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Review

Dynamic coupling of oscillatory neural activity and its roles in visual attention

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Oscillatory neural activity is believed to have a central role in information processing in the mammalian brain. While early studies often focussed on the function of individual frequency bands, there is emerging appreciation for the role of simultaneous activity in many distinct frequency bands and the interactions between them in high-level cognitive functions. Here, we focus on the role of cross-frequency coupling (CFC) in visual attention. First, we propose a framework that reconciles previous contrasting findings, showing how CFC could have a functional role on both intra- and interareal scales. Second, we outline how CFC between distinct frequency bands could label different submodalities of sensory information. Overall, our scheme provides a novel perspective of how interfrequency interaction contributes to efficient and dynamic processing of information across the brain.

Highlights

Rhythmic neuronal activity has long been proposed to have a central role in information processing in the mammalian brain. Recent studies have documented a multitude of simultaneously active frequency bands.

These frequency components are often coupled, with the phase of a lower frequency modulating the power of a higher frequency rhythm [phase–amplitude coupling (PAC)]. We suggest that such coupling allows different scales of neural populations to interact and enables high-level cognitive functions, including selective attention.

We propose a scheme that outlines how changes in PAC during attention helps in sensory signal discrimination in early visual areas and in signal transmission in higher areas.

We suggest that dynamic coupling of distinct frequency bands provides a mechanism to functionally label and flexibly route signals from different sensory submodalities.

The buzzing brain

Since Berger's early description of electrical potentials recorded from the scalp [1], oscillating neuronal activity in the brain has been described at various spatiotemporal scales on the basis of several electrophysiological methods, including electroencephalography (EEG), electrocorticography (ECoG), local field potentials (LFP), as well as multi-unit (MU) and single-unit recordings. These studies have documented a range of periodicities in brain activity, from slow, delta frequencies (1–4 Hz), through theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz) frequencies, to faster gamma (30–220 Hz) frequencies (reviewed in [2]). Their possible functions have been a source of intense scientific debate, but there is now substantial evidence that the brains of humans and nonhuman primates process information in a rhythmic fashion, which causes perceptual sensitivity and behavioural performance to fluctuate in time [3,4]. While early studies that ushered in the recent surge of interest in brain rhythms [5,6] often focussed on lower gamma frequencies (–<80 Hz), which are prominent, for instance, in the primary visual cortex (V1) during visual stimulus presentation, a variety of active frequency bands have been observed across different cortical and subcortical areas [7–13]. Furthermore, within the same cortical area, often different and non-overlapping ranges of frequencies have simultaneous functional roles [10,14,15] and, in some cases, different frequencies dominate during different stimulus conditions [16].

Here, we explore ways in which different frequency ranges could interact to promote information processing in the brain. One well-recognised process is for the phase or amplitude of one frequency to modulate the frequency or amplitude of another oscillation, an interaction known as CFC [17,18]. Here, we elaborate on two possible roles of CFC in selective attention in the visual system. One is for CFC to be mediating the effect of attention in increasing discrimination between different signals and also in effective signal transmission between cortical areas. The other possibility is that coupling between distinct frequency ranges may tag different types of information arriving at a common target. These suggestions form a heuristic framework for future research investigating neuronal oscillations.

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Role of phase-amplitude coupling (PAC) in sensory processing

Attentional role of PAC: facilitation or suppression?

One of the important contributions to our understanding of the role of neural oscillations is the suggestion that CFC can be an efficient form of interaction between separate brain areas [17,18]. Most commonly, this is achieved by PAC (i.e., modulating the power of a higher frequency oscillation along the phase of a lower frequency rhythm) (Figure 1). Such nesting of higher oscillations within a lower frequency rhythm can also occur within a brain area, enabling the coordination of activity of large-scale neural ensembles with the activity of local neural populations [15,18–20]. A neuronal network that generates a low frequency rhythm (e.g., theta) could modulate a higher frequency response (e.g., gamma) in projection neurons of the area (i.e., long axonal projecting neurons responsible for local processing as well as interareal transmission of information, as opposed to interneurons [21]). The activity of this circuit itself can be under the modulating influence of other factors, such as attention (Figure 1). Such PACs have been documented in both humans and nonhuman primates.

Human studies have revealed PAC in many brain regions, in which the low frequencies that provide the phase and the high frequencies the amplitudes of which are being modulated may be from the same or different brain regions [19,22–26]. In humans, PAC has also been shown to be correlated with functional connectivity between different brain regions as assessed via blood oxygen level-dependent (BOLD) signals in fMRI [27]. Furthermore, it has been suggested that PAC coordinates activity between different association areas (frontal and parietal regions) and that of visual areas, particularly in attention-demanding tasks [23]. Similarly, PAC has been observed to mediate the role of the thalamus in coordinating cortical regions that exchange information [26]. Studies have also sought to clarify the underlying neural mechanism of interareal communication via the coupling of the low-frequency oscillations (theta and alpha) of the areas [28–30].

