

1 A theta rhythm in awake macaque V1 and V4
2 and its attentional modulation

3 **Georgios Spyropoulos^a, Conrado A. Bosman^{b,c}, Pascal Fries^{a,b,1}**

4 ^aErnst Strüngmann Institute (ESI) for Neuroscience in Cooperation with Max Planck Society,
5 Deutschordenstraße 46, 60528 Frankfurt, Germany, ^bDonders Institute for Brain, Cognition and Behaviour,
6 Radboud University Nijmegen, Kapittelweg 29, 6525 EN Nijmegen, Netherlands, and ^cSwammerdam Institute for
7 Life Sciences, Center for Neuroscience, Faculty of Science, University of Amsterdam, Sciencepark 904, 1098 XH
8 Amsterdam, Netherlands.

9 ¹To whom correspondence should be addressed. E-mail: pascal.fries@esi-frankfurt.de.

10

11 **Abstract**

12 Theta-rhythmic neuronal synchronization has been described in hippocampus and high-level
13 visual areas. Recent studies suggest that theta in visual areas might originate in V1. We
14 analyzed simultaneous electrocorticographic (ECoG) grid recordings of local field potentials
15 from areas V1 and V4 of two macaque monkeys performing a selective visual attention task.
16 We found a ≈ 4 Hz theta rhythm, which was strongest at sites showing visually induced gamma-
17 band activity. This theta rhythm was coherent between V1 and V4, with a predominant
18 V1-to-V4 Granger causal influence. Locally, theta phase was correlated with power in a narrow
19 gamma-frequency band. These theta-rhythmic processes were reduced by selective attention
20 to a visual stimulus contralateral to the recorded visual areas. This attentional effect was
21 substantial, particularly compared to other reported effects of attention in area V1. We
22 investigated, whether microsaccades (MSs) play a role in the generation or attentional
23 modulation of theta. Stratification of MS rate between attention conditions, or elimination of
24 MS-affected data epochs left the main results essentially unchanged. Thus, we find an
25 MS-independent theta rhythm in the visually driven part of V1, which rhythmically modulates
26 local gamma and entrains V4, and which is strongly reduced by attention.

27 **Introduction**

28 Neuronal activity shows rhythmic structure in several characteristic frequency bands (1).
29 These different rhythms have often been linked to areas and/or functions, in which they
30 predominate (2). The theta rhythm has primarily been described in high-level areas of awake
31 mammalian brains in the context of higher cognitive functions. A particularly strong theta
32 rhythm exists in rodent medial temporal lobe (MTL), in particular the hippocampus and
33 entorhinal cortex (3, 4). This theta is found during exploratory behavior, and has been
34 implicated in episodic memory (5-7). A similar theta rhythm also exists in the MTL of non-
35 human and human primates during virtual maze navigation (8) and visual exploration (9, 10),
36 and has been linked to episodic memory encoding (10-12) and working memory maintenance
37 (13, 14).

38 Hippocampal theta is synchronized with a theta rhythm in prefrontal cortex (PFC) (15-17).
39 Theta in PFC and strongly connected structures like the anterior cingulate cortex (ACC) and
40 the posterior parietal cortex has been described when subjects exert executive control (18-
41 23).

42 The theta rhythm in non-human primate PFC shows long-distance synchronization to a theta
43 rhythm in area V4 (24, 25). This PFC-V4 theta-band synchronization and the V4 theta rhythm
44 is pronounced during the delay period of a visual working memory task, that is, in the absence
45 of visual stimulation. In inferotemporal cortex, a theta rhythm has been described that is
46 phase-locked to stimulus onset (26).

47 A theta rhythm at 3-5 Hz has also been described in mid-level visual areas V4 and V5/MT
48 during selective visual attention tasks. A study in macaque area MT reported that the power
49 of high-frequency (30-120 Hz) LFP components is modulated by the phase of low-frequency
50 (1-8 Hz) components, and that this modulation is reduced by attention to the visual stimulus

51 activating the recorded neurons (27). A study in macaque area V4 showed spike-field and
52 spike-spike coherence at 2-4 Hz and straddling the lower end of the spectrum (28). This local
53 low-frequency synchronization was enhanced by visual stimulation; furthermore, it was
54 reduced by attention in the absence of visual stimulation. A subsequent study reported that
55 the 4 Hz phase of LFP in macaque V4 modulates the gamma-band synchronization between
56 areas V4 and V1 (29). Also theta-band Granger causality (GC) influences around 4 Hz between
57 V1 and V4 are stronger in the feedforward direction (30). This suggests that a 4 Hz rhythm
58 might emerge in area V1 and entrain higher areas. Interestingly, a previous study found that
59 microsaccades occur at a 3-4 Hz rhythm and lead to evoked responses and perturbations in
60 local synchronization in both, areas V1 and V4 (31). This MS-related V1 4 Hz rhythm temporally
61 structures also the V1-V2 interaction by co-modulating respective gamma power and
62 frequency (32).

