common input from neuromodulatory brainstem centres³⁸. More recent evidence shows that correlations between remote fMRI signals can also occur at faster timescales that reflect specific perceptual and cognitive processes^{26,202–204}. Again, these correlations probably reflect a correlation between amplitudes of band-limited activity; however, measurements to test this hypothesis have not yet been performed.

brain areas^{45–50,63,64}. Information about the environment encoded in sensory cortices is routed to motor structures in a feedforward fashion^{45–50}. However, these sensorimotor transformations are strongly shaped by feedback from association and premotor cortices to early sensory cortices. The mapping of sensory information onto actions is flexibly adapted by these feedback interactions to both the decision-maker's internal state and the situational context^{42,50–62}. For example, 'top-down' feedback signals selectively bias the information flow such that only the goal-relevant evidence is mapped onto motor actions^{65,66}. Such feedback to sensory cortices may even occur spontaneously, when the task does not require it^{54–56}. Further, real-life sensory-guided behaviour involves active sampling of the sensory environment⁶⁷, and here, momentary sensory inputs are strongly shaped by motor actions (for example, saccades, whisking or sniffing)⁶⁸ as well as motor plans^{69,70}.

Traditionally, studies of the neuronal basis of sensory-guided behaviour have been segregated according to the primary direction of information flow. Studies of sensorimotor decision-making have primarily focused on the 'bottom-up' transformation of sensory information into action plans, whereas studies of top-down attention primarily focus on the top-down selection of sensory information. In the following section, we first follow this distinction when reviewing recent studies of large-scale neuronal interactions. We then discuss the mechanistic connections between the neuronal interactions identified in these two lines of research.

Sensorimotor decision-making. A number of influential single-unit studies in monkeys have focused on characterizing the feedforward transformations of sensory signals into motor plans during sensorimotor decisions^{45,46,48,49}. These studies suggest that the temporal integration of sensory information that lies at the heart of this decision process is distributed across several recurrently interconnected cortical association areas, most importantly the posterior parietal cortex (PPC) and dorsolateral prefrontal cortex (DLPFC)^{45–49}. Recent studies in humans and monkeys have adopted analogous experimental strategies to investigate the large-scale cortical interactions during sensorimotor decisions.

One example is a series of studies that combined MEG with source reconstruction in humans^{42,50,71–73}. In

one of the studies⁴², subjects had to decide whether there was a coherent visual motion signal embedded in visual 'noise' presented on a screen and report their decisions by pressing a button with one of their hands. Owing to the difficulty of this task, subjects had to integrate the weak 'evidence' for motion over time^{51,74,75}. Amplitude correlation of local oscillations during decision formation provided insight into the large-scale interactions between sensory and motor stages. Preceding the button press, lateralized gamma-band (~60–100 Hz) and beta-band (~12–35 Hz) activity associated with the upcoming choice gradually built up in the subjects' left and right motor cortices⁴². The build-up of this choice-predictive activity reflected the temporal integral of the stimulus response in the area MT⁴², and gamma-band activity in this area encoded the strength of visual motion⁷¹ (FIG. 2a). This direct evidence for the temporal integration of sensory evidence into motor plans could only have been obtained by directly analysing the interactions between two 'stages' (that is, sensory and motor stages) of the decision process^{51,74,75}.

Several studies have suggested a role for large-scale coupling in the beta-band in sensorimotor integration^{76–78}. A different analysis of the MEG data on visual motion detection (discussed above) implicated large-scale oscillations in a lower beta-band (12–25 Hz) in connecting the sensory and motor processing stages of the decision process⁷². While subjects were forming the decision, beta-band oscillations were enhanced in the PPC and DLPFC before correct choices relative to incorrect choices (FIG. 2b). Moreover, interactions between the PPC and DLPFC — as assessed by their amplitude correlation in the beta-band — predicted the correctness of the upcoming choice. One possible interpretation of this result is that the large-scale, frontoparietal beta-band oscillations that occur during decision formation reflect reverberant network interactions that actively maintain past sensory evidence^{50,72,79}. Notably, these large-scale beta-band oscillations are distinct from the choice-predictive suppression of local beta-band oscillations in the motor cortex⁴², which seems to reflect a focal suppression of intrinsic rhythms by cortical activation⁸⁰.

Multi-area recordings from the monkey cortex provide further support for the idea that large-scale beta-band oscillations are involved in sensorimotor decisions. A recent study⁸¹ showed decision-related beta-band

1/f spectrum

A spectrum for which the power P is inversely proportional to frequency f : $P(f) \propto 1/f^a$, $a > 0$.

Posterior parietal cortex

(PPC). An associative brain region that is centrally involved in spatial processing and controlling selective attention.

Area MT

A region in the extrastriate visual cortex of the primate brain that is centrally involved in neuronal processing and perception of visual motion.

Local field potentials (LFPs). The low-frequency components of the extracellular voltage. The LFP mainly reflects average postsynaptic potentials surrounding the electrode tip.

activity during a well-characterized somatosensory discrimination task^{48,82}. In each trial of this task, monkeys received two vibrotactile stimuli, separated by a brief delay, to the right hand and had to indicate with a left-hand button press whether the second stimulus was of higher or lower frequency than the first stimulus. During stimulus presentation, beta-band oscillations

(~15–30 Hz) in the local field potentials (LFPs) of several frontal cortical areas varied with the stimulus frequency. Furthermore, during the decision-making period (that is, after stimulus presentation), beta-band oscillations in medial prefrontal and primary motor cortices reflected the monkeys' upcoming perceptual choice. These large-scale beta-band modulations were absent in a control condition in which the monkeys received the same vibrotactile stimuli and had to make a motor response but no perceptual decision about the stimuli. The decision-related beta-activity reflected the upcoming choice, irrespective of its correctness. In that respect, this otherwise similar spectral fingerprint differed from the large-scale performance-related beta-band activity observed during visual motion detection discussed above⁷². Experiments using similar tasks in human MEG and monkey LFP studies are needed to determine the causes of this apparent dissociation.

Frontal–parietal beta-band oscillations also seem to be instrumental for decisions that are not directly instructed by external stimuli⁸³ (FIG. 2c). When monkeys were free to choose a sequence of reach movements to visual targets displayed on a screen, coherence between spikes and LFPs in the premotor cortex and in a specific region of the PPC (the 'parietal reach region') increased transiently around 15 Hz. This coherence increase was stronger during the 'free search' condition than during a control condition in which the monkeys had to follow a visually instructed movement sequence. The authors suggested that the free decision process more strongly recruited a large-scale frontoparietal decision circuit⁸³. Interactions in this decision circuit may specifically involve the beta-band.

Top-down attention. Several recent studies have begun to characterize the cortical long-range interactions that underlie top-down attention in the primate brain. One MEG study⁷³ demonstrated that attention selectively modulates large-scale cortical phase coherence in the human brain (FIG. 3a). Subjects were simultaneously presented with two weak motion stimuli in the left and right visual hemifield. At the beginning of each trial, a cue instructed subjects to attend to one of the two stimuli and to assess its motion direction. The authors combined MEG with source reconstruction to characterize the phase coherence between visual cortical area MT and two attentional control regions, the PPC and the frontal eye field (FEF)⁷³. Attention selectively enhanced gamma-band phase coherence between these regions in the hemisphere that processed the attended stimulus (FIG. 3a). This enhancement was complemented by a reduction of coherence in lower (that is, alpha and beta) frequency ranges. Attention also modulated local oscillatory activity (that is, signal power) in these brain regions, with different frequency bands being involved before and during stimulus presentation⁷³. By contrast, long-range coherence was similarly modulated before and during stimulus presentation and thus seemed to be largely stimulus-independent. These findings suggest that attention establishes gamma-band coherence between specific neuronal populations in frontal, parietal and visual

Box 2 | Challenges in characterizing large-scale neuronal interactions

Signal-to-noise ratio

The signal-to-noise ratio (SNR) poses a serious but often ignored potential confounding factor for all assessments of neuronal interactions based on measures of neuronal mass activity. Measures such as the local field potential (LFP), electroencephalography (EEG), magnetoencephalography (MEG) or blood oxygen level-dependent (BOLD) functional MRI (fMRI) not only reflect activity of the neuronal population of interest ('signal') but also activity that is not of interest ('noise'). Consequently, changes in measured correlations can be driven by changes in the SNR. For example, even if the true correlation between two populations of interest does not change, a mere increase in the amplitude of their activity leads to an increase in the SNR and thus to an increase in the measured correlation (for a detailed discussion, see REF. 87). One strategy to control for this confounding factor is to focus on characterizing changes in correlation only if they are not paralleled by changes in the amplitude of the local neuronal signals^{87,95,204}.

Multiple-comparison problems

Large numbers of comparisons across the brain are common in brain-imaging techniques. But the more comparisons that are performed, the higher the probability that false-positives will be detected. This multiple-comparison problem is often severely aggravated when studying neuronal interactions because the number of interactions grows quadratically with the number of potentially interacting regions. Like SNR confounding factors, this problem is not limited to the characterization of neuronal oscillations but also applies to other approaches (for example, fMRI). Typical strategies to circumvent this problem are to focus on a few regions of interest and to apply rigorous statistical techniques that efficiently account for multiple comparisons⁸⁷.

Field spread

Field spread refers to the fact that electrical potentials and magnetic fields generated by neuronal activity are not only measured in the direct vicinity of neuronal sources but can also be measured at distant sites, depending on the conductive properties of the interposed media. This substantially limits the interpretation of sensor-level EEG and MEG data with respect to underlying neuronal sources. For example, responses in the primary auditory cortex (that is, the temporal lobe) are most strongly measured at central and peripheral EEG electrodes, but not actually at electrodes over the temporal cortex²⁰⁵. Thus, coherent activity at distant EEG or MEG sensors should be interpreted with caution, as it may merely reflect activity from a single neuronal source rather than coherence of activity at distinct sources²⁰⁶. Applying spatial filtering techniques to EEG or MEG data, such as surface Laplacian or source reconstruction techniques, can help to minimize the problem of volume conduction. Because volume conduction is always instantaneous, an effective strategy for addressing this confounding factor is to confine the analysis to non-instantaneous correlations, as in analyses of directed interactions or of the phase-lagged part of coherence²⁰⁷.

Saccadic spike potentials

Saccadic spike potentials are electromagnetic signals that are produced by extraocular muscle contractions at the onset of saccadic or microsaccadic eye movements²⁰⁸. The waveform of these spike potentials contains the most signal power in a broad gamma-band (~20–90 Hz) and, because of field spread (see above), spike potentials are strongly picked up at frontal, parietal and occipital EEG electrodes^{209–211}. The rate of microsaccades is modulated by stimulus presentation and cognitive factors^{212,213}. With their topography, spectral characteristic and temporal modulation, spike potentials closely resemble neuronal gamma-band activity. Indeed, several EEG findings that had previously been interpreted as neuronal gamma-band activity are likely to reflect saccadic spike-potentials^{209,210}. Thus, it is crucial to carefully control for saccadic spike-potential artefacts in any EEG or MEG²¹⁴ experiments that investigate oscillatory activity in the gamma-band. Rejection of contaminated data segments, source analysis⁸⁷ and independent component analysis (ICA)-based spike-potential removal¹¹⁰ provide useful approaches.

Frontal eye field (FEF). A region in the frontal cortex that controls saccadic eye movements and the focus of visuospatial attention in the primate brain.

cortices and that this coherence mediates the selection of task-relevant visual information.