In nonhuman primates, in which targeted access to functionally specific areas and recording neural activity at high spatial and temporal resolutions is possible, PAC has been documented

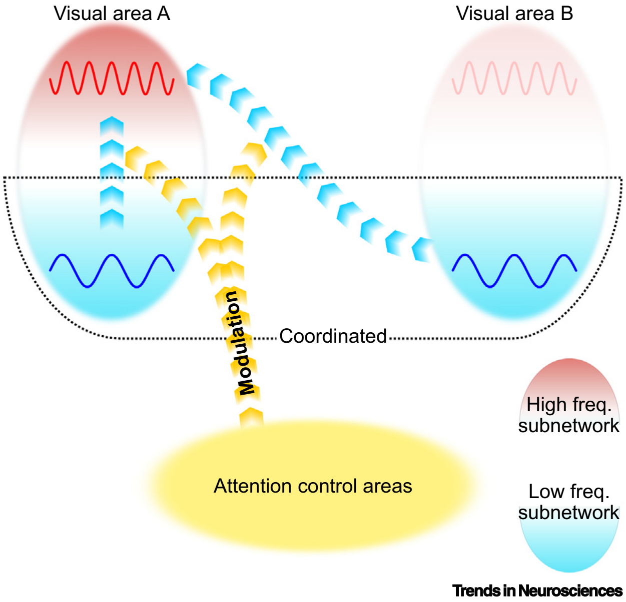

Figure 1. Modulation of inter/intra-areal cross-frequency coupling (CFC) as the mechanism by which top-down attention operates. CFC is postulated to be a process by which regulatory low-frequency activity-generating subnetworks (in blue) within each individual visual area control the temporal pattern of local processing subnetworks (in red), which produce high-frequency oscillatory activities. A local subnetwork active within the high-frequency range (e.g., in Visual area A) may be temporally regulated via projections from slow oscillating networks either within the same visual area or from another visual area (Visual area B). Such projections (either within or interareal, shown by blue arrows here) may be influenced by top-down signals from attention control areas/networks, including the visual thalamus, lateral intraparietal cortex–frontal eye field (LIP–FEF) complex, or the claustrum. Visual areas A and B shown here refer to regions belonging to the same visual pathway, either dorsal or ventral.

in several brain regions. In this review, we focus primarily on work in the visual system, in which the roles of PAC in the context of visual processing have been relatively more thoroughly documented. We address processes along both of the two main streams of visual information processing (Box 1), including visual areas V1 [10], middle temporal area (MT) [15], V4 [10], lateral intraparietal cortex (LIP) [14], and frontal eye field (FEF) [14], and the hippocampus [31,32]. Figure 2 summarises key findings on PAC in most of these areas. The frequencies of these oscillatory activities cover a large spectrum, from low frequencies (<30 Hz), which are known to involve larger populations of neurons, to higher frequencies (>40 Hz), which are thought to represent the activity within smaller, local neural circuits. However, although the role of PAC in visual processing has received much attention, its exact function in visuomotor processing remains incompletely understood.

One important approach to studying the role of PAC in regulating sensory information processing is to examine its function in the processing of sensory stimuli by selective attention. However, most studies have examined neural synchrony between different attention conditions only in terms of the changes within a specific frequency band, be it in feedforward or feedback pathways within the visual system [8,11,12,33–37]. We focus here on recent studies that have examined the coupling between different frequency bands (i.e., PAC) in intracortical recordings of single neurons and local populations from many precisely identified cortical areas in nonhuman primates. Some of these studies in the visual cortex of rhesus monkeys have shown that selective attention decreases the coupling of gamma oscillations to the phase of low-frequency oscillations (<30 Hz) in LFPs [10,15]. For instance, in area MT, directing the focus of attention into the RF of a neuron decreases the PAC between delta-theta (2–6 Hz) and gamma (40–100 Hz) frequencies within the local population of neurons [15]. This decrease in PAC correlated with an increase in the neural discriminability of visual stimuli. Similar results were observed for areas V1 and V4 [10]. While these studies suggest a suppressive role for PAC in the case of attention, studies in higher order visual-processing cortical areas point to a different function. A study examining the interplay in the macaque frontoparietal network during spatial attention tasks showed that, with areas FEF and LIP, which are known to be involved in controlling attentional processing in sensory areas, PAC between theta (4–8 Hz) and higher frequencies (30–35 Hz for FEF and 15–55 Hz for LIP) increases with selective attention [14] (see [23] for comparable results in human prefrontal cortex). The authors suggested that this increased PAC helps improve the communication between visual association areas. However, it is noteworthy that in contrast to the enhanced interareal PAC, the authors also observed that, within FEF, attention in fact decreases PAC between theta (4–8 Hz) phase and low-beta (13–17 Hz) power.