63 Thus, several studies suggest a theta rhythm in V1, by e.g. showing a theta modulation of V1-
64 V4 or V1-V2 interactions. Here, we analyzed simultaneous LFP recordings from awake
65 macaque V1 and V4. We investigated whether the respective LFP power and phase-locking
66 spectra actually show theta peaks, how this is related to visually induced activity, whether
67 local gamma-band power is modulated by theta phase, to which degree these theta-related
68 phenomena are independent of MSs, and whether they are modulated by selective visual
69 attention.

70 **Results**

71 **Macaque areas V1 and V4 show a theta rhythm.** We first calculated power spectra averaged
72 over all electrodes on V1 and V4 from periods, during which the monkey fixated and covertly
73 monitored one of two simultaneously presented drifting grating stimuli (see Materials and
74 Methods for the definition of “electrodes” versus “sites” and the attribution of electrodes and
75 sites to areas). Those average power spectra exhibited clear peaks in the gamma and the beta
76 range, with peak frequencies specific to each monkey; however, they did not exhibit clear
77 peaks in the theta-frequency range (Fig. 1A,B). We have previously found that power spectra
78 can fail to reveal rhythms that are nevertheless unequivocally detectable with metrics of
79 phase locking (35, 50). Here, we quantified phase locking by means of the pairwise phase
80 consistency metric (PPC, see Materials and Methods). We calculated PPC spectra averaged
81 over all possible pairs of sites within and between V1 and V4. The average PPC spectra
82 confirmed the gamma and beta peaks and in addition revealed clear theta peaks around 4 Hz
83 (Fig. 1C,D). Thus, awake macaque visual cortex shows a distinct theta rhythm, when activated
84 by a visual stimulus.

85
86 **Selective attention reduces theta.** Previous studies reported similar theta or low-frequency
87 rhythms in awake macaque areas V4 and MT, which were reduced by selective attention (27,
88 51). Theta might be generated in those extrastriate areas, or it might alternatively emerge
89 already at earlier stages of the visual system. A previous study has found that Granger-
90 causality between visual areas in the theta band is stronger in the feedforward than feedback

91 direction (30). Thus, theta in extrastriate cortex might actually be driven by theta in primary
92 visual cortex. Therefore, we investigated the theta rhythm separately in areas V1 and V4, and
93 we tested if it was affected by selective attention. Raw power spectra averaged over all V1
94 electrodes showed a shallow bump around 4 Hz (Fig. 2A). This V1 theta rhythm was reduced
95 when attention was directed to the contralateral visual stimulus, which was driving part of the
96 V1 electrodes. A similar pattern was found in V4: There was a very shallow bump with an
97 attentional reduction close to 4 Hz (Fig. 2B).

98 To reduce the $1/f^n$ component of the power spectrum, we estimated it by robust regression
99 and subtracted it from the total power (52). We followed this approach and found that in the
100 absence of attention, there were distinct peaks around 4 Hz in both V1 and V4 (Fig. 2C,D).
101 Those peaks were reduced when attention was directed to the contralateral hemifield.
102 We also calculated low-frequency phase-locking (PPC) spectra separately for pairs of sites
103 within V1 or V4 and between V1 and V4, and we investigated whether this phase locking is
104 affected by selective attention. The PPC spectra showed theta peaks for pairs of sites within
105 and between V1 and V4, and this theta-band PPC was reduced by attention (Fig. 3).