Enhanced coherence of the FEF with the visual cortex may reflect attentional selection of sensory signals by feedback from the FEF to the visual cortex, as well

as the feedforward influence of the selected neuronal population in the visual cortex to the corresponding FEF population, thus supporting the covert reorienting of attention and/or the preparation of an eye movement to the attended stimulus^{70,84}. Evidence for both of these aspects was provided in a study⁸⁵ of the interactions between the FEF and visual area V4 during a visuospatial attention task in monkeys (FIG. 3b). In accordance with the MEG results discussed above⁷³, top-down attention enhanced gamma-band coherence between the FEF and V4. Gamma-band oscillations in both areas were phase-shifted by ~10 ms. Given synaptic and conduction delays, this time shift may be optimal for spikes in one region to affect neurons at peak depolarization in the other region. Moreover, an analysis of the direction of inter-regional gamma-band interactions based on Granger causality suggested that immediately after a cue to shift attention, feedback from the FEF to V4 dominated. Later, during processing of the attended stimulus, feedforward influences from V4 to the FEF became dominant (FIG. 3b). Thus, after an initial top-down bias of sensory processing stages, long-range gamma-band coherence seems to primarily mediate the enhanced bottom-up routing of attended sensory signals.

The above two studies^{73,85} provide converging evidence that the gamma frequency range is instrumental in mediating the cortical long-range interactions underlying top-down attention. However, other findings also suggest an important role for lower frequencies, in particular the beta- and theta-bands. One human MEG study⁸⁶ investigated the neuronal basis of the attentional blink (FIG. 3c). When subjects successfully detected target letters in a rapid visual stream of letters, coherent beta-band oscillations (13–18 Hz) were enhanced between MEG sensors overlying the temporal cortex, DLPFC and PPC. Thus, fluctuations in the strength of large-scale beta-band coherence may reflect fluctuations in visual attention that, in turn, cause fluctuations in behavioural performance.

An EEG study⁸⁷ of cortical coherence during perception of an ambiguous audiovisual stimulus also suggests that top-down attention can be mediated by coherent beta-band oscillations across frontoparietal networks. In each trial, participants watched a screen on which two bars approached, briefly overlapped and moved apart again. At the time of overlap of the bars, a brief click sound was played. Participants perceived this stimulus either as two passing or bouncing bars, with the percept spontaneously changing from trial to trial. Around the time when the stimulus became perceptually ambiguous, beta-band coherence (15–23 Hz) was enhanced across a large-scale cortical network including bilateral FEF, PPC and visual area MT (FIG. 3d). Furthermore, the strength of beta-band coherence in this network predicted the subjects' percept: stronger beta-band coherence predicted the subjects perceiving the bars as bouncing, whereas weaker coherence predicted the percept of passing bars. As the FEF and PPC are centrally involved in controlling top-down attention^{57,59–61}, fluctuations of large-scale beta-band coherence may reflect fluctuations of attention that determine the bi-stable percept.

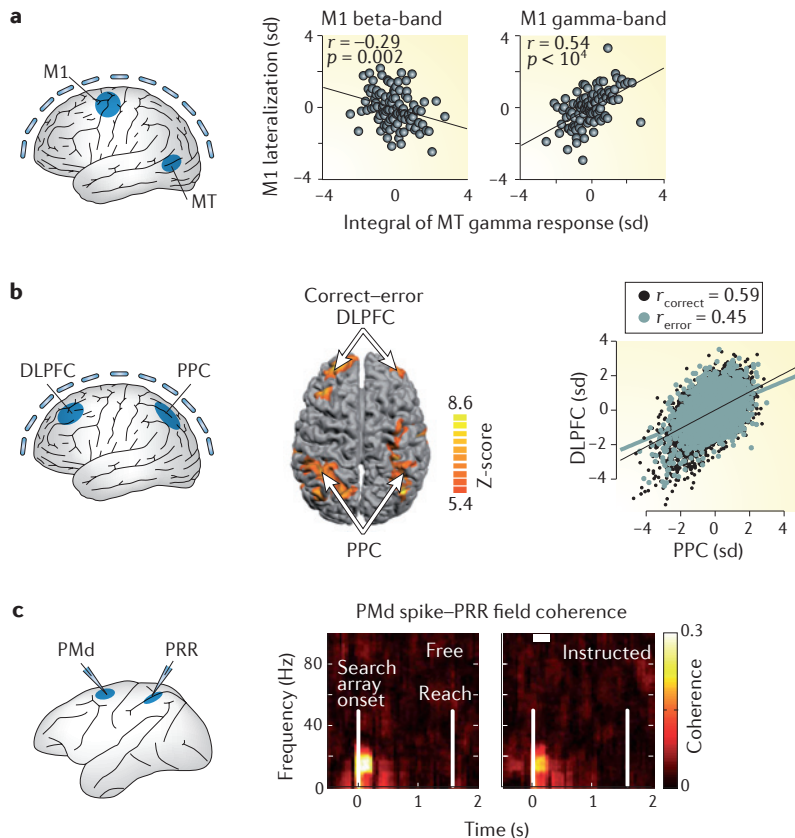
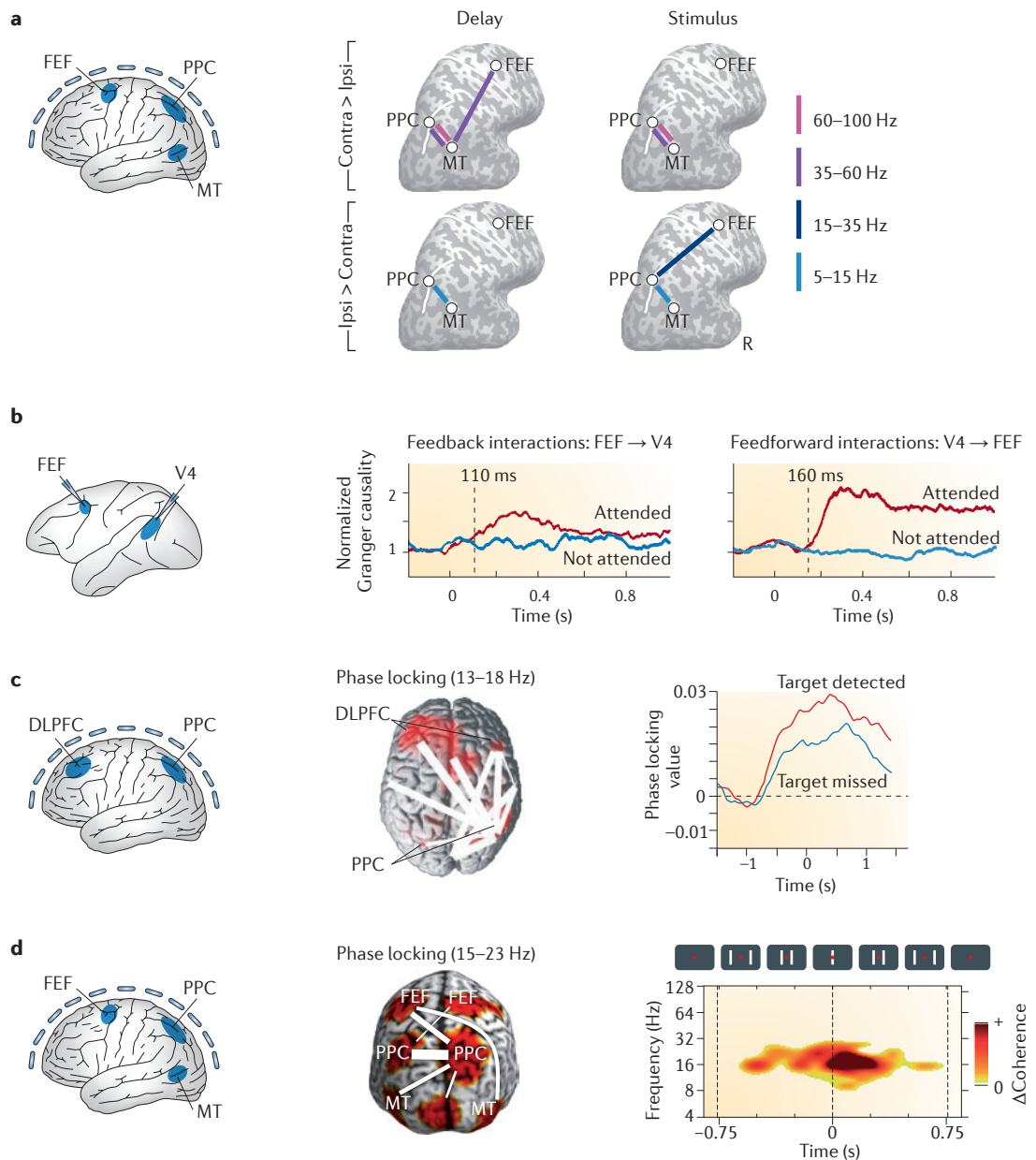


Figure 2 | Cortical network dynamics underlying sensorimotor decisions.

a | Long-range interactions between sensory and motor processing stages during perceptual decision-making in humans. Neuronal activity in the motor cortex (M1) and area MT (left panel) was reconstructed from the magnetoencephalogram of subjects performing a visual motion-detection task. Gamma-band activity in area MT reflects the strength of visual motion⁷¹, and the hemispheric lateralization of gamma- and beta-band activity in M1 reflects the upcoming manual motor response. The temporal integral of MT gamma-band activity across the stimulus-viewing interval predicted M1 lateralization in the beta-band and gamma-band at the end of stimulus viewing. This suggests that the temporal integration of sensory evidence encoded in area MT underlies the interaction of MT and M1. **b** | Frontoparietal beta-band (12–24 Hz) activity reflects perceptual decision-making processes. During stimulus viewing in the same motion-detection task as in **a**, beta-band activity reconstructed from the magnetoencephalogram in dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC) (left panel) was stronger for correct than for erroneous detection decisions (middle panel). Also, stronger interactions between DLPFC and PPC, as quantified by the amplitude correlation of beta-band activity between these stages, predicted correct decisions (right panel). **c** | Frontoparietal beta-band coherence around 15 Hz reflects decision-making during motor planning. Local field potentials (LFPs) and spiking activity were simultaneously recorded in dorsal premotor cortex (PMd) and the parietal reach region (PRR) in macaque monkeys (left panel) performing an instructed or free motor choice task. Immediately following the display of a search array, beta-band coherence between spikes in PMd and LFPs in PRR was enhanced during free choices (left graph) compared with instructed (right graph) choices. The graphs in **a** are reproduced, with permission, from REF. 42 © (2009) Elsevier. The middle panel of **b** is reproduced, with permission, from REF. 72 © (2007) American Physiological Society. The graphs in **c** are reproduced, with permission, from REF. 83 © (2008) Macmillan Publishers Ltd. All rights reserved. sd, standard deviation.



Two invasive studies in monkeys provide further support for the importance of long-range beta-coherence in top-down visual attention. The first study⁸⁸ simultaneously recorded neuronal activity from area MT and the lateral intraparietal area (area LIP) (a region of the PPC) during a visual delayed match-to-sample task in monkeys. High beta-band coherence (20–35 Hz) was selectively enhanced between those neuronal populations in MT and LIP that encoded the remembered visual location. The discrepancy between the enhancement of coherence in the beta-band in this study and the gamma-band enhancements reported in REFS 73,85 may be related to the different behavioural tasks (delayed match-to-sample versus instructed spatial attention tasks). Indeed, another study⁸⁹ found that the frequency of long-range interactions changes with different directions of visuomotor processing. Here, the authors

compared the coherence between the DLPFC and the LIP in a task that required top-down attention to find a visual target ('top-down task') and in a task in which attention was attracted to a salient target in a bottom-up fashion ('bottom-up task'). The top-down task was associated with enhanced coherence between the LIP and DLPFC in the beta-band (22–34 Hz), whereas the bottom-up task was associated with enhanced coherence in the gamma-band (35–55 Hz). Thus, this study suggests that bottom-up and top-down visuomotor processing may rely on interactions between the DLPFC and the PPC in the gamma- and beta-band, respectively.