Hypothesis 1 on role of PAC: enhancing intra-areal neural discrimination versus improving interareal communication

The studies summarised above document conflicting findings, with some claiming that attention is linked to an enhanced PAC, while others see a suppression. However, a common pattern has also emerged across these studies: the high-frequency ranges that show an up- or downregulation have very little or no overlap. Thus, during windows of focused attention, one set of frequencies (13–17 Hz in FEF, 40–100 Hz in MT, and 60–100 Hz in V4) show enhanced PAC to local theta or delta-theta rhythms, while another set of frequencies (15–55 Hz in LIP and 30–35 Hz in FEF) show reduced PAC to local theta rhythms. Other frequency ranges (e.g., beta [8,38] and high gamma [39,40]) have also been observed to have a functional role in visual cortex under attention. We suggest that, across the entire range of frequencies, the PACs of different frequency pairs serve distinct roles in the processing of visual information. This notion is consistent with previous observations, using human ECoG, that distinct high-frequency oscillations (HFO) are locked to two distinct phases of the low-frequency oscillations (separated by as far as 180°), indicative of different activity time windows of the local circuits, corresponding to each of the two high-

Box 1. Two cortical streams and attention

One of the best understood patterns of functional connectivity between cortical areas of the primate is the functional dichotomy of projections leading from the visual area V1 into higher areas [80–84]. The dorsal pathway, projecting into the parietal cortex, is concerned largely with the spatial and dynamic properties essential for action in an everchanging environment, while the ventral pathway, projecting into the inferotemporal cortex, is concerned mainly with visual features and objects necessary for perception and awareness. Figure I shows these pathways in the macaque brain.

Attentional modulation of PAC is observed across a multitude of visuo/motor brain areas in both cortical streams, suggesting a widespread functional role of PAC across the brain. The following is a list of the macaque visuo/motor brain areas in which PAC has been most studied.

V1

V1 is involved in the processing of basic visual features, such as the colour, size, or orientation of a visual stimulus. Weak, but significant effects of selective attention have been observed in V1 [85–87].

V4

An extrastriate visual area located in the ventral visual pathway, V4 is involved in processing shapes and complex aspects of colour perception. Substantial effects of selective attention on the activity of single neurons and neural populations have been consistently observed in V4 [88,89].

MT

MT is an extrastriate visual area located in the dorsal visual pathway, with neurons predominantly selective to visual motion parameters and stereoscopic depth. Substantial attentional modulation at the level of both single neurons and population activity has been observed in MT for spatial, feature-based, and object-based attention [90–92].

LIP and FEF

LIP and FEF are visuomotor areas involved in transmitting attentional control signals to visual areas and decision signals to other areas for action. LIP is strongly interconnected with MT, and FEF has been documented to modulate V4 activity [51]. LIP and FEF are parts of the frontoparietal attention network, which controls the focus of endogenous and exogenous attention [12,93,94].

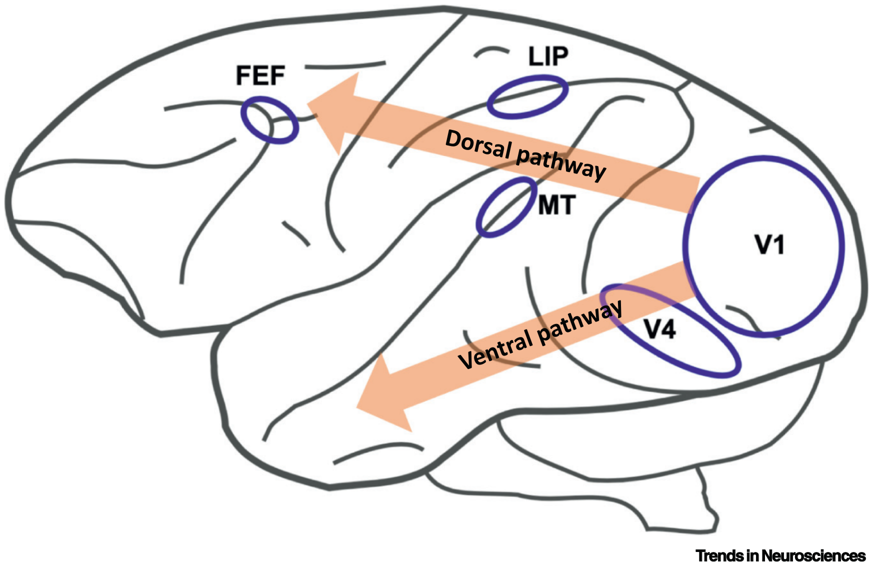

Figure I. Schematic of dorsal and ventral cortical streams in the macaque brain. The figure shows the visual information reaching the primary visual cortex (V1) progressing along a series of extra-striate areas in two streams, one dorsal and one ventral. The middle temporal area (MT), lateral intraparietal cortex (LIP), and frontal eye field (FEF) are some of the areas along the dorsal pathway, and area V4 is one of the areas in the ventral stream.