106
107 **Theta is spatially coextensive with visually induced gamma.** Because theta was modulated
108 by attention, while attention was directed to visual stimuli, we next investigated whether
109 theta was related to visually induced activity. The ECoG covered large parts of V1,
110 corresponding to large parts of the representation of the lower right visual quadrant, from the
111 fovea out to about six degrees of visual angle. This allowed us to test whether theta was
112 coextensive with visually driven activity. A given ECoG electrode does not provide
113 conventional spike recordings, yet it does provide gamma power enhancements selectively
114 for particular stimulus positions, that is, gamma power enhancements with circumscribed
115 receptive fields (RFs) (29, 37). The electrodes over V1 had varying overlap with the employed
116 grating patch, which resulted in a topographic map of visually induced gamma-band power
117 with a clear peak at the representation of the stimulus (Fig. 4A). When we calculated a
118 corresponding topographic map of theta power (after robust regression of the $1/f^n$
119 component and its removal), it also showed a clear spatial peak (Fig. 4B). We calculated the
120 spatial correlation (Spearman rank correlation) between low-frequency components (power
121 residuals) and visually induced gamma power, across electrodes, separately for V1 and V4, for
122 each attention condition, and for each of the low frequency components up to 10 Hz. The
123 resulting correlation spectra reveal that across the spatial extension of both V1 and V4, visually
124 induced gamma is positively correlated with theta when attention is ipsilateral (Fig. 4C,D, blue
125 lines). In addition, visually induced gamma is negatively correlated with power around 1-4 Hz
126 when attention is contralateral, and in V4 also when attention is ipsilateral (Fig. 4C,D). To
127 ensure that the correlations shown in Figure 4C, D are not due to broadband power
128 correlations, the analyses used gamma from the pre-cue period and theta power from the
129 post-cue period (both with visual stimulation), that is, from non-overlapping trial epochs.
130 Results are essentially the same if the post-cue period is used for both (data not shown).

131

132 **Theta-band Granger causality is stronger in the feedforward direction and reduced by**
133 **attention.** The PPC analysis revealed clear theta peaks for the visually driven sites, and a
134 previous study found theta-band GC between visual areas to be generally stronger in the
135 feedforward direction (30). Therefore, we next investigated in detail the GC between V1 and
136 V4 in the low-frequency range and separately for the two attention conditions. Figure 5A
137 shows the GC spectra averaged over all V1-V4 site pairs, pooled across both attention
138 conditions, and separately for the feedforward (V1-to-V4; green line) and feedback (V4-to-V1;
139 black line) directions. These GC spectra reveal clear theta peaks, and they confirm that GC is
140 stronger in the feedforward than feedback direction. To investigate whether this asymmetry
141 in GC is due to differences in theta power between V1 and V4, we stratified theta power
142 between the two areas. After stratification, the result remained qualitatively unchanged (data
143 not shown).

144 Figure 5B shows the feedforward GC spectra separately for the two attention conditions. It
145 reveals that feedforward GC in the theta band is enhanced when attention is to the ipsilateral
146 stimulus. Figure 5C shows that the same pattern of attention effects exists for the feedback
147 GC.

148
149 **Theta-gamma phase-amplitude coupling and its attentional modulation.** Several previous
150 studies have found that the theta phase modulates gamma power, that is, there is theta-
151 gamma phase-amplitude coupling, or PAC (13, 16, 19, 53). One of those studies also reported
152 that theta-gamma PAC in area MT is decreased with attention to the activating stimulus (27).
153 We investigated whether the theta rhythm described above for V1 and V4 modulates gamma
154 power, and whether this is affected by selective attention. As described above, we found that
155 theta is spatially coextensive with visually induced gamma and reduced by attention.
156 Therefore, to explore whether theta phase modulates gamma amplitude, we first selected
157 conditions with maximal theta strength, that is, visual stimulation with a non-attended
158 stimulus. Figure 6A shows for one example electrode the raw spectral power as a function of
159 time relative to the theta trough. This reveals that the amplitude of visually induced gamma-
160 band power is modulated systematically by theta phase. Figure 6B shows the resulting PAC,
161 averaged over all electrodes in V1 and V4, and over both attentional conditions. It reveals a
162 distinct peak of PAC between theta phase and gamma power. We note that the theta-
163 rhythmic modulation of gamma was most pronounced for the high-frequency end of the
164 gamma band. In addition, this analysis reveals PAC between the phase around 1 Hz and power
165 in several frequency bands; this 1 Hz component is likely related to the temporal frequency of
166 the drifting gratings (see Materials and Methods).

167 Figure 7 shows PAC separately for areas V1 and V4 and for the two attention conditions. In
168 V1, there was a PAC peak for phase-frequencies around 4 Hz (Fig. 7A,B). This theta-gamma
169 PAC was strongly reduced by attention (Fig. 7C). There were additional significant PAC
170 components at lower phase frequencies, which partly also showed significant attentional
171 effects. As mentioned above, these slower components are likely related to the temporal
172 frequency of the drifting gratings. In contrast to V1, V4 did not show significant theta-gamma
173 PAC, and also no significant PAC difference between attention conditions (Fig. 7D-F).