Two human EEG studies suggest that feedback interactions in the theta-band between areas of the medial frontal cortex and visual cortex also contribute to the top-down control of visually guided behaviour. One study⁴³ recorded EEG in children performing a

Granger causality

A statistical measure that quantifies directed and potentially causal interactions between two simultaneous signals based on their mutual predictability.

Attentional blink

The phenomenon that a second target is often missed when presented ~200–500 ms after a first target in a rapid stream of visual stimuli.

◀ **Figure 3 | Cortical network dynamics underlying top-down attention.**

a | Long-range coherence among the prefrontal, parietal and visual cortex during a spatial attention task in humans. Neuronal activity in the frontal eye field (FEF), posterior parietal cortex (PPC) and area MT was reconstructed from the magnetoencephalogram (left panel) of subjects performing a demanding visual motion-discrimination task during which stimuli were shown in the left and right visual hemifield. During a delay interval following the cue to shift attention ('Delay', middle panels), long-range phase coherence in the gamma-band (35–100 Hz) between the PPC, area MT and FEF was enhanced in the hemisphere contralateral to the attended visual hemifield compared with the non-attended hemifield (top). At the same time, low-frequency alpha-band coherence (5–15 Hz) between area MT and PPC was suppressed in the attended hemifield compared with the non-attended hemifield (bottom). Similarly, during stimulus presentation ('Stimulus', right panels), attention enhanced long-range coherence in the gamma-band between the PPC and area MT in the contralateral hemifield (top) and suppressed coherence in lower frequency ranges among the PPC, FEF and area MT in the contralateral hemifield (bottom). **b** | Directed gamma-band (40–60 Hz) interactions between the prefrontal and visual cortex during spatial attention. Local field potentials (LFPs) were simultaneously recorded from the FEF and visual area V4 (left panel) of macaque monkeys attending to one of several visual targets. Following the cue indicating which target to attend, feedback interactions in the gamma-band (quantified by Granger causality) were enhanced between those neuronal populations in the FEF and V4 that encoded the attended target (middle panel). Approximately 50 ms later, feedforward interactions in the gamma-band were also selectively enhanced between these neuronal populations (right panel). **c** | Frontoparietal beta-band (13–18 Hz) coherence during the attentional blink in humans. Neuronal activity in the dorsolateral prefrontal cortex (DLPFC) and PPC was reconstructed from the magnetoencephalogram (left panel) of subjects detecting target letters in a rapid serial visual stream. The rapid and successive presentation of target letters causes subjects to miss a substantial fraction of the targets. Correct target detection was associated with enhanced long-range beta-band coherence (quantified by the phase-locking value) between DLPFC and PPC (middle and right panel). **d** | Long-range beta-band coherence (15–23 Hz) between the frontoparietal (FEF and PPC) and visual cortex (area MT) (left panel) during processing of an ambiguous visual motion stimulus. Neuronal activity was reconstructed from the electroencephalogram of human subjects presented with two moving bars that could be perceived either as bouncing or passing (see stimulus schematic at the top of the right panel). Long-range coherence was enhanced in a widespread cortical network including bilateral FEF, PPC and MT (middle panel). Coherence within this network was enhanced for approximately 1 second around the time of bar overlap in the beta-band from approximately 15 to 23 Hz (right panel). Beta-band coherence in this network predicted whether the subjects perceived the bars as bouncing or passing. The middle and right panels of **a** are reproduced, with permission, from REF. 73 © (2008) Elsevier. The middle and right panel of **b** are reproduced, with permission, from REF. 85 © (2009) American Association for the Advancement of Science. The middle and right panel of **c** are reproduced, with permission, from REF. 86 © (2004) National Academy of Sciences. The middle and right panel of **d** are reproduced, with permission, from REF. 87 © (2011) Elsevier.

cross-modal attention task that required them to shift their attention between visual and auditory stimuli. Alpha-band activity over the visual cortex predicted behavioural performance and was suppressed during visual attention as compared to auditory attention. This accords well with the notion that local alpha oscillations in early sensory regions reflect a 'pulsed' functional inhibition of irrelevant processing streams^{23,90–94}. Moreover, the amplitude of alpha-band activity over the visual cortex was inversely correlated with medial frontal theta-band activity. This amplitude correlation was missing in children with attention deficit hyperactivity disorder (ADHD)⁴⁴. The notion that the medial frontal cortex exerts top-down control over the visual cortex through theta-band oscillations receives further support from another EEG study⁹⁵. Here, during a visual go/no-go task, enhanced theta-band coherence and

Go/no-go task

A task that requires a subject to perform a behavioural response (for example, button press) when one stimulus type appears, but to withhold a response when another stimulus type appears.

directed interactions from medial frontal to occipital cortex occurred immediately after a response error had been made. The strength of these theta-band interactions predicted behavioural performance in the subsequent trial, in line with models of prefrontal control over sensorimotor processing⁶⁵.

The studies reviewed in the preceding sections illustrate that phase coherence and amplitude correlation of cortical oscillations provide insight into the interactions between brain regions that underlie cognitive processes. The traditional approach in neuroscience has focused on characterizing in detail how sensory, cognitive and motor variables are encoded in individual brain regions (FIG. 4a). By contrast, the studies reviewed here have provided a glimpse into the large-scale neuronal interactions that transform these variables to produce cognition and goal-directed sensory-guided behaviour.

All of the studies discussed in this Review have demonstrated that the large-scale neuronal interactions underlying goal-directed sensory-guided behaviour occur within specific frequency bands. But the pattern of these frequency-specific effects is complex: different frequency bands have been implicated in the same cognitive process and different cognitive processes seem to involve identical frequency ranges. How can these findings be reconciled? And what do they teach us about the neuronal basis of sensory-guided behaviour and cognition? Answering these questions requires consideration of the factors that govern the different frequency bands of large-scale cortical oscillations. There are currently two main perspectives on these factors: the first perspective focuses on the functional properties of large-scale neuronal interactions, and the second perspective focuses on the biophysical properties of neuronal circuits.

Functional properties of interactions

Directionality of interactions. It has been suggested that different frequencies of large-scale coherent oscillations reflect different directions of cortical information flow^{24,89,96–98}. Specifically, coherent gamma and beta (or alpha) oscillations have been implicated in feedforward and feedback interactions, respectively. This notion is supported by theoretical^{96,99,100} and experimental evidence^{89,97,101}. On the basis of laminar recordings in the cat visual system, gamma-band coherence and coherence at lower frequencies have been linked to bottom-up and top-down directed interactions, respectively⁹⁷. Furthermore, in the frontoparietal network, gamma-band coherence has been specifically demonstrated during bottom-up directed visuomotor processing, whereas beta-band coherence was found during top-down directed processing⁸⁹. Also, feedback interactions during multisensory processing have been associated with beta-band activity¹⁰¹. As we discuss below, this notion accords well with recent evidence on the laminar specificity of cortical rhythms and long-range interactions. However, this notion is challenged by experiments that specifically implicate long-range gamma-band coherence in top-down processing^{85,102}. Further studies are required to probe how consistently different frequencies (in particular gamma and beta) are associated with feedforward and feedback interactions.

Timescale of processing. It has been hypothesized that large-scale beta-band oscillations reflect the maintenance of information across long timescales, whereas gamma-band activity reflects the encoding of local variables that may vary over short timescales (for example, owing to sensory inputs)^{50,72}. A related account postulates that large-scale beta-band oscillations reflect maintenance of the status quo in large-scale cortical networks, whereas gamma-band oscillations predominate if changes in the stimulus are expected¹⁰³. In line with these notions, beta oscillations have been observed in occipital, inferotemporal and prefrontal cortex during short-term memory tasks^{104–110} (see REF. 111 for a comprehensive review on memory and neuronal oscillations in various frequency ranges). Active maintenance of information is not only crucial for accomplishing short-term memory tasks, but is also a general building block of cognition. For example, it is necessary for guiding the

focus of attention based on behavioural goals⁶⁶, for forming decisions based on past evidence, and for ‘keeping online’ the mapping between sensory inputs and motor actions required by the context at hand. Indeed, the studies discussed here consistently implicate large-scale beta oscillations in top-down attention^{86,88,89} and sensorimotor decision-making^{72,83,87}. Consistent with this notion, *in vitro*¹¹² and modelling¹¹³ studies suggest that the neural mechanisms that generate local beta-band oscillations may be particularly suited for maintaining persistent activity even in the absence of external inputs. It should be noted that the factors ‘timescale of processing’ and ‘directionality of interactions’ are not mutually exclusive but, in fact, may be closely related. For example, intrinsic cognitive processes may typically evolve on relatively long timescales and drive feedback interactions in recurrent cortico–cortical loops.

Rhythmicity of cognitive processes. Cortical oscillations may reflect not only rhythmic neuronal activity during continuous cognitive processes but also the rhythmic dynamics of cognitive processing itself^{21,67,114,115}. It has been suggested that, in addition to a ‘continuous’ mode, sensory processing can operate in a ‘rhythmic’ mode in which the phases of neuronal oscillations across sensory pathways are aligned to amplify the processing of behaviourally relevant rhythmic sensory inputs^{21,67}. These rhythmic inputs may result either from the inherent temporal structure of sensory streams (for example, speech¹¹⁶) or, during a mode of ‘active sensing’, from the rhythmic motor sampling of the environment (for example, saccades¹¹⁷, whisking^{118,119} or sniffing¹²⁰). In line with this notion, low-frequency oscillations (~3 Hz) in the primary visual and auditory cortices of monkeys are entrained by attended rhythmic inputs in either the preferred or non-preferred modality^{121,122} — this mechanism may be particularly suited to enhancing the integration of sensory information across modalities¹²². Other findings also support this idea. For example: rhythmic microsaccades that trigger retinal transients are correlated with the phase of slow LFP fluctuations (~3 Hz) across visual areas V1 and V4 in monkeys¹¹⁷; covert shifts of attention during visual search are aligned to the phase of beta-band oscillations in monkey FEF¹²³; the phase of theta-band oscillations in the human auditory system tracks the dynamics of incoming speech signals¹¹⁶; slow oscillations in primary sensory cortex are correlated with whisker position during active whisking in rodents^{118,119}; and slow theta-band oscillations in the rodent olfactory system are aligned with the respiratory cycle during sniffing¹²⁰. In most of these cases^{117,120–122}, the phase of the slow oscillations modulates the amplitude of (faster) gamma oscillations such that the gamma oscillations co-occur with the incoming sensory information. EEG recordings in humans also show that the perception of visual stimuli is rhythmically modulated by the phase of slow cortical oscillations in the alpha^{90–93,114,124} and theta¹²⁵ range. The evidence that slow cortical oscillations reflect rhythmic sampling of sensory information is consistent with psychophysical data on the timescale of sensory processing. Indeed, the timescales