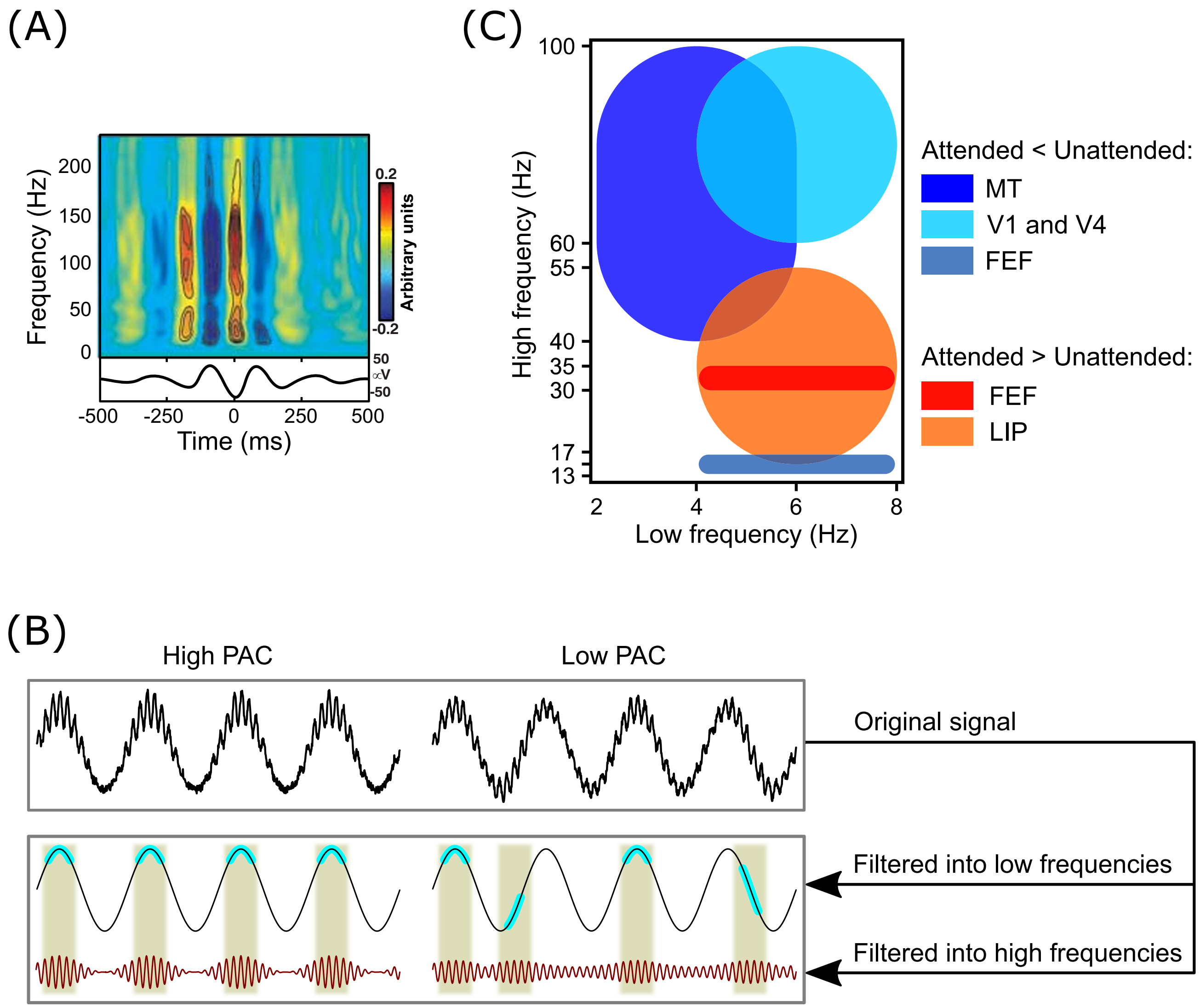

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Figure 2. Strength of phase-amplitude coupling (PAC) differs under different attention conditions. (A) Coupling of the power of high-frequency oscillations to the phase of low-frequency rhythms. Reproduced from [19]. (B) Types of PAC. A sample synthetic signal is filtered within low- and high-frequency bands. At high PAC, the high-frequency component reaches its maximum power at a specific phase of the low-frequency component (here, the peak phase highlighted in blue on the low-frequency trace) and the high-frequency power is considerably dampened at other phases of the low-frequency component. By contrast, in the low PAC condition, the high-frequency component is distributed across varying phases of the low-frequency component; that is, not only is the gamma frequency component distributed across all time points (rather than occurring in an all-or-none fashion), but its amplitude maxima also coincide with different phases of the low frequency component. (C) Summary of studies of the effect of spatial attention on the strength of PAC in different visual cortical areas of the macaque. Cooler colours represent a decrease in PAC when attention is shifted toward the receptive field (RF) [in the middle temporal area (MT) [15], areas V1 and V4 [10], and frontal eye field (FEF) [14]]. Warmer colours indicate an increase in PAC when attending toward the RF [in FEF and lateral intraparietal cortex (LIP) [14]).

frequency components [41]. This would allow PAC to have a dual role through the coupling of distinct frequency pairs: enhancing neural discrimination and improving interareal communication (Figure 3).

In our hypothetical scheme showing the effect on signal discrimination in unattended and attended task conditions (Figure 3, top panel), peaks of gamma bursts (representative of the