174

175 **Visual theta remains after microsaccade removal.** It has previously been shown that theta-
176 band rhythmicity is present in the sequence of microsaccades (MSs) (31, 32). MSs cause a
177 movement of the retinal image and an MS-related response in the LFP and the multi-unit
178 activity (31). MSs also modulate the strength of gamma-band activity (31, 32). Thus, the MS
179 rhythm may underlie both the theta rhythm and the theta-gamma PAC observed here. To
180 investigate this, we first quantified the phase-locking between MSs and the LFP in V1.
181 Figure 8A shows the MS-LFP PPC spectrum and reveals a clear theta peak. If neuronal activity
182 and phase locking in the theta band were due to driving by theta-rhythmic MSs, then removal
183 of epochs with MSs should diminish the observed theta rhythmicity. To test this, we excluded
184 MSs with increasing stringency and investigated the effect on the observed neuronal theta
185 rhythmicity. We detected MSs and excluded data recorded between MS onset and 0.5 s
186 thereafter. This substantially reduced the amount of available data. We calculated low-
187 frequency PPC spectra within V1 for the attend-away condition for 1) all available epochs
188 (N=1917 epochs), 2) epochs excluding MSs exceeding average eye speed by 5 SD (N=827
189 epochs), 3) epochs excluding MSs exceeding average eye speed by 3 SD (N=446 epochs).
190 Figure 8B reveals that excluding MSs with increasing stringency did not decrease theta
191 rhythmicity in V1. These results strongly suggest that, while there is phase locking between
192 MSs and cortical theta, the cortical theta exists independently of the occurrence of MSs (31).
193 Figure 9 investigates the influence of MS removal (at 5 SD to retain acceptable statistical
194 sensitivity) on further metrics of visual theta. The main results remained essentially
195 unchanged: Low-frequency power spectra (after robust regression of $1/f^n$ and removal) show
196 theta peaks for attention ipsilateral, which are reduced by attention to the contralateral
197 stimulus (Fig. 9A,B); PPC spectra show theta peaks for all cases (Fig. 9C-E), and significant
198 attentional reduction; PAC in area V1 shows a peak for theta-band phase frequencies and
199 gamma-band amplitude frequencies only when attention is directed to the ipsilateral stimulus
200 (Fig. 9F,G,H). When we excluded MSs exceeding average eye speed by merely 3 SD, i.e. when
201 we applied an even more stringent MS removal, the results remained qualitatively unchanged
202 (data not shown). Only the reduction of theta-band V1-V4 PPC with attention did not any more
203 reach significance, probably due to strongly reduced statistical sensitivity.

204

205 **Control for microsaccade rate.** In addition, we performed an alternative control, by equating
206 the MS rate, that is, the MS temporal density, between attention conditions. This specifically
207 controls for potential MS rate differences between attention conditions. Figure 9A shows the
208 cumulative distribution of MS rate over the respective number of data epochs (see Materials
209 and Methods for MS rate estimation). MS rate actually differed between attention conditions.
210 We therefore stratified the data (see Materials and Methods) to arrive at two equally sized
211 sets of epochs with an essentially equal distribution of MS rates (dashed lines in Fig. 9A). After
212 stratification, almost all main results remained essentially unchanged (Fig. 9B-G). Note that V4
213 theta power (after robust regression of $1/f^n$ and removal) did not show a significant
214 attentional effect, yet such an effect was significant for V4-V4 PPC. When we stratified based

215 on MSs detected by a 3 SD threshold, all results remained qualitatively the same as without
216 stratification.

217

218 **Control for theta power.** Finally, we controlled for the possibility that the effects of attention
219 on theta PPC, theta GC or theta-gamma PAC were explained by the effects of attention on
220 theta power. Specifically, theta power was enhanced with ipsilateral attention, which might
221 enhance the sensitivity of PPC, GC and/or PAC quantification, which might in turn explain the
222 enhanced PPC, GC and/or PAC values with ipsilateral attention. To investigate this possibility,
223 we stratified for theta power between attention conditions. After stratification, attention
224 conditions did not any more differ significantly in either theta PPC (V1-V1, V4-V4 or V1-V4),
225 theta GC (V1-to-V4 or V4-to-V1) or theta-gamma PAC (in V1 or V4). This is consistent with two
226 interpretations. One interpretation relates to the signal-to-noise ratio (SNR) of theta. The
227 enhanced theta power in the attend-away condition might increase the sensitivity of the theta
228 PPC and the theta-gamma PAC quantification and thereby explain the attention effect on
229 those metrics. An alternative interpretation relates to the relative amount of time with strong
230 theta power. The enhanced theta power in the attend-away condition might correspond to
231 more time spent in a regime of strong theta rhythmicity. This might conceivably be a genuine
232 difference between attention conditions. If this is the case, stratification for theta power
233 artificially removes this genuine difference. There is no unequivocal way to distinguish
234 between these two interpretations.