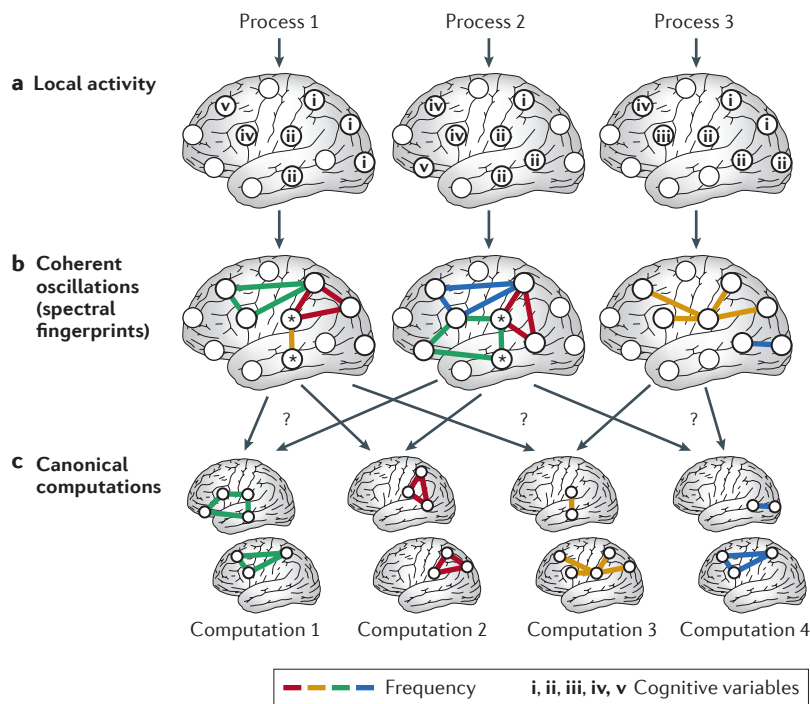


Figure 4 | Large-scale spectral fingerprints of cognitive processes. Schematic illustration of how coherent oscillations provide ‘spectral fingerprints’ for regrouping of cognitive processes 1–3. **a** | Studies of neuronal activity in individual brain regions (circles) elucidate the activation of different regions (bold circles) and the encoding of various cognitive variables (Roman numerals) during different cognitive processes. Several cognitive variables (for example, different sensory features) are simultaneously encoded in each region, but for simplicity only one variable is depicted per region. Note that the pattern of local activity and encoding can be similar between processes. **b** | Coherent oscillations allow for the characterization of the interactions between different brain regions (coloured lines) during different cognitive processes. The frequency of these oscillations (indicated by the colours) allows the corresponding network interactions to be classified and, thus, for the cognitive processes to be regrouped. For simplicity, only interactions in one frequency range are depicted between pairs of regions. The two regions marked by asterisks illustrate that different frequency-specific interactions (yellow versus green lines) can dissociate cognitive processes that show identical effects at the level of local activity (compare with the marked regions in **a**). **c** | The different frequencies of coherent oscillations may allow for the identification of corresponding canonical computations that underlie cognitive processes.

Box 3 | Circuit mechanisms of local cortical oscillations

A combination of *in vivo*, *in vitro* and modelling approaches has substantially advanced our understanding of the circuit mechanisms that underlie local cortical oscillations, in particular those in the gamma-band. Converging evidence^{96,126,133,141–147} suggests that local cortical gamma-band oscillations result from local excitatory–inhibitory feedback loops between pyramidal neurons and fast-spiking interneurons. The frequency of these local interactions in the gamma-band is determined by the time constant of inhibitory GABA_A conductances^{96,126,133,142–147,154} and the balance between excitation and inhibition¹⁴¹.

The mechanisms underlying local cortical oscillations in other frequency ranges are currently less clear. Recent *in vitro* and modelling studies suggest a separation of the beta-band into lower (beta1) and higher (beta2) frequency ranges and have identified potential underlying circuit mechanisms^{100,112,113,135,140}. Beta2 oscillations seem to originate primarily from deep cortical layers and, depending on the cortical region at hand, may require either chemical or purely electrical synaptic interactions^{100,135}. Beta1 oscillations may result from the concatenation of those local circuit interactions across deep and superficial layers, which also generate local gamma and beta2 oscillations^{112,140}. An alternative model suggests that local beta-band oscillations result from local interactions between alpha-rhythmic feedforward and feedback inputs in a cortical column⁹⁹. Likewise, the mechanisms underlying cortical alpha oscillations are still poorly understood and may differ substantially across cortical regions. The available evidence suggests that in early sensory regions, alpha oscillations result not only from cortico–cortical interactions but also from the interplay between alpha rhythms generated in deep cortical layers^{136–139,187,188,215} and in the thalamus^{187,188,215,216}. In higher-order sensory regions, alpha oscillations seem to primarily originate from superficial cortical generators¹³⁶.

of forms of active sensing (for example, saccades, whisking or sniffing) and of the corresponding slow oscillations match well with the timescales of integration of sensory information measured in several perceptual decision-making tasks⁶⁸.

Biophysical circuit properties

Ultimately, the frequencies of all neuronal network interactions are determined by the biophysical properties of the underlying neuronal circuits. It has been suggested that the spatial distance — and hence conduction delays — between distant network nodes may be a key factor in determining the frequency range of cortical network interactions^{126,127}. Longer conduction delays between distant brain regions may limit the frequency of large-scale network oscillations to below the gamma-band (that is, beta or lower). Indeed, theoretical^{126,128} and experimental^{38,127} evidence supports the notion that the frequency of coherent oscillations drops as the spatial scale of processing increases. However, several recent empirical demonstrations of fast gamma-band coherence between distant cortical regions^{73,85,87,89,102,129} indicate that physical distance is probably not the only factor at work.

Local oscillations provide the basic temporal scaffolding for interactions between distant brain regions. Thus, the frequency of these local oscillations, which are determined by the biophysical properties of the local circuits, may also be an important factor in determining the frequencies of large-scale interactions. Considerable progress has been made in understanding the detailed circuit mechanisms underlying local cortical oscillations, in particular in the gamma-band (BOX 3). However, little is known about how these local circuit mechanisms shape the frequencies of large-scale neuronal interactions.

Large-scale spectral fingerprints

Here, we attempt to synthesize the two different perspectives outlined above into a common framework. At the heart of this framework lie neuronal circuit mechanisms at different levels of organization (for example, channel kinetics, local circuit motifs and large-scale network architectures)^{13,20,24,25}. Our framework is based on two key assumptions: first, that the biophysical properties of such circuit mechanisms determine the frequency bands of neuronal oscillations; and second, that the same circuit mechanisms determine canonical computations that constitute the elementary building blocks of cognition — that is, these computations can be combined and applied to different inputs in different neuronal networks to yield various different cognitive functions.

Two examples illustrate this idea. First, different directional modes of processing ('bottom-up' versus 'top-down') and the associated frequencies of coherent oscillations may result from the specific laminar profiles of local rhythms and inter-regional connections²⁴. Feedforward and feedback connections originate primarily in superficial and deep cortical layers, respectively^{130,131}, but a growing body of evidence suggests that specific oscillatory rhythms (as measured by the LFP) and corresponding local patterns of oscillatory neuronal synchronization are expressed with different strengths across cortical laminae. In particular, in early sensory cortices, gamma oscillations seem to dominate in superficial layers^{98,132–135}, whereas slower rhythms in the alpha-band^{98,132,136–139} and beta-band^{100,135,140} seem to dominate in deep layers. Thus, gamma-band oscillations and feedforward projections in superficial layers may lead to bottom-up interactions in the gamma-band. Conversely, slower rhythms and feedback projections in deep layers may underlie top-down interactions in slower frequency ranges in particular in the beta-band. The laminar specificity of cortical oscillations and long-range projections may thus be key for linking different directions of information processing with different frequency bands of large-scale coherent cortical oscillations^{24,96–98}.

Second, the concept of canonical computations may also apply to local oscillations in individual cortical regions²⁵. Local gamma oscillations provide an intriguing example. Recurrent excitatory–inhibitory network interactions in a local patch of cortex may determine both the frequency of gamma-band oscillations and the transformation of neuronal signals in that patch of cortex. As outlined above, the frequency of gamma-band oscillations is determined by the decay time of rhythmic local inhibition^{96,126,133,141–147}. The same local inhibition seems to mediate local computations, such as 'divisive normalization', that govern the encoding of sensory, cognitive or motor variables throughout the cerebral cortex^{148–153}. Thus, local cortical gamma-band oscillations may index a generic cortical computation underlying local encoding of information²⁵.

In both of these examples, cortical oscillations index canonical computations, that is, processes at a functional level of description (for example, feedback or normalization) below the one that is commonly used to describe cognition. The ideas outlined above suggest that the

frequency bands of coherent large-scale oscillations constitute fingerprints of these canonical computations (FIG. 4). Thus, we refer to these large-scale oscillations as ‘spectral fingerprints’. Spectral fingerprints provide valuable information about the circuit mechanisms of cognition, regardless of whether or not they have a direct computational role.

Spectral fingerprints at work. If these ideas are correct, spectral fingerprints point to an intermediate level of description, a level in between the processes defined by cognitive psychology and the underlying neuronal circuit interactions. This level of description may yield a new taxonomy of cognitive processes in terms of their mechanistic building blocks (FIG. 4). The studies on decision-making and attention discussed above provide examples for how the notion of spectral fingerprints may contribute to novel views on the underlying canonical computations.

These studies suggest that processes that are often conceptualized as monolithic entities across different tasks may turn out to be associated with distinct large-scale cortical network interactions. This is indicated, for example, by the different large-scale oscillations associated with top-down attention as discussed above. Depending on the task, this process has been associated with long-range coherence in the beta-band^{86–89} or in the gamma-band^{73,85}. This suggests that spectral fingerprints can distinguish processes that seem to be similar at the behavioural level and even at the level of neuronal processing in individual brain regions (compare the two regions marked by asterisks in FIG. 4). It is the different frequency ranges of their interaction that point to the different underlying computations. For example, interactions in the gamma- and beta-band may index the bottom-up and top-down directed cortical information flows, respectively, that predominate in different behavioural tasks.

Conversely, spectral fingerprints may enable the identification of canonical computations that are shared among cognitive processes that have typically been considered as distinct entities in cognitive neuroscience (FIG. 4c). For example, the studies discussed here consistently demonstrate the presence of beta-band interactions between posterior parietal and frontal cortices during both sensorimotor decision-making^{72,83,87} and top-down attention^{86,88,89}. We speculate that for both processes, large-scale beta-band activity indicates identical canonical computations in these networks. For example, both processes may involve the maintenance of information (decision variables or sensory–motor contingencies) through large-scale reverberation in recurrent networks⁷⁹, and for both processes, these reverberations may drive top-down interactions along the sensorimotor hierarchy (see above). More specifically, during decision-formation, high-level decision or motor stages may send specific top-down signals to sensory stages⁵⁵ that are similar to the top-down signals in top-down attention tasks. In other words, even for sensorimotor tasks that are classically thought to only require bottom-up information flow, the brain recruits top-down interactions^{54–56}. Therefore, at the level of these large-scale interactions,

decision-making and attention may be highly similar, and large-scale correlated beta-band oscillations may be a fingerprint of this common canonical computation.

Currently, the extent to which canonical computations can be inferred from spectral fingerprints is unknown. The strength of this inference will depend on how specific the link between frequencies and circuit mechanisms turns out to be. Even for the same underlying computation the exact frequency of large-scale oscillations can be highly variable, which may complicate a direct inference^{141,154,155}. Moreover, although some frequency bands may be tightly linked to specific circuit mechanisms, this relationship may be less clear for other bands. Finally, the link between fingerprints and canonical computations does not necessarily generalize across cortical networks. A particular frequency band may reflect one canonical computation in some anatomical networks, but may reflect a different mechanism in other networks. There may even be characteristic frequencies for specific anatomical networks that do not generalize to other networks. For example, theta-band phase coherence has been consistently implicated in interactions between the prefrontal cortex and hippocampus^{156–161} and may thus reflect a characteristic frequency for this specific anatomical network.