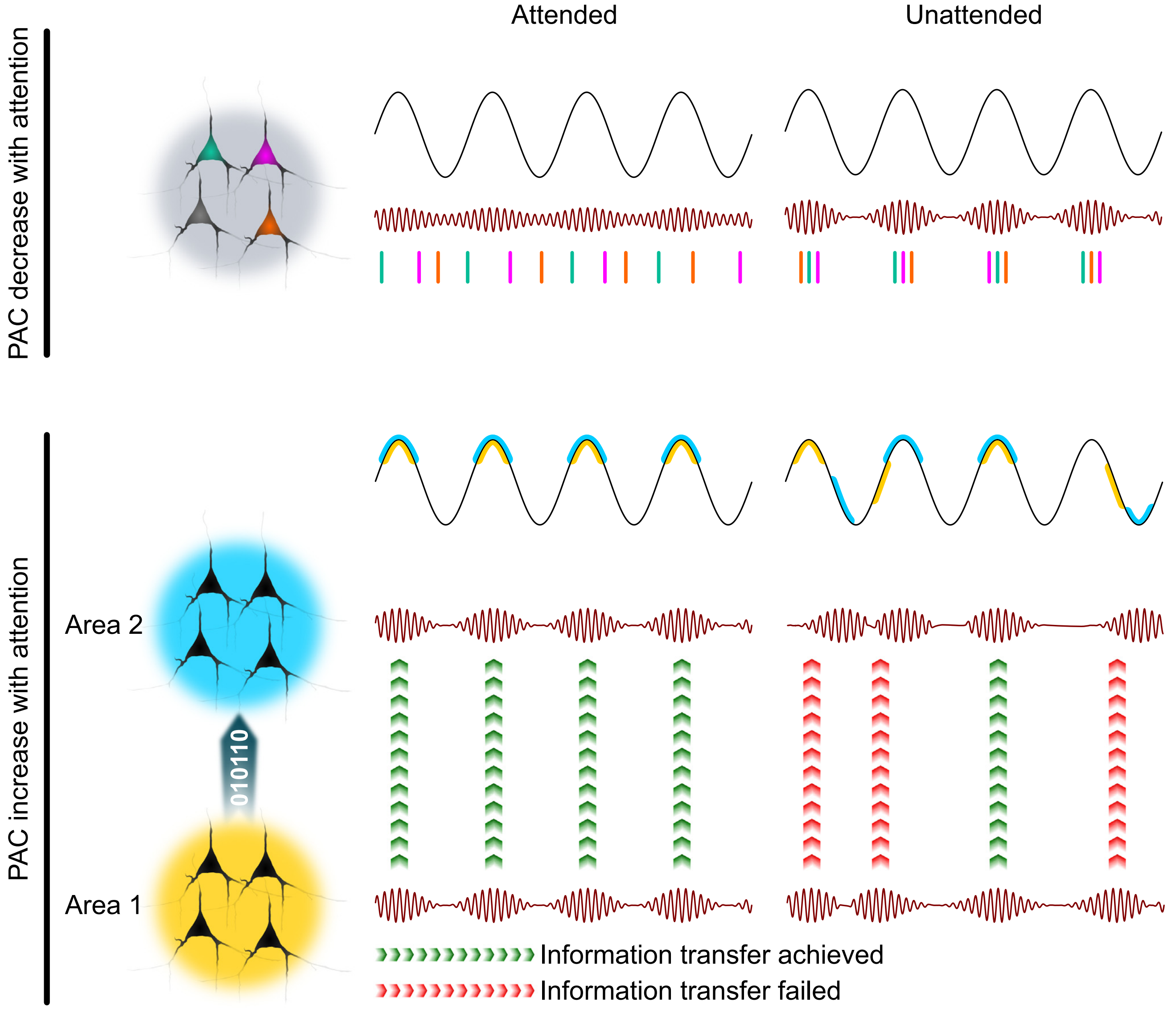

Figure 3. Hypothetical scheme for a dual role for phase-amplitude coupling (PAC) in attention. The top panel depicts PAC reduction with attention, where modulation of neuronal responses are compared between a condition in which attention is focussed on the receptive field of a neuron in a visual area (attended) versus when attention is thrown outside the receptive field of the neuron (unattended). The maximum high-frequency power is shown to coincide with a specific phase (here, peak) of the low-frequency oscillation in both attention conditions. However, in the attended case, the high-frequency oscillations are distributed in time, whereas they occur in an all-or-none manner in the unattended condition. Note that the average power (in time) is equal in the two conditions. Given the simultaneity of spikes and gamma oscillations (i.e., different neurons being more likely to fire when high-frequency oscillations occur), neighbouring neurons fire more synchronously in the unattended condition, in which high-frequency oscillations occur only in limited time-windows. By contrast, the single neurons fire sparsely and in less synchrony with each other when high-frequency oscillations are unevenly distributed in time. The bottom panel illustrates PAC enhancement between areas that occurs with attention. Here, while the high-frequency component follows an all-or-none regime in both attention conditions, the preferred low-frequency phase is constant in the attended condition, while it varies in the unattended condition. In the context of information transmission from a sensory area (here, area 1) to an association area (here, area 2), time-windows of highest excitability (with a stronger high-frequency component) coincide in the attended condition, allowing area 2 to successfully receive the signals transmitted by area 1. However, in the unattended condition, excitability windows for areas 1 and 2 are straggled from each other, preventing an efficient between-area transfer of information. The yellow and blue highlights show the periods of peak high gamma activity in areas 1 and 2, respectively. For simplicity, this figure does not include the mechanism for the theoretical possibility indicated in Figure 1 of a low-frequency oscillation in one area directly modulating high-frequency oscillations in another area.

co-occurrence of the spiking activities of neighbouring neurons) occur at specific phases of the low-frequency oscillations. However, the two attention conditions differ in terms of their gamma frequency distribution in time. In the absence of attention, gamma bursts occur in an all-or-none manner (with some epochs without any gamma burst and other epochs with strong gamma power), while, in the presence of attention, gamma activity is distributed across the whole low-frequency cycle and occurs at all low-frequency phases. Therefore, the unattended condition mediates a temporally localised occurrence of spiking activity in a simultaneous, although redundant, manner across neighbouring neurons, while, in the attended condition, neurons generate spikes with poor temporal synchrony. This view is consistent with the suggestion that stronger interneuronal synchrony (as in the unattended condition shown in the top panel of Figure 3) mediates poorer information capacity, whereas a weaker interneuronal synchrony (as in the attended condition) mediates greater information capacity [42]. Such sparse coding is believed to be an efficient way of coding information and increasing signal discriminability [43,44].