235 Note that the increased theta power in the attend-away condition most likely reflects an
236 increased theta-rhythmic synchronization among local neurons. In general, power increases
237 can be due to increases in synchronization or increases in the activity of the involved neurons.
238 However, V1 and V4 neurons, when activated with one stimulus in their RFs as done here,
239 show neuronal activity that increases with attention or stays unchanged (54).

240 **Discussion**

241 We demonstrated the presence of a ≈ 4 Hz theta rhythm in awake macaque V4 and V1. This
242 theta rhythm was present selectively in sites driven by the visual stimulus, such that the spatial
243 map of theta co-extended with the map of visually induced gamma-band activity. In V1, theta
244 rhythmically modulated local gamma-band activity and thereby most likely the gamma-
245 associated local processing of visual information. Theta rhythms in V1 and V4 synchronized,
246 and an analysis of GC revealed a predominant feedforward influence. Theta rhythmicity was
247 substantially reduced by selective attention to a visual stimulus contralateral to the recorded
248 areas. Visual cortical theta showed phase locking with MSs. Yet, exclusion of MS effects left
249 all main theta-related observations essentially unchanged.

250 We were somewhat surprised to find that theta shows a clear spatial correlation or
251 coextension with visually induced gamma-band power. There were reasons to assume that a
252 putative theta rhythm might be global across visual cortex. Hippocampal recordings suggest
253 that theta is global in this structure, travelling as a wave from dorsal to ventral parts (55, 56).
254 Also, there is the general notion that slower rhythms are more global than faster rhythms (57,

255 58). Yet, our finding of a spatially specific theta, which is coupled to gamma by spatial
256 extension and also through PAC, is also in agreement with one previous study: Inter-areal GC
257 influences in both theta and gamma are typically stronger in the anatomically defined
258 feedforward than feedback direction (30).

259 The PAC analysis showed theta-gamma coupling that peaked for an amplitude-frequency at
260 the high-frequency end of the visually induced gamma band activity. Thus, theta-rhythmic
261 modulation was most apparent for this high-frequency part of the overall gamma peak. This
262 might reflect a physiological asymmetry or be related to signal-to-noise ratio. Physiologically,
263 it is conceivable that the modulation is in fact stronger at the upper flank of the gamma peak
264 than at the lower flank, which would be equivalent to an asymmetric broadening of the
265 gamma peak towards higher frequencies. Alternatively, the gamma-band peak is modulated
266 in its entirety, yet the PAC metric ends up larger for the upper than the lower flank, e.g.
267 because the gamma peak is superimposed on unmodulated (or less modulated) $1/f^n$ power. If
268 we consider the $1/f^n$ component of the power spectrum as noise, this noise is larger for the
269 lower than the upper flank.

270 In addition, it is interesting to investigate the precise frequency of the observed theta rhythm.
271 The basic spectra of power (residuals) and phase locking showed peaks close to 4 Hz. The
272 analysis of spatial correlation between theta power and visually-induced gamma power
273 showed a broader peak that includes 4 Hz, yet extends up to 8 Hz. This suggests that the
274 underlying phenomenon might actually occupy this broader frequency range, with theta
275 merely peaking at 4 Hz for the particular stimulus and task conditions used here. Whether
276 other stimuli or tasks make theta in V1 and/or V4 shift in frequency is an interesting topic for
277 further study. In any case, the 4-8 Hz range found in the spatial correlation analysis is an
278 interesting link to the classical hippocampal theta, which occupies this range. Hippocampal
279 theta in fact shifts in frequency, e.g. depending on running speed (62, 63).

280 The mechanisms behind the observed visual cortical theta rhythm and its attentional
281 modulation are not yet clear. The mechanisms underlying hippocampal theta have been
282 studied in great detail (64), and hippocampal theta is partly synchronized to neocortex, e.g. to
283 entorhinal and prefrontal areas. It is conceivable that this theta synchronizes further to
284 intermediate and lower visual areas, yet we deem it unlikely that this is the source of the theta
285 observed here. Such a mechanism would most likely not generate the spatial coextension
286 between theta and gamma, and the predominant GC direction from V1 to V4, which we
287 observed here. The present results place further constraints on potential mechanisms: The
288 fact that removing MSs left the main results essentially unchanged suggests that theta in visual
289 cortex does not merely reflect theta-rhythmic MSs. Rather, the clear spatial co-extension
290 between theta power and visually induced gamma suggests a role for visually driven activity
291 in theta generation.