Conclusions and future directions

We have focused our concept of spectral fingerprints on phase-coherent oscillations between different cortical regions, but this notion may extend to other frequency-specific measures of neuronal population activity as well. First, the local power of oscillations may also serve as a spectral fingerprint of canonical computations²⁵. We have discussed local gamma-band activity as a showcase for this notion. However, evidence suggests that long-range coherence and local power in various frequency bands can be dissociated^{173,83,87,89}. Thus, frequency-specific local power and large-scale coherence may provide independent information about neural computations. Second, frequency-specific amplitude correlations between cortical regions also seem to be informative about underlying network computations. It remains to be determined to what extent amplitude correlation provides redundant or complementary information as compared to phase coherence. Third, interactions between different frequency bands may also index specific cortical computations. Interactions between frequencies can occur as phase–phase, phase–amplitude or amplitude–amplitude coupling¹⁶². Coupling between the phase of slower rhythms and the amplitude of faster rhythms (a phenomenon that is often referred to as ‘nesting’) seems to be ubiquitous across various cortical systems^{36,109,116,120,122,163–171}. This type of cross-frequency interaction provides a mechanism by which slower rhythms coordinate local or faster computations that are expressed at higher frequencies. As outlined above, evidence suggests that slow rhythms reflect rhythmic cognitive processes such as the rhythmic sampling of sensory information. Thus, phase–amplitude coupling may be a fingerprint of the temporal coordination — by slower rhythmic cognitive processes — of canonical

computations that are reflected at higher frequencies. Other types of cross-frequency interactions (for example, phase–phase or amplitude–amplitude) may serve as fingerprints of interactions between different canonical computations expressed in the interacting frequency bands.

Identifying the spectral fingerprints of the canonical computations of cognition would have important implications beyond basic neuroscience. Many neuropsychiatric disorders probably result from dysfunctions of specific network computations. Currently, neuropsychiatric disorders are classified at a phenomenological level¹⁷², and most biomarkers of these disorders do not capture the heart of the underlying network dysfunction. The spectral fingerprints of neuronal interactions may turn out to be sensitive markers of such disorders. Indeed, a rapidly growing body of evidence indicates that local oscillations and their large-scale coherence are altered in various diseases, including schizophrenia, Alzheimer's disease and autism spectrum disorders (see REFS 173–175 for reviews). In schizophrenia, impaired local oscillations^{176,177} and large-scale coherence¹⁷⁸ in the gamma-band seem to provide a spectral fingerprint of deficient GABAergic transmission^{173,179,180}.

The studies reviewed here provide a glimpse into the large-scale circuit dynamics that mediate cognition. They also raise important new questions for future research. First, more studies are required to link large-scale oscillations to well-controlled cognitive processes. What explains the variability in the frequency ranges of large-scale oscillations that have been identified for apparently similar cognitive processes? And is there a set of large-scale fingerprints that are common to seemingly

distinct cognitive processes? A broader basis of empirical studies will help to identify consistent links between frequency-specific large-scale interactions and specific cognitive processes. Second, more studies are required to unravel the circuit mechanisms that underlie large-scale cortical oscillations. What roles do layer- and cell-specific projections between cortical regions have? How specific is the link between the frequencies of local and large-scale oscillations and the underlying circuit mechanisms? And what is the relationship between the frequencies of local oscillations and their large-scale coherence or amplitude–correlation? Third, how do subcortical systems shape the spectral fingerprints of cognitive processes in the cerebral cortex? It has become clear in recent years that brainstem neuromodulatory systems are not merely unspecific regulators of coarse behavioural states but have important roles in cognitive processes such as attention and decision-making^{181–184}. These neuromodulatory systems alter the frequency range and strength of local cortical oscillations^{40,100,185}, and it is therefore likely that they shape the frequencies of large-scale cortical interactions during cognition. The thalamus may also have an important role in shaping large-scale cortical oscillations¹⁸⁶. Cortical alpha-band^{136,139,187,188} and beta-band^{189–191} oscillations seem to involve reciprocal thalamo–cortical loops. Furthermore, higher-order thalamic nuclei such as the pulvinar may be crucial for synchronizing oscillations^{186,191–197} and facilitating information transfer¹⁹⁸ between distant cortical regions. Answering these questions will further our understanding of large-scale correlated oscillations as fingerprints of the canonical computations underlying cognition.

- Crick, F. & Koch, C. A framework for consciousness. *Nature Neurosci.* **6**, 119–126 (2003).
- Singer, W. & Gray, C. M. Visual feature integration and the temporal correlation hypothesis. *Annu. Rev. Neurosci.* **18**, 555–586 (1995).
- von der Malsburg, C. The correlation theory of brain function. in *Internal Report 81-2* (Max-Planck-Institute for Biophysical Chemistry, 1981).
- Eckhorn, R. *et al.* Coherent oscillations: a mechanism of feature linking in the visual cortex? Multiple electrode and correlation analyses in the cat. *Biol. Cybern.* **60**, 121–130 (1988).
- Engel, A. K., Kreiter, A. K., König, P. & Singer, W. Synchronization of oscillatory neuronal responses between striate and extrastriate visual cortical areas of the cat. *Proc. Natl Acad. Sci. USA* **88**, 6048–6052 (1991).
- Gray, C. M., König, P., Engel, A. K. & Singer, W. Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature* **338**, 334–337 (1989).
- Engel, A. K., König, P. & Singer, W. Direct physiological evidence for scene segmentation by temporal coding. *Proc. Natl Acad. Sci. USA* **88**, 9136–9140 (1991).
- Kreiter, A. K. & Singer, W. Stimulus-dependent synchronization of neuronal responses in the visual cortex of the awake macaque monkey. *J. Neurosci.* **16**, 2381–2396 (1996).
- Castelo-Branco, M., Goebel, R., Neuenschwander, S. & Singer, W. Neural synchrony correlates with surface segregation rules. *Nature* **405**, 685–689 (2000).
- Lamme, V. A. & Spekreijse, H. Neuronal synchrony does not represent texture segregation. *Nature* **396**, 362–366 (1998).
- Palanca, B. J. & DeAngelis, G. C. Does neuronal synchrony underlie visual feature grouping? *Neuron* **46**, 333–346 (2005).
- Thiele, A. & Stoner, G. Neuronal synchrony does not correlate with motion coherence in cortical area MT. *Nature* **421**, 366–370 (2003).
- Varela, F., Lachaux, J. P., Rodriguez, E. & Martinerie, J. The brainweb: phase synchronization and large-scale integration. *Nature Rev. Neurosci.* **2**, 229–239 (2001).
- Engel, A. K., Fries, P. & Singer, W. Dynamic predictions: oscillations and synchrony in top-down processing. *Nature Rev. Neurosci.* **2**, 704–716 (2001).
- Salinas, E. & Sejnowski, T. J. Correlated neuronal activity and the flow of neural information. *Nature Rev. Neurosci.* **2**, 539–550 (2001).
- Driver, J. & Noesselt, T. Multisensory interplay reveals crossmodal influences on 'sensory-specific' brain regions, neural responses, and judgments. *Neuron* **57**, 11–23 (2008).
- Ghazanfar, A. A. & Schroeder, C. E. Is neocortex essentially multisensory? *Trends Cogn. Sci.* **10**, 278–285 (2006).
- Schroeder, C. E. & Foxe, J. Multisensory contributions to low-level, 'unisensory' processing. *Curr. Opin. Neurobiol.* **15**, 454–458 (2005).
- Senkowski, D., Schneider, T. R., Foxe, J. J. & Engel, A. K. Crossmodal binding through neural coherence: implications for multisensory processing. *Trends Neurosci.* **31**, 401–409 (2008).
- Buzsáki, G. & Draguhn, A. Neuronal oscillations in cortical networks. *Science* **304**, 1926–1929 (2004).
- Schroeder, C. E. & Lakatos, P. Low-frequency neuronal oscillations as instruments of sensory selection. *Trends Neurosci.* **32**, 9–18 (2008).
- Fries, P. Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annu. Rev. Neurosci.* **32**, 209–224 (2009).
- Jensen, O. & Mazaheri, A. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. *Front. Hum. Neurosci.* **4**, 186 (2010).
- Wang, X. J. Neurophysiological and computational principles of cortical rhythms in cognition. *Physiol. Rev.* **90**, 1195–1268 (2010).
- Donner, T. H. & Siegel, M. A framework for local cortical oscillation patterns. *Trends Cogn. Sci.* **15**, 191–199 (2011).
- Friston, K. Beyond phrenology: what can neuroimaging tell us about distributed circuitry? *Annu. Rev. Neurosci.* **25**, 221–250 (2002).
- Fries, P. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends Cogn. Sci.* **9**, 474–480 (2005).
- Abeles, M. Role of the cortical neuron: integrator or coincidence detector? *Isr. J. Med. Sci.* **18**, 83–92 (1982).
- König, P., Engel, A. K. & Singer, W. Integrator or coincidence detector? The role of the cortical neuron revisited. *Trends Neurosci.* **19**, 130–137 (1996).
- 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).
- Alonso, J. M., Usrey, W. M. & Reid, R. C. Precisely correlated firing in cells of the lateral geniculate nucleus. *Nature* **383**, 815–819 (1996).
- Bruno, R. M. & Sakmann, B. Cortex is driven by weak but synchronously active thalamocortical synapses. *Science* **312**, 1622–1627 (2006).
- Salinas, E. & Sejnowski, T. J. Impact of correlated synaptic input on output firing rate and variability in simple neuronal models. *J. Neurosci.* **20**, 6193–6209 (2000).
- Womelsdorf, T. *et al.* Modulation of neuronal interactions through neuronal synchronization. *Science* **316**, 1609–1612 (2007).
- Haider, B. & McCormick, D. A. Rapid neocortical dynamics: cellular and network mechanisms. *Neuron* **62**, 171–189 (2009).