To improve interareal communication (Figure 3, bottom panel) the strength of PAC changes in a different way. Here, gamma activity occurs in both attention conditions in an all-or-none manner, but the gamma bursts are aligned to different phases of the low-frequency component, with all gamma bursts at a specific preferred phase for the attended condition and at different phases in the absence of attention.

This dual function of PAC in attention, occurring across different frequency pairs, serves to transfer information from one area/ensemble to another area/ensemble (as in bottom panel of Figure 3), after adequate neural discrimination of different signals has been achieved (as shown in the top panel of Figure 3). Thus, the two sets of frequency pairs (represented by the cooler and warmer colours in Figure 2C) may represent a highly relevant dichotomy in functional brain connectivity. Future studies are needed to determine whether both PAC functions happen simultaneously within one region or only one of them. The presence of the two types of PAC modulation can be assessed by calculating the degree of the all-or-none distribution of the gamma power across time. A similar degree of such behaviour of the gamma power between the two attention conditions would support an improved interareal communication, whereas a marked difference would be indicative of a PAC modulation supporting enhanced discrimination. Similarly, oscillations may vary in terms of their length. In particular, in lower frequency bands, they could be short-lived, barely present for more than one cycle, or, in higher frequency bands, they may last for dozens of cycles. Understanding the functional relevance of this variation and its differential amplification requires further studies.

The dual role of PAC within distinct coupled frequency pairs agrees with studies showing that different low-frequency ranges are used to transmit signals through different directions. It has been shown that the theta range is harnessed for bottom-up transmissions and the alpha–beta range for top-down projections [45,46]. Similarly, the two contrasting types of PAC may be directed at the different requirements at early and late levels of information processing in the visual system. All reduction of PAC involving gamma frequencies during attention is in early visual areas (V1, V4, and MT; Figure 2), whereas the enhancement of PAC involving gamma frequencies is in higher areas (LIP and FEF). As noted above, reduced PAC suppresses highly synchronised bursts of neuronal responses at gamma frequencies and contributes to greater discrimination among the local population of neurons. However, such sparse coding has its limitations [47] and can be a handicap in higher areas that are closer to decision-making for motor outputs. Here, integration between different inputs and a flexible dense code are likely to be more useful. This is consistent with the experimental data summarised in Figure 2, with activity in the gamma frequencies being more in phase with the theta frequency during attention in the frontoparietal network.

Hypothesis 2 on role of PAC: allowing high-order cortical areas to distinguish incoming signals related to different submodalities via different frequencies

We have described the above aspects and roles of PAC in the context of differentially modulating sensory information processing, particularly for target versus distractor stimuli in visual tasks involving attentional allocation. Next, we address a potential role of PAC in allowing higher order cortical areas to identify and distinguish incoming neuronal signals encoding different modalities, such as different sensory features. We first review recent evidence for a role of distinct frequencies in such a process. Next, we suggest a mechanism that could allow the nervous system to leverage these frequencies to maintain modality information, even when a cortical area simultaneously receives information from multiple modalities.

Two cortical streams and multiple brain rhythms

Despite the fundamental dorsoventral dichotomy of cortical visual information processing described in Box 1, there is extensive communication between the two streams via: (i) feedback projections to common upstream areas such as V1; (ii) corticocortical interactions between the two processing streams; and (iii) the convergence of the streams at the level of the prefrontal cortex [48–50]. Studies of single neuron activity and LFPs recorded simultaneously across different visual areas have suggested that the neural basis of interareal functional interaction is synchronised oscillations between the areas [7,8,12,51]. There is now a rapidly growing body of evidence for the presence of, and changes in the strength of, neural synchrony during processing of incoming sensory signals [10,13,15,52–55] and top-down modulation related to cognitive functions, such as attention [56–58] and predictive coding [59]. It has also been suggested that the oscillation frequencies encountered in different cortical areas are different and depend on task demands [60]. For instance, networks that involve feedforward and feedback information transmission use alpha–beta frequencies for feedback and theta–gamma oscillations for feedforward communication [45,46]. Different frequency ranges may even be used to tag different information pathways toward the same target area (Figure 4).