292 The theta rhythms in V1 and V4 were reduced by selective attention to a contralateral
293 stimulus. Attention effects are typically smaller in V1 than in higher visual areas (for otherwise
294 comparable conditions). This holds for firing rates (54, 59) and gamma-band synchronization
295 (60). In fact, for gamma-band synchronization, different studies in V1 have reported
296 attentional increases (60), decreases (61) or the absence of an effect (29). By contrast, the

297 attentional effects on theta appeared to be of similar strength in V4 and V1, entailing an
298 unusually strong attention effect for V1.

299 Many studies have reported reductions in alpha power at the neuronal representation of
300 visual stimuli or visual attention (28, 65). The attentional reduction of theta observed here
301 might be a related phenomenon at a slightly lower frequency. However, whereas visually
302 driven neuronal ensembles show reduced alpha (28), we found that they show enhanced
303 theta (Fig. 4). This observation supports an alternative scenario. Recent studies have shown
304 that attention samples visual stimuli at a theta rhythm. When human subjects have to detect
305 the appearance of a faint stimulus at a peripheral location, their detection performance is
306 modulated by the phase of a 7-8 Hz rhythm with a maximum over frontal cortex (66). This
307 might reflect an ≈ 8 Hz rhythmic attentional sampling. In support of this, three subsequent
308 studies have shown that two simultaneously monitored stimuli are attentionally sampled in
309 alternation, each at ≈ 4 Hz (67-69). A further study estimated the temporal sampling frequency
310 of attention, and found it to be around 7 Hz for a single attended stimulus, 4 Hz for two and
311 2.6 Hz for three (70). These numbers are consistent with a single attentional sampling
312 mechanism that is multiplexed over the to-be-attended stimuli. Such a scenario would also
313 explain theta-rhythmic modulations of firing rates in inferotemporal (IT) cortex during the
314 presentation of two stimuli (26). When IT neurons respond to one stimulus, and a second
315 stimulus is added onto the screen, firing rates start oscillating at ≈ 4 Hz in a way that suggests
316 that attention is drawn to the newly presented stimulus and subsequently alternates between
317 the two stimuli. At first glance, these results might seem to suggest that visual cortical theta
318 should be stronger for the attended stimulus, in contrast to our findings. Yet, the fact that
319 divided attention tasks reveal theta-rhythmic sampling does not mean that attended stimuli
320 are affected by stronger theta-rhythmic modulation than non-attended stimuli. The
321 mentioned recordings in IT showed strong theta rhythmicity when two stimuli were
322 presented, but weaker theta rhythmicity when a single stimulus was presented and thereby
323 received full attention. Based on these and the present results, we propose that attention is
324 more sustained, yet still weakly theta rhythmic, at the attended location, and that it theta-
325 rhythmically scans the space around it, to explore other stimuli. As a consequence, non-
326 attended stimuli receive attentional processing benefits only when they are attentionally
327 scanned, leading to relatively strong theta rhythmicity. This scanning hypothesis is consistent
328 with theta-rhythmic modulations of detection performance when one location on an
329 extended stimulus is attended, while another location on the same object is not attended: The
330 non-attended location is consistently sampled at an 8 Hz rhythm, yet with a 90 degree phase
331 offset in the 8 Hz cycle to the attended location (69).

332 Future studies will need to investigate whether attentional control structures show an ≈ 8 Hz
333 sampling rhythm that is coherent to the sampled stimulus representations in visual cortex. As
334 mentioned above, the ≈ 8 Hz EEG component, whose phase predicts human detection
335 performance, is strongest over frontal areas (66). Also, spike and LFP recordings in macaque
336 parietal cortex have recently revealed a similar theta rhythm (21, 22). If such theta-rhythmic
337 top-down influences were to be found, it will be interesting to understand how they fit with
338 the predominantly bottom-up directed theta influences observed between visual areas (30).

339 One possibility is that control structures exert a theta-rhythmic perturbation on early and even
340 primary visual cortex, which then percolates up through the hierarchy of visual areas.

341 **Materials and Methods**

342 **Subjects, stimuli and task.** Two adult male macaque monkeys participated in this study. All
343 procedures were in accordance with Dutch and European regulations for the protection of
344 animals and were approved by the animal ethics committee of Radboud University Nijmegen
345 (Netherlands). The data analyzed here have been (partially) used in previous studies (29, 30,
346 33-40).