36. Lakatos, P. *et al.* An oscillatory hierarchy controlling neuronal excitability and stimulus processing in the auditory cortex. *J. Neurophysiol.* **94**, 1904–1911 (2005).
37. Bruns, A., Eckhorn, R., Jokeit, H. & Ebner, A. Amplitude envelope correlation detects coupling among incoherent brain signals. *Neuroreport* **11**, 1509–1514 (2000).
38. Leopold, D. A., Murayama, Y. & Logothetis, N. K. Very slow activity fluctuations in monkey visual cortex: implications for functional brain imaging. *Cereb. Cortex* **13**, 422–433 (2003).
39. Shmuel, A. & Leopold, D. A. Neuronal correlates of spontaneous fluctuations in fMRI signals in monkey visual cortex: implications for functional connectivity at rest. *Hum. Brain Mapp.* **29**, 751–761 (2008).
40. Munk, M. H., 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).
41. de Lange, F. P., Jensen, O., Bauer, M. & Toni, I. Interactions between posterior gamma and frontal alpha/beta oscillations during imagined actions. *Front. Hum. Neurosci.* **2**, 7 (2008).
42. Donner, T. H., Siegel, M., Fries, P. & Engel, A. K. Buildup of choice-predictive activity in human motor cortex during perceptual decision making. *Curr. Biol.* **19**, 1581–1585 (2009).
This human MEG study was the first to directly link sensory and motor processing stages during visual decision-making, strongly suggesting a temporal integration of sensory evidence into motor plans.
43. Mazaheri, A. *et al.* Functional disconnection of frontal cortex and visual cortex in attention-deficit/hyperactivity disorder. *Biol. Psychiatry* **67**, 617–623 (2010).
This human EEG study assessed amplitude correlation between local oscillatory signatures to show that reduced fronto–occipital interactions reflect attentional control deficits in children with ADHD.
44. Mazaheri, A., Nieuwenhuis, I. L., van Dijk, H. & Jensen, O. Prestimulus alpha and mu activity predicts failure to inhibit motor responses. *Hum. Brain Mapp.* **30**, 1791–1800 (2009).
45. Glimcher, P. W. The neurobiology of visual-saccadic decision making. *Annu. Rev. Neurosci.* **26**, 133–179 (2003).
46. Gold, J. I. & Shadlen, M. N. The neural basis of decision making. *Annu. Rev. Neurosci.* **30**, 535–574 (2007).
47. Heekeren, H. R., Marrett, S. & Ungerleider, L. G. The neural systems that mediate human perceptual decision making. *Nature Rev. Neurosci.* **9**, 467–479 (2008).
48. Romo, R. & Salinas, E. Flutter discrimination: neural codes, perception, memory and decision making. *Nature Rev. Neurosci.* **4**, 203–218 (2003).
49. Schall, J. D. Neural basis of deciding, choosing and acting. *Nature Rev. Neurosci.* **2**, 33–42 (2001).
50. Siegel, M., Engel, A. K. & Donner, T. H. Cortical network dynamics of perceptual decision-making in the human brain. *Front. Hum. Neurosci.* **5**, 21 (2011).
51. Gold, J. I. & Shadlen, M. N. Neural computations that underlie decisions about sensory stimuli. *Trends Cogn. Sci.* **5**, 10–16 (2001).
52. Horwitz, G. D., Batista, A. P. & Newsome, W. T. Representation of an abstract perceptual decision in macaque superior colliculus. *J. Neurophysiol.* **91**, 2281–2296 (2004).
53. Kim, J. N. & Shadlen, M. N. Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. *Nature Neurosci.* **2**, 176–185 (1999).
54. Donner, T. H., Sagi, D., Bonneh, Y. S. & Heeger, D. J. Opposite neural signatures of motion-induced blindness in human dorsal and ventral visual cortex. *J. Neurosci.* **28**, 10298–10310 (2008).
55. Nienborg, H. & Cumming, B. G. Decision-related activity in sensory neurons reflects more than a neuron's causal effect. *Nature* **459**, 89–92 (2009).
56. Ress, D. & Heeger, D. J. Neuronal correlates of perception in early visual cortex. *Nature Neurosci.* **6**, 414–420 (2003).
57. Corbetta, M. & Shulman, G. L. Control of goal-directed and stimulus-driven attention in the brain. *Nature Rev. Neurosci.* **3**, 201–215 (2002).
58. Driver, J., Blankenburg, F., Bestmann, S., Vanduffel, W. & Ruff, C. C. Concurrent brain-stimulation and neuroimaging for studies of cognition. *Trends Cogn. Sci.* **13**, 319–327 (2009).
59. Kastner, S. & Ungerleider, L. G. Mechanisms of visual attention in the human cortex. *Annu. Rev. Neurosci.* **23**, 315–341 (2000).
60. Moore, T. & Armstrong, K. M. Selective gating of visual signals by microstimulation of frontal cortex. *Nature* **421**, 370–373 (2003).
61. Serences, J. T. & Yantis, S. Selective visual attention and perceptual coherence. *Trends Cogn. Sci.* **10**, 38–45 (2006).
62. Zanto, T. P., Rubens, M. T., Thangavel, A. & Gazzaley, A. Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. *Nature Neurosci.* **14**, 656–661 (2011).
63. Bressler, S. L., Coppola, R. & Nakamura, R. Episodic multiregional cortical coherence at multiple frequencies during visual task performance. *Nature* **366**, 153–156 (1993).
64. Roelfsema, P. R., Engel, A. K., König, P. & Singer, W. Visuomotor integration is associated with zero time-lag synchronization among cortical areas. *Nature* **385**, 157–161 (1997).
65. Miller, E. K. & Cohen, J. D. An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* **24**, 167–202 (2001).
66. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* **18**, 193–222 (1995).
67. Schroeder, C. E., Wilson, D. A., Radman, T., Scharfman, H. & Lakatos, P. Dynamics of active sensing and perceptual selection. *Curr. Opin. Neurobiol.* **20**, 172–176 (2010).
68. Uchida, N., Kepecs, A. & Mainen, Z. F. Seeing at a glance, smelling in a whiff: rapid forms of perceptual decision making. *Nature Rev. Neurosci.* **7**, 485–491 (2006).
69. Rizzolatti, G., Riggio, L., Dascola, I. & Umiltà, C. Reorienting attention across the horizontal and vertical meridians: evidence in favor of a premotor theory of attention. *Neuropsychologia* **25**, 31–40 (1987).
70. Moore, T., Armstrong, K. M. & Fallah, M. Visuomotor origins of covert spatial attention. *Neuron* **40**, 671–683 (2003).
71. Siegel, M., Donner, T. H., Oostenveld, R., Fries, P. & Engel, A. K. High-frequency activity in human visual cortex is modulated by visual motion strength. *Cereb. Cortex* **17**, 732–741 (2007).
72. Donner, T. H. *et al.* Population activity in the human dorsal pathway predicts the accuracy of visual motion detection. *J. Neurophysiol.* **98**, 345–359 (2007).
73. Siegel, M., Donner, T. H., Oostenveld, R., Fries, P. & Engel, A. K. Neuronal synchronization along the dorsal visual pathway reflects the focus of spatial attention. *Neuron* **60**, 709–719 (2008).
This human MEG study was the first to demonstrate that visuospatial attention modulates long-range coherence between frontal, parietal and visual cortices in a spatially selective fashion.
74. Usher, M. & McClelland, J. L. The time course of perceptual choice: the leaky, competing accumulator model. *Psychol. Rev.* **108**, 550–592 (2001).
75. Smith, P. L. & Ratcliff, R. Psychology and neurobiology of simple decisions. *Trends Neurosci.* **27**, 161–168 (2004).
76. Aoki, F., Fetz, E. E., Shupe, L., Lettich, E. & Ojemann, G. A. Changes in power and coherence of brain activity in human sensorimotor cortex during performance of visuomotor tasks. *Biosystems* **63**, 89–99 (2001).
77. Brovelli, A. *et al.* Beta oscillations in a large-scale sensorimotor cortical network: directional influences revealed by Granger causality. *Proc. Natl Acad. Sci. USA* **101**, 9849–9854 (2004).
78. Murthy, V. N. & Fetz, E. E. Coherent 25- to 35-Hz oscillations in the sensorimotor cortex of awake behaving monkeys. *Proc. Natl Acad. Sci. USA* **89**, 5670–5674 (1992).
79. Wang, X. J. Decision making in recurrent neuronal circuits. *Neuron* **60**, 215–234 (2008).
80. Pfurtscheller, G. & Lopes da Silva, F. H. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol.* **110**, 1842–1857 (1999).
81. Haegens, S. *et al.* Beta oscillations in the monkey sensorimotor network reflect somatosensory decision making. *Proc. Natl Acad. Sci. USA* **108**, 10708–10713 (2011).
This monkey electrophysiology study demonstrated decision-related modulations of beta-band oscillations across several frontal areas during a vibro-tactile discrimination task.
82. Hernandez, A. *et al.* Decoding a perceptual decision process across cortex. *Neuron* **66**, 300–314 (2010).
83. Pesaran, B., Nelson, M. J. & Andersen, R. A. Free choice activates a decision circuit between frontal and parietal cortex. *Nature* **453**, 406–409 (2008).
This monkey electrophysiology study was the first to link large-scale multi-area recordings to decision-making and reported enhanced frontoparietal beta-band coherence during free decisions as compared to instructed decisions.
84. Rizzolatti, G., Riggio, L. & Sheliga, B. M. in *Attention and Performance* (ed. Moscovitch, C. U. M.) 231–265 (MIT Press, Cambridge, Massachusetts, USA, 1994).
85. Gregoriou, G. G., Gots, S. J., Zhou, H. & Desimone, R. High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science* **324**, 1207–1210 (2009).
This monkey electrophysiology study demonstrated spatially selective attentional modulation of coherence between frontal and visual cortices and characterized in detail the temporal dynamics and directionality of oscillatory interactions.
86. Gross, J. *et al.* Modulation of long-range neural synchrony reflects temporal limitations of visual attention in humans. *Proc. Natl Acad. Sci. USA* **101**, 13050–13055 (2004).
This human MEG study was the first to demonstrate that frontoparietal beta-band coherence predicts performance in a demanding visual detection task.
87. Hipp, J. F., Engel, A. K. & Siegel, M. Oscillatory synchronization in large-scale cortical networks predicts perception. *Neuron* **69**, 587–596 (2011).
This human EEG study identified a large-scale coherent beta-band network across frontoparietal and visual cortices by using a new analysis approach that allows for imaging interacting networks across a full pair-wise cortico–cortical space.
88. Saalmann, Y. B., Pigarev, I. N. & Vidyasagar, T. R. Neural mechanisms of visual attention: how top-down feedback highlights relevant locations. *Science* **316**, 1612–1615 (2007).
89. Buschman, T. J. & Miller, E. K. Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science* **315**, 1860–1862 (2007).
This monkey electrophysiology study was the first to directly compare bottom-up and top-down attention and demonstrated frontoparietal coherence in the gamma- and beta-band for bottom-up and top-down attention, respectively.
90. Lindsley, D. B. Psychological phenomena and the electroencephalogram. *Electroencephalogr. Clin. Neurophysiol.* **4**, 443–456 (1952).
91. Nunn, C. M. & Osselton, J. W. The influence of the EEG alpha rhythm on the perception of visual stimuli. *Psychophysiology* **11**, 294–303 (1974).
92. Busch, N. A., Dubois, J. & VanRullen, R. The phase of ongoing EEG oscillations predicts visual perception. *J. Neurosci.* **29**, 7869–7876 (2009).
93. Mathewson, K. E., Gratton, G., Fabiani, M., Beck, D. M. & Ro, T. To see or not to see: prestimulus alpha phase predicts visual awareness. *J. Neurosci.* **29**, 2725–2732 (2009).
94. Worden, M. S., Foxe, J. J., Wang, N. & Simpson, G. V. Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. *J. Neurosci.* **20**, RC63 (2000).
95. Cohen, M. X., van Gaal, S., Ridderinkhof, K. R. & Lamme, V. A. Unconscious errors enhance prefrontal-occipital oscillatory synchrony. *Front. Hum. Neurosci.* **3**, 54 (2009).
96. Siegel, M., Kording, K. P. & König, P. Integrating top-down and bottom-up sensory processing by somato-dendritic interactions. *J. Comput. Neurosci.* **8**, 161–173 (2000).
97. von Stein, A., Chiang, C. & König, P. Top-down processing mediated by interareal synchronization. *Proc. Natl Acad. Sci. USA* **97**, 14748–14753 (2000).
98. Buffalo, E. A., Fries, P., Landman, R., Buschman, T. J. & Desimone, R. Laminar differences in gamma and alpha coherence in the ventral stream. *Proc. Natl Acad. Sci. USA* **108**, 11262–11267 (2011).
99. Jones, S. R. *et al.* Quantitative analysis and biophysically realistic neural modeling of the MEG mu rhythm: rhythmicogenesis and modulation of sensory-evoked responses. *J. Neurophysiol.* **102**, 3554–3572 (2009).
100. Roopun, A. K. *et al.* Cholinergic neuromodulation controls directed temporal communication in neocortex *in vitro*. *Front. Neural Circuits* **4**, 8 (2010).