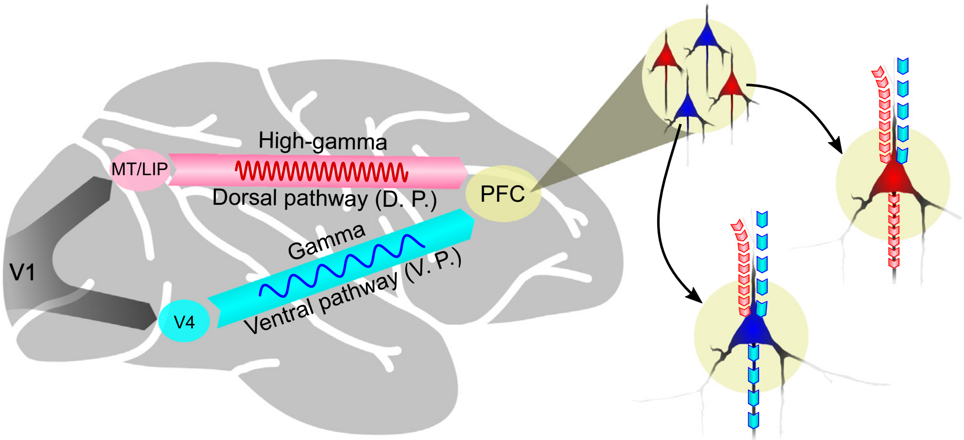

Figure 4. Routing of distinct information types to different associative neuron types via frequency channels. Blue and red streams indicate information sourced from the ventral and dorsal visual pathways, respectively, of the macaque brain taken as representing the general primate cortical architecture. Prefrontal cortex (PFC) neurons are hypothesised to be of at least two different types: gamma detectors (in blue) and high gamma detectors (in red). In the panel on the right, a gamma-detecting neuron (in dark blue), with an intrinsic resonance frequency in the gamma range, selectively relays spikes that are coupled to the phase of gamma oscillations, and high gamma-detecting neurons (in dark red) pass on those spikes that are phase-coupled to the intrinsic high gamma oscillatory activity. Abbreviations: FEF, frontal eye field; LIP, lateral intraparietal cortex; MT, middle temporal area.

Cortical association areas [e.g., lateral prefrontal cortex and LIP) receive and integrate information from a multitude of brain regions, each often preferentially processing a distinct sensory feature dimension (e.g., colour in area V4 and visual motion in area MT). This raises the important question of how neural signals encoding such different visual dimensions are distinguished once they converge at the same higher order cortical area. It was recently suggested that this is achieved by tagging the incoming sensory signals by pathway-specific frequencies of oscillatory activity [39]. Specifically, the ventral visual pathway, carrying information about visual orientation and colour communicates via gamma frequencies (40–70 Hz) [52,61]. By contrast, the dorsal visual pathway, encoding visual motion parameters, transmits information via higher gamma frequency ranges (180–220 Hz [39] and 70–250 Hz [40]). At the receiving end, prefrontal areas could use different neuron types with different resonance properties to selectively receive the signals of different frequencies. This would ensure that the spikes encoding different visual information are segregated across these neuron types for further selective processing. Figure 4 visualises how different neuron types may distinguish the inputs from different brain areas. This model also allows for a selective processing of the different information types.

When attention is directed toward colour, V4 spikes phase-lock to the gamma frequency, whereas, when a motion signal is attended, spikes couple to the phase of high gamma frequency. This enables the corresponding gamma or high gamma cells in prefrontal cortex to selectively receive the currently attended information. Another alternative (not shown in Figure 4) may be that the same set of output neurons with a specific function may choose one or the other sensory input by a change in their resonance frequency. Such transient changes in resonance frequency can be brought about by a change in circuit dynamics depending upon task demands [62–64]. The first account means that a selective processing of colour/motion is implemented at the source area (V4/MT) via a selective phase-coupling of spikes to the corresponding frequency band, whereas the latter would need a control signal at the level of higher association areas to determine which of the source signals to selectively receive.

Tagging of different sources of information via different frequencies has been shown in the hippocampus of rodents, where CA3 and the entorhinal cortex use distinct frequency ranges (25–50 Hz and 65–140 Hz, respectively) to communicate with CA1 [65]. Recently, it was also shown that the lateral and medial entorhinal rodent cortex, which, among other functions, convey information on the ‘what’ and ‘where’ of objects, route the two information types via distinct slow-gamma (30–50 Hz) and fast-gamma (100–150 Hz) bands toward the hippocampus [66].

Distinguishing higher frequency rhythms from artefacts due to spiking activity and non-sinusoidal oscillations

When discussing the role of high gamma frequencies, it has been a frequent point of contention that higher frequency components of LFP signals may include or represent leakage of the waveform of action potentials (i.e., during periods of high firing rates, the frequency components of the spike waveform can get reflected in the high gamma frequency ranges of the LFP) [67–69]. The higher frequency (>100 Hz) component of human LFPs (has also been proposed as an important biological signature of cognitive functions [70,71], although the source of these oscillations has been elusive. Two recent studies have shed light on this matter. In one study [39], extensive analytical controls established that the high gamma frequencies do exist as LFPs and do not arise from spike leakage. In the other study [40], the time period of occurrence of the high gamma oscillations showed very little overlap with the occurrence of high spike activity in mediating feature-based attention.