347 Stimuli and behavior were controlled by the software CORTEX (<http://dally.nimh.nih.gov>).
348 Stimuli were presented on a CRT monitor at 120 Hz non-interlaced. When the monkey
349 touched a bar, a gray fixation point appeared at the center of the screen. When the monkey
350 brought its gaze into a fixation window around the fixation point (0.85 degree radius in
351 monkey K; 1 deg radius in monkey P), a pre-stimulus baseline of 0.8 s started. If the monkey's
352 gaze left the fixation window at any time, the trial was terminated. The measured eye
353 positions during correct trials used for analysis differed only by an average of 0.03 deg of visual
354 angle between the two attention conditions. After the baseline period, two physically
355 isoluminant patches of drifting sinusoidal grating appeared (diameter= 3 degrees, spatial
356 frequency ≈ 1 cycles/degree, drift velocity ≈ 1 degree/s, resulting temporal frequency
357 ≈ 1 cycle/s, contrast= 100%). The two grating patches chosen for a given recording session
358 always had equal eccentricity, size, contrast, spatial frequency and drift velocity. The two
359 gratings always had orientations that were orthogonal to each other, and they had drift
360 directions that were incompatible with a Chevron pattern moving behind two apertures, to
361 avoid pre-attentive binding. In any given trial, one grating was tinted yellow, the other blue,
362 with the color assigned randomly across trials. The yellow and blue colors were physically
363 equiluminant. After 1-1.5 s (0.8-1.3 s in monkey P), the fixation point changed color to match
364 the color of one of the two gratings, thereby indicating this grating as the relevant stimulus
365 and the other as irrelevant. For each trial, two independent change times for the two stimuli
366 were determined randomly between stimulus onset and 4.5 s after cue onset, according to a
367 slowly rising hazard rate. If the relevant stimulus changed (before or after the irrelevant
368 stimulus changed), and the monkey released the bar within 0.15-0.5 s thereafter, the trial was
369 terminated and a reward was given. If the monkey released the bar at any other time, the trial
370 was terminated without reward. The stimulus changes were small changes in the grating
371 pattern, with the stripes undergoing a gentle bend. During the bend, the outer ends of the
372 grating stripes lagged increasingly behind the center of the stripes, until the lag reached
373 0.1 degree at 75 ms after the start of the bend. Over the course of another 75 ms, the stripes
374 straightened again.

375 Several sessions (either separate or after attention-task sessions) were devoted to the
376 mapping of receptive fields (RFs), using 60 patches of moving grating. Receptive field positions
377 were stable across recording sessions (29).

378

379 **Neurophysiological recordings and signal preprocessing.** Neuronal recordings were made
380 from two left hemispheres in two monkeys through a micromachined 252-channel
381 electrocorticographic electrode array (ECoG) implanted subdurally. The details of the
382 production and the electrochemical properties have been described in a separate paper (41).
383 Briefly, ECoG grids were 10 micron thick polyimide foils with 0.3 micron thick Platinum
384 electrodes and conductive lanes embedded. Electrodes had an exposed surface with a
385 diameter of 1 mm and a center-to-center spacing of 2-3 mm. Electrodes were arranged in
386 lanes, and two neighboring lanes ran parallel on one “finger” of the polyimide foil (30). The
387 structuring in separate fingers avoided wrinkling of the ECoG on the brain surface and
388 corresponding pressure points. For ECoG implantation, a 6.5x4 cm craniotomy over the left
389 hemisphere in each monkey was performed under aseptic conditions with isoflurane
390 anesthesia. The dura was opened and the ECoG was placed directly onto the brain under visual
391 control. Several high resolution photos were taken before and after placement of the ECoG
392 for later coregistration of ECoG signals with brain regions. After ECoG implantation, both the
393 bone and the dural flap were placed back and secured in place. After a recovery period of
394 approximately three weeks, we started with neuronal recordings.
395 Signals obtained from the 252-electrode grid were amplified 20 times by eight Plexon
396 headstage amplifiers (Plexon, USA), high-pass filtered at 0.159 Hz, low-pass filtered at 8 kHz
397 and digitized at 32 kHz by a Neuralynx Digital Lynx system (Neuralynx, USA). LFP signals were
398 obtained by low-pass filtering at 200 Hz and downsampling to 1 kHz. Powerline artifacts were
399 removed by digital notch filtering. The actual spectral data analysis included spectral
400 smoothing that rendered the original notch invisible.

401
402 **Data analysis general.** All analyses were done in MATLAB (The MathWorks, USA) and using
403 FieldTrip (42) (<http://fieldtrip.fcdonders.nl>).