101. Kayser, C. & Logothetis, N. K. Directed interactions between auditory and superior temporal cortices and their role in sensory integration. *Front. Integr. Neurosci.* **3**, 7 (2009).
102. Maier, J. X., Chandrasekaran, C. & Ghazanfar, A. A. Integration of bimodal looming signals through neuronal coherence in the temporal lobe. *Curr. Biol.* **18**, 963–968 (2008).
103. Engel, A. K. & Fries, P. Beta-band oscillations—signalling the status quo? *Curr. Opin. Neurobiol.* **20**, 156–165 (2010).
104. Palva, J. M., Monto, S., Kulashkhar, S. & Palva, S. Neuronal synchrony reveals working memory networks and predicts individual memory capacity. *Proc. Natl Acad. Sci. USA* **107**, 7580–7585 (2010).
105. Spitzer, B., Wacker, E. & Blankenburg, F. Oscillatory correlates of vibrotactile frequency processing in human working memory. *J. Neurosci.* **30**, 4496–4502 (2010).
106. Spitzer, B. & Blankenburg, F. Stimulus-dependent EEG activity reflects internal updating of tactile working memory in humans. *Proc. Natl Acad. Sci. USA* **108**, 8444–8449 (2011).
107. Palva, S., Kulashkhar, S., Hamalainen, M. & Palva, J. M. Localization of cortical phase and amplitude dynamics during visual working memory encoding and retention. *J. Neurosci.* **31**, 5013–5025 (2011).
108. Tallon-Baudry, C., Mandon, S., Freiwald, W. A. & Kreiter, A. K. Oscillatory synchrony in the monkey temporal lobe correlates with performance in a visual short-term memory task. *Cereb. Cortex* **14**, 713–720 (2004).
109. Siegel, M., Warden, M. R. & Miller, E. K. Phase-dependent neuronal coding of objects in short-term memory. *Proc. Natl Acad. Sci. USA* **106**, 21341–21346 (2009).
110. Tallon-Baudry, C., Bertrand, O. & Fischer, C. Oscillatory synchrony between human extrastriate areas during visual short-term memory maintenance. *J. Neurosci.* **21**, RC177 (2001).
111. Fell, J. & Axmacher, N. The role of phase synchronization in memory processes. *Nature Rev. Neurosci.* **12**, 105–118 (2011).
112. Roopun, A. K. *et al.* Period concatenation underlies interactions between gamma and beta rhythms in neocortex. *Front. Cell Neurosci.* **2**, 1 (2008).
113. Kopell, N., Whittington, M. A. & Kramer, M. A. Neuronal assembly dynamics in the beta1 frequency range permits short-term memory. *Proc. Natl Acad. Sci. USA* **108**, 3779–3784 (2011).
114. VanRullen, R. & Koch, C. Is perception discrete or continuous? *Trends Cogn. Sci.* **7**, 207–213 (2003).
115. Buschman, T. J. & Miller, E. K. Shifting the spotlight of attention: evidence for discrete computations in cognition. *Front. Hum. Neurosci.* **4**, 194 (2010).
116. Luo, H. & Poeppel, D. Phase patterns of neuronal responses reliably discriminate speech in human auditory cortex. *Neuron* **54**, 1001–1010 (2007).
117. Bosman, C. A., Womelsdorf, T., Desimone, R. & Fries, P. A microaccadic rhythm modulates gamma-band synchronization and behavior. *J. Neurosci.* **29**, 9471–9480 (2009).
118. Crochet, S. & Petersen, C. C. Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neurosci.* **9**, 608–610 (2006).
119. Ganguly, K. & Kleinfeld, D. Goal-directed whisking increases phase-locking between vibrissa movement and electrical activity in primary sensory cortex in rat. *Proc. Natl Acad. Sci. USA* **101**, 12348–12353 (2004).
120. Kay, L. M. *et al.* Olfactory oscillations: the what, how and what for. *Trends Neurosci.* **32**, 207–214 (2009).
121. Lakatos, P., Karmos, G., Mehta, A. D., Ulbert, I. & Schroeder, C. E. Entrainment of neuronal oscillations as a mechanism of attentional selection. *Science* **320**, 110–113 (2008).
122. Lakatos, P. *et al.* The leading sense: supramodal control of neurophysiological context by attention. *Neuron* **64**, 419–430 (2009).
123. Buschman, T. J. & Miller, E. K. Serial, covert shifts of attention during visual search are reflected by the frontal eye fields and correlated with population oscillations. *Neuron* **63**, 386–396 (2009).
124. Varela, F. J., Toro, A., John, E. R. & Schwartz, E. L. Perceptual framing and cortical alpha rhythm. *Neuropsychologia* **19**, 675–686 (1981).
125. Busch, N. A. & VanRullen, R. Spontaneous EEG oscillations reveal periodic sampling of visual attention. *Proc. Natl Acad. Sci. USA* **107**, 16048–16053 (2010).
126. Kopell, N., Ermentrout, G. B., Whittington, M. A. & Traub, R. D. Gamma rhythms and beta rhythms have different synchronization properties. *Proc. Natl Acad. Sci. USA* **97**, 1867–1872 (2000).
127. 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 (2000).
128. Miller, R. Theory of the normal waking EEG: from single neurones to waveforms in the alpha, beta and gamma frequency ranges. *Int. J. Psychophysiol.* **64**, 18–23 (2007).
129. Ghazanfar, A. A., Chandrasekaran, C. & Logothetis, N. K. Interactions between the superior temporal sulcus and auditory cortex mediate dynamic face/voice integration in rhesus monkeys. *J. Neurosci.* **28**, 4457–4469 (2008).
130. Felleman, D. J. & Van Essen, D. C. Distributed hierarchical processing in the primate cerebral cortex. *Cereb. Cortex* **1**, 1–47 (1991).
131. Barone, P., Batardiere, A., Knoblauch, K. & Kennedy, H. Laminar distribution of neurons in extrastriate areas projecting to visual areas V1 and V4 correlates with the hierarchical rank and indicates the operation of a distance rule. *J. Neurosci.* **20**, 3263–3281 (2000).
132. van Kerkoerle, T. J., Self, M., Poort, J., van der Togt, C. & Roelfsema, P. R. High frequencies flow in the feed-forward direction through the different layers of monkey primary visual cortex while low frequencies flow in the recurrent direction. *Soc. Neurosci. Abstr.* **270.8** (Washington, DC, 12–16 Nov 2011).
133. Buhl, E. H., Tamas, G. & Fisahn, A. Cholinergic activation and tonic excitation induce persistent gamma oscillations in mouse somatosensory cortex *in vitro*. *J. Physiol.* **513**, 117–126 (1998).
134. Maier, A., Adams, G. K., Aura, C. & Leopold, D. A. Distinct superficial and deep laminar domains of activity in the visual cortex during rest and stimulation. *Front. Syst. Neurosci.* **4**, 31 (2010).
135. Roopun, A. K. *et al.* A beta2-frequency (20–30 Hz) oscillation in nonsynaptic networks of somatosensory cortex. *Proc. Natl Acad. Sci. USA* **103**, 15646–15650 (2006).
136. Bollimunta, A., Chen, Y., Schroeder, C. E. & Ding, M. Neuronal mechanisms of cortical alpha oscillations in awake-behaving macaques. *J. Neurosci.* **28**, 9976–9988 (2008).
137. Lopes Da Silva, F. H. & Storm Van Leeuwen, W. The cortical source of the alpha rhythm. *Neurosci. Lett.* **6**, 237–241 (1977).
138. Silva, L. R., Amitai, Y. & Connors, B. W. Intrinsic oscillations of neocortex generated by layer 5 pyramidal neurons. *Science* **251**, 432–435 (1991).
139. Sun, W. & Dan, Y. Layer-specific network oscillation and spatiotemporal receptive field in the visual cortex. *Proc. Natl Acad. Sci. USA* **106**, 17986–17991 (2009).
140. Kramer, M. A. *et al.* Rhythm generation through period concatenation in rat somatosensory cortex. *PLoS Comput. Biol.* **4**, e1000169 (2008).
141. Atallah, B. V. & Scanziani, M. Instantaneous modulation of gamma oscillation frequency by balancing excitation with inhibition. *Neuron* **62**, 566–577 (2009).
142. Whittington, M. A., Traub, R. D., Kopell, N., Ermentrout, B. & Buhl, E. H. Inhibition-based rhythms: experimental and mathematical observations on network dynamics. *Int. J. Psychophysiol.* **38**, 315–336 (2000).
143. Whittington, M. A., Stanford, I. M., Colling, S. B., Jefferys, J. G. & Traub, R. D. Spatiotemporal patterns of gamma frequency oscillations tetanically induced in the rat hippocampal slice. *J. Physiol.* **502**, 591–607 (1997).
144. Bartos, M., Vida, I. & Jonas, P. Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. *Nature Rev. Neurosci.* **8**, 45–56 (2007).
145. Cardin, J. A. *et al.* Driving fast-spiking cells induces gamma rhythm and controls sensory responses. *Nature* **459**, 663–667 (2009).
146. Hasenstaub, A. *et al.* Inhibitory postsynaptic potentials carry synchronized frequency information in active cortical networks. *Neuron* **47**, 423–435 (2005).
147. Sohal, V. S., Zhang, F., Yizhar, O. & Deisseroth, K. Parvalbumin neurons and gamma rhythms enhance cortical circuit performance. *Nature* **459**, 698–702 (2009).
148. Heeger, D. J., Simoncelli, E. P. & Movshon, J. A. Computational models of cortical visual processing. *Proc. Natl Acad. Sci. USA* **93**, 623–627 (1996).
149. Shapley, R., Hawken, M. & Ringach, D. L. Dynamics of orientation selectivity in the primary visual cortex and the importance of cortical inhibition. *Neuron* **38**, 689–699 (2003).
150. Louie, K., Grattan, L. E. & Glimcher, P. W. Reward value-based gain control: divisive normalization in parietal cortex. *J. Neurosci.* **31**, 10627–10639 (2011).
151. Reynolds, J. H. & Heeger, D. J. The normalization model of attention. *Neuron* **61**, 168–185 (2009).
152. Zoccolan, D., Cox, D. D. & DiCarlo, J. J. Multiple object response normalization in monkey inferotemporal cortex. *J. Neurosci.* **25**, 8150–8164 (2005).
153. Ohshiro, T., Angelaki, D. E. & DeAngelis, G. C. A normalization model of multisensory integration. *Nature Neurosci.* **14**, 775–782 (2011).
154. Ray, S. & Maunsell, J. H. Differences in gamma frequencies across visual cortex restrict their possible use in computation. *Neuron* **67**, 885–896 (2010).
155. Siegel, M. & König, P. A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. *J. Neurosci.* **23**, 4251–4260 (2003).
156. Hyman, J. M., Zilli, E. A., Paley, A. M. & Hasselmo, M. E. Medial prefrontal cortex cells show dynamic modulation with the hippocampal theta rhythm dependent on behavior. *Hippocampus* **15**, 739–749 (2005).
157. Jones, M. W. & Wilson, M. A. Theta rhythms coordinate hippocampal-prefrontal interactions in a spatial memory task. *PLoS Biol.* **3**, e402 (2005).
158. Poch, C., Fuentemilla, L., Barnes, G. R. & Duzel, E. Hippocampal theta-phase modulation of replay correlates with configural-relational short-term memory performance. *J. Neurosci.* **31**, 7038–7042 (2011).
159. Siapas, A. G., Lubenov, E. V. & Wilson, M. A. Prefrontal phase locking to hippocampal theta oscillations. *Neuron* **46**, 141–151 (2005).
160. Sirota, A. *et al.* Entrainment of neocortical neurons and gamma oscillations by the hippocampal theta rhythm. *Neuron* **60**, 683–697 (2008).
161. Buzsáki, G. Theta oscillations in the hippocampus. *Neuron* **33**, 325–340 (2002).
162. Jensen, O. & Colgin, L. L. Cross-frequency coupling between neuronal oscillations. *Trends Cogn. Sci.* **11**, 267–269 (2007).
163. Canolty, R. T. *et al.* High gamma power is phase-locked to theta oscillations in human neocortex. *Science* **313**, 1626–1628 (2006).
164. Saleh, M., Reimer, J., Penn, R., Ojakangas, C. L. & Hatsopoulos, N. G. Fast and slow oscillations in human primary motor cortex predict ongoing behaviorally relevant cues. *Neuron* **65**, 461–471 (2010).
165. Cohen, M. X., Elger, C. E. & Fell, J. Oscillatory activity and phase-amplitude coupling in the human medial frontal cortex during decision making. *J. Cogn. Neurosci.* **21**, 390–402 (2009).
166. Voytek, B. *et al.* Shifts in gamma phase-amplitude coupling frequency from theta to alpha over posterior cortex during visual tasks. *Front. Hum. Neurosci.* **4**, 191 (2010).
167. Handel, B. & Haarmeier, T. Cross-frequency coupling of brain oscillations indicates the success in visual motion discrimination. *Neuroimage* **45**, 1040–1046 (2009).
168. Osipova, D., Hermes, D. & Jensen, O. Gamma power is phase-locked to posterior alpha activity. *PLoS ONE* **3**, e3990 (2008).
169. Schack, B., Vath, N., Petsche, H., Geissler, H. G. & Moller, E. Phase-coupling of theta-gamma EEG rhythms during short-term memory processing. *Int. J. Psychophysiol.* **44**, 143–163 (2002).
170. Demiralp, T. *et al.* Gamma amplitudes are coupled to theta phase in human EEG during visual perception. *Int. J. Psychophysiol.* **64**, 24–30 (2007).
171. Mormann, F. *et al.* Phase/amplitude reset and theta-gamma interaction in the human medial temporal lobe during a continuous word recognition memory task. *Hippocampus* **15**, 890–900 (2005).
172. American Psychiatric Association. *Diagnosics and Statistical Manual of Mental Disorders* 4th edn (American Psychiatric Press, Washington, DC, 2000).
173. Uhlhaas, P. J. & Singer, W. Abnormal neural oscillations and synchrony in schizophrenia. *Nature Rev. Neurosci.* **11**, 100–113 (2010).
174. Lizio, R. *et al.* Electroencephalographic rhythms in Alzheimer's disease. *Int. J. Alzheimers Dis.* **2011**, 927573 (2011).