It has been suggested that high-frequency bands with no obvious peak in the spectral domain (so-called 'broadband signals') involve stereotyped sharp transients, which are interpreted as sinusoidal components in Fourier analyses [72]. These transients (nonphasic components) have been shown to induce artificial PACs across cortex [73]. In such cases, a change in transient responses due to association with external or internal events may lead to artificial differential quantifications of PAC. Therefore, it is important for future studies to both remove such non-sinusoidal components using template-matching approaches, and to identify and extract truly sinusoidal components using a battery of different approaches [67].

Source and function of the phase-providing rhythm in CFC

Even though PAC has consistently been observed across brain areas, the exact low-frequency component driving the gamma/high gamma frequency components varies across brain areas, from as low as delta (1–4 Hz) up to the beta range (12–30 Hz) [32,41,74–76]. This suggests that the low-frequency component of PAC, along with the frequency of the high-frequency component, have the role of a region-specific signature. An association area may take advantage of this fact to keep different pieces of information segregated, by virtue of PAC coupling for each information content being represented by a distinct frequency pair (Figure 5). In the specific case illustrated above, in which colour and motion direction information are transmitted to a downstream area via different HFOs, we speculate that gamma and high gamma frequencies within an association area (such as prefrontal cortex) are coupled to different low-frequency ranges (e.g., gamma oscillations may be coupled to theta–alpha range and high gamma frequencies to the beta range). This is supported by previous studies that observed V4 and MT spikes to communicate interareally via coupling to theta [10,77] and beta/low gamma [8,38], respectively, and is consistent with the recent suggestion of the pervasive role of these low-frequency oscillations in governing sustained attention [14].

Yet another function that has been suggested for PAC is that low-frequency signals from the pulvinar, a part of the visual thalamus [7,26], as well as the claustrum [78], boost neural synchrony between areas and also orchestrate the precise timing needed for many cognitive functions, such as visual search. This scheme has the advantage that, although the connections between cortical areas may not be structurally and functionally tight enough to develop sufficient

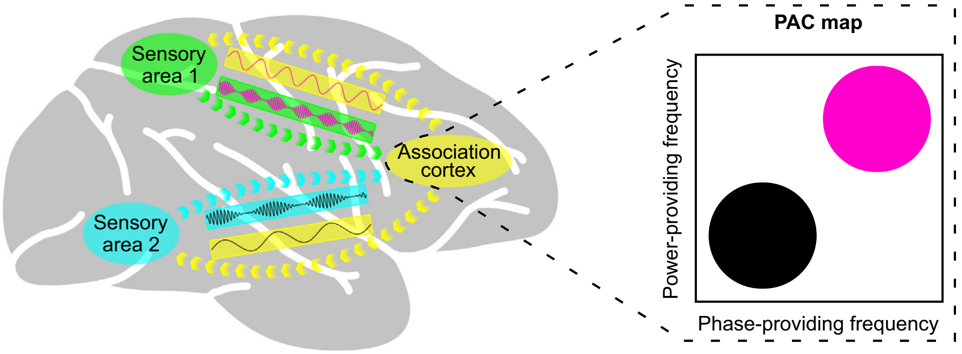

Figure 5. Tagging of information type/source via phase-amplitude coupling (PAC) of different frequencies. Different sensory areas may use distinct high-frequency channels to transmit their encoded information to the association cortex. The higher order cortex, in turn, may use different frequency channels within the low-frequency range to independently send top-down signals to each of the sensory areas (left panel). These distinct low-frequency channels are speculated to be used within the association cortex to maintain the separation of the distinctive inputs as well as propagating them separately to yet other downstream target areas. This hypothesis predicts distinct patches of PAC of separate frequency pairs within the map of PAC strengths at different frequency pairs in the association cortex (right panel).

synchrony, the entraining role given by the pulvinar or claustrum can help them attain a degree of synchrony that will be functionally useful. Critical to this function, in the case of the claustrum, is the unique claustral morphology [79], within both the claustrum and its cortical targets, which are features considered to be characteristic of a system designed to amplify correlated neuronal activity.

Concluding remarks

Oscillation of neural activity has been recognised as a ubiquitous phenomenon in the mammalian brain, and recordings from nonhuman primates have revealed a broad spectrum of oscillatory patterns, not only in the range of frequencies and the coupling pairs, but also how they relate to different behavioural conditions. Across the brain, the frequencies involved in PAC range from slow delta waves to high gamma frequencies of more than 200 Hz. We propose that such diversity enables the brain to use specific coupling pairs for selecting specific types of information and for different functions (see Outstanding questions).

Recent studies support the account that PAC is a central mechanism for linking neuronal oscillations with the temporal pattern of single neuronal activity in the context of information processing and transmission in the mammalian brain. However, much still needs to be clarified about the role of PAC and high gamma frequencies.

Outstanding questions

Does PAC create separate local reference frames by coupling to different low-frequency carriers? For example, is information about the place and motion of a visual stimulus processed within a different low-frequency band compared with that carrying information of shape and identity?

Is the neural activity encoding distinct feature dimensions with different upstream sensory areas modulated by different PAC frequency pairs?

Does PAC mediate the selective transmission of information belonging to each feature dimension/submodality to later stages of processing?

Does PAC modulate the temporal distribution of gamma or the phase preference of gamma relative to low frequencies?

How applicable are the insights gained from studies in the visual system to other sensory modalities?

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Declaration of interests

The authors declare no competing interests in relation to this work.

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