175. Uhlhaas, P. J. & Singer, W. Neural synchrony in brain disorders: relevance for cognitive dysfunctions and pathophysiology. *Neuron* **52**, 155–168 (2006).
176. Haenschel, C. *et al.* Cortical oscillatory activity is critical for working memory as revealed by deficits in early-onset schizophrenia. *J. Neurosci.* **29**, 9481–9489 (2009).
177. Cho, R. Y., Konecky, R. O. & Carter, C. S. Impairments in frontal cortical gamma synchrony and cognitive control in schizophrenia. *Proc. Natl Acad. Sci. USA* **103**, 19878–19883 (2006).
178. Spencer, K. M. *et al.* Abnormal neural synchrony in schizophrenia. *J. Neurosci.* **23**, 7407–7411 (2003).
179. Lewis, D. A., Hashimoto, T. & Volk, D. W. Cortical inhibitory neurons and schizophrenia. *Nature Rev. Neurosci.* **6**, 312–324 (2003).
180. Vierling-Claassen, D., Siekmeier, P., Stufflebeam, S. & Kopell, N. Modeling GABA alterations in schizophrenia: a link between impaired inhibition and altered gamma and beta range auditory entrainment. *J. Neurophysiol.* **99**, 2656–2671 (2008).
181. Aston-Jones, G. & Cohen, J. D. An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. *Annu. Rev. Neurosci.* **28**, 403–450 (2005).
182. Goard, M. & Dan, Y. Basal forebrain activation enhances cortical coding of natural scenes. *Nature Neurosci.* **12**, 1444–1449 (2009).
183. Yu, A. J. & Dayan, P. Uncertainty, neuromodulation, and attention. *Neuron* **46**, 681–692 (2005).
184. Sara, S. J. The locus coeruleus and noradrenergic modulation of cognition. *Nature Rev. Neurosci.* **10**, 211–223 (2009).
185. Rodriguez, R., Kallenbach, U., Singer, W. & Munk, M. H. Short- and long-term effects of cholinergic modulation on gamma oscillations and response synchronization in the visual cortex. *J. Neurosci.* **24**, 10369–10378 (2004).
186. Saalman, Y. B. & Kastner, S. Cognitive and perceptual functions of the visual thalamus. *Neuron* **71**, 209–223 (2011).
187. Bollimunta, A., Mo, J., Schroeder, C. E. & Ding, M. Neuronal mechanisms and attentional modulation of corticothalamic alpha oscillations. *J. Neurosci.* **31**, 4935–4943 (2011).
188. Lorincz, M. L., Kekesi, K. A., Juhász, G., Crunelli, V. & Hughes, S. W. Temporal framing of thalamic relay-mode firing by phasic inhibition during the alpha rhythm. *Neuron* **63**, 683–696 (2009).
189. Bekisz, M. & Wrobel, A. Coupling of beta and gamma activity in corticothalamic system of cats attending to visual stimuli. *Neuroreport* **10**, 3589–3594 (1999).
190. Wrobel, A. Beta activity: a carrier for visual attention. *Acta Neurobiol. Exp. (Wars)* **60**, 247–260 (2000).
191. Wrobel, A., Ghazaryan, A., Bekisz, M., Bogdan, W. & Kaminski, J. Two streams of attention-dependent beta activity in the striate recipient zone of cat's lateral posterior-pulvinar complex. *J. Neurosci.* **27**, 2230–2240 (2007).
192. Jones, E. G. The thalamic matrix and thalamocortical synchrony. *Trends Neurosci.* **24**, 595–601 (2001).
193. Lopes da Silva, F. H., Vos, J. E., Mooibroek, J. & Van Rotterdam, A. Relative contributions of intracortical and thalamo-cortical processes in the generation of alpha rhythms, revealed by partial coherence analysis. *Electroencephalogr. Clin. Neurophysiol.* **50**, 449–456 (1980).
194. Shipp, S. The functional logic of cortico-pulvinar connections. *Phil. Trans. R. Soc. Lond. B* **358**, 1605–1624 (2003).
195. Molotchnikoff, S. & Shumikhina, S. The lateral posterior-pulvinar complex modulation of stimulus-dependent oscillations in the cat visual cortex. *Vision Res.* **36**, 2037–2046 (1996).
196. Shumikhina, S. & Molotchnikoff, S. Pulvinar participates in synchronizing neural assemblies in the visual cortex, in cats. *Neurosci. Lett.* **272**, 135–139 (1999).
197. Vicente, R., Gollo, L. L., Mirasso, C. R., Fischer, I. & Pipa, G. Dynamical relaying can yield zero time lag neuronal synchrony despite long conduction delays. *Proc. Natl Acad. Sci. USA* **105**, 17157–17162 (2008).
198. Theyel, B. B., Llano, D. A. & Sherman, S. M. The corticothalamic circuit drives higher-order cortex in the mouse. *Nature Neurosci.* **13**, 84–88 (2010).
199. Nir, Y. *et al.* Coupling between neuronal firing rate, gamma LFP, and BOLD fMRI is related to interneuronal correlations. *Curr. Biol.* **17**, 1275–1285 (2007).
200. Nir, Y. *et al.* Interhemispheric correlations of slow spontaneous neuronal fluctuations revealed in human sensory cortex. *Nature Neurosci.* **11**, 1100–1108 (2008).
201. Fox, M. D. & Raichle, M. E. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Rev. Neurosci.* **8**, 700–711 (2007).
202. Haynes, J. D., Driver, J. & Rees, G. Visibility reflects dynamic changes of effective connectivity between V1 and fusiform cortex. *Neuron* **46**, 811–821 (2005).
203. Haynes, J. D., Tregellas, J. & Rees, G. Attentional integration between anatomically distinct stimulus representations in early visual cortex. *Proc. Natl Acad. Sci. USA* **102**, 14925–14930 (2005).
204. Freeman, J., Donner, T. H. & Heeger, D. J. Inter-area correlations in the ventral visual pathway reflect feature integration. *J. Vis.* **11** (4), 15 (2011).
205. Pantev, C. *et al.* Specific tonotopic organizations of different areas of the human auditory cortex revealed by simultaneous magnetic and electric recordings. *Electroencephalogr. Clin. Neurophysiol.* **94**, 26–40 (1995).
206. Schoffelen, J. M. & Gross, J. Source connectivity analysis with MEG and EEG. *Hum. Brain Mapp.* **30**, 1857–1865 (2009).
207. Nolte, G. *et al.* Identifying true brain interaction from EEG data using the imaginary part of coherence. *Clin. Neurophysiol.* **115**, 2292–2307 (2004).
208. Blinn, K. A. Focal anterior temporal spikes from external rectus muscle. *Electroencephalogr. Clin. Neurophysiol.* **7**, 299–302 (1955).
209. Yuval-Greenberg, S., Tomer, O., Keren, A. S., Nelken, I. & Deouell, L. Y. Transient induced gamma-band response in EEG as a manifestation of miniature saccades. *Neuron* **58**, 429–441 (2008).
210. Keren, A. S., Yuval-Greenberg, S. & Deouell, L. Y. Saccadic spike potentials in gamma-band EEG: characterization, detection and suppression. *NeuroImage* **49**, 2248–2263 (2010).
211. Reva, N. V. & Aftanas, L. I. The coincidence between late non-phase-locked gamma synchronization response and saccadic eye movements. *Int. J. Psychophysiol.* **51**, 215–222 (2004).
212. Engbert, R. & Kliegl, R. Microsaccades uncover the orientation of covert attention. *Vision Res.* **43**, 1035–1045 (2003).
213. Valsecchi, M., Betta, E. & Turatto, M. Visual oddballs induce prolonged microsaccadic inhibition. *Exp. Brain Res.* **177**, 196–208 (2007).
214. Carl, C., Acik, A., König, P., Engel, A. K. & Hipp, J. F. The saccadic spike artifact in MEG. *NeuroImage* **59**, 1657–1667 (2011).
215. Hughes, S. W. & Crunelli, V. Thalamic mechanisms of EEG alpha rhythms and their pathological implications. *Neuroscientist* **11**, 357–372 (2005).
216. Lopes da Silva, F. H., van Lierop, T. H., Schrijer, C. F. & van Leeuwen, W. S. Organization of thalamic and cortical alpha rhythms: spectra and coherences. *Electroencephalogr. Clin. Neurophysiol.* **35**, 627–639 (1973).

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Competing interests statement

The authors declare no competing financial interests.

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