404 **Recording electrodes versus recording sites.** During recordings, all ECoG electrodes were
405 referenced against one silver ball implanted epidurally over the other hemisphere. This
406 common reference could lead to artifactual correlations between the signals of separate
407 electrodes. Therefore, all metrics of interaction between distant groups of neurons, that is the
408 pairwise phase consistency (PPC) and Granger causality (GC), were applied after removing the
409 common reference by local bipolar differentiation. That is, the signals from two immediately
410 neighboring electrodes were subtracted from each other. We refer to the ECoG contacts as
411 “electrodes” and to the local bipolar derivations as “recording sites” or just “sites”. All analyses
412 of local neuronal activity used directly the signals recorded from the electrodes, to minimize
413 preprocessing and to minimize reduction in theta amplitude due to theta phase alignment
414 between neighboring electrodes.

415 **Selection of electrodes and sites.** The ECoG grids provided dense coverage of dorsal V1, the
416 superficial part of dorsal V2, dorsal V4 and posterior TEO (29, 30). For simplicity, we refer to
417 V1 and V2 sites as V1, and to V4 and TEO sites as V4. Monkey K had 45 electrodes on V1,

418 resulting in 40 bipolar sites, and 24 electrodes on V4, resulting in 19 sites. Monkey P had
419 72 electrodes on V1, resulting in 64 sites, and 26 electrodes on V4, resulting in 21 sites.

420 **Normalization of signals across electrodes and recording sessions.** Signal amplitude could
421 vary across electrodes because several separate headstages were used. Furthermore, signal
422 amplitude of a given electrode could vary across sessions, probably due to variable quality of
423 contact to the cortical surface. To equalize the contribution of different electrodes and
424 sessions, we applied a z-transform: For each electrode and session, the raw LFP signal was
425 demeaned and divided by its standard deviation.

426 **Segmenting data into epochs.** Each successfully completed trial contained three periods: The
427 pre-stimulus, the pre-cue and the post-cue period. The pre-stimulus period was the time
428 between fixation onset and stimulus onset. During the pre-stimulus period, monkeys fixated
429 on a fixation point on a gray screen, and there was no stimulus presented and no cue had been
430 nor was presented during that time. The pre-cue period was the time between stimulus onset
431 and cue onset. During the pre-cue period, monkeys kept fixation, the stimuli were
432 continuously present, one tinted yellow the other blue, chosen randomly, and the fixation
433 point had not yet assumed a color, and thereby the attentional cue had not been given. The
434 post-cue period was the time between cue onset and target change. During the post-cue
435 period, monkeys kept fixation, the stimuli were continuously present with their tints and the
436 fixation point was tinted in one of these colors, thereby providing the attentional cue. On
437 approximately half of the trials, the post-cue period contained a distracter change, and the
438 data immediately following this event were excluded as explained below. The pre-stimulus,
439 pre-cue and post-cue periods all were of variable length across trials. The spectral analysis was
440 based on epochs of fixed lengths. Therefore, the described task periods were cut into non-
441 overlapping epochs. We aimed at excluding data soon after events, like stimulus onset, cue
442 onset and distracter change, to minimize effects of post-event transients and non-
443 stationarities on the metrics of rhythmicity and synchronization. Therefore, periods were cut
444 into non-overlapping epochs, starting from the end of the period and stopping, before an
445 epoch would have included data less than 0.5 s after those events. In general, we cut epochs
446 of 1 s length, to achieve a fundamental spectral resolution (Rayleigh frequency) of one Hertz.
447 This was used for the analysis of PPC, GC and phase-amplitude coupling (PAC). The PAC
448 analysis required the prior estimation of the power time course, for which we employed
449 window lengths of ± 2.5 cycles per frequency. In this case, epochs were cut such that the power
450 estimation windows excluded data less than 0.5 s after events. The estimation of power
451 spectra was based on 1.6 s epochs, because theta peaks were visible but less conspicuous
452 when 1 s epochs were used.

453 **Spectral estimation.** Epochs were Hann tapered and Fourier transformed. For the PAC
454 analysis, the ± 2.5 cycle long windows were also treated in this way. For the analysis of the
455 spatial correlation between theta power and stimulus induced gamma power, the gamma-
456 power estimation used multitaper spectral estimation with seven tapers taken from the
457 discrete prolate spheroidal sequence, defined on 0.5 s long epochs (43).

458 **Robust regression.** We reduced the $1/f^n$ background in power spectra by estimating the $1/f^n$
459 component and subtracting it. Specifically, for each electrode separately, we pooled attention
460 conditions and fitted a line to the log-log power plot between 0.625 and 10 Hz, using robust
461 regression as implemented in the MATLAB “robustfit” function with default settings. Robust
462 regression uses an iterative procedure that lends less weight to data that are far from the
463 fitted function. Subsequently, the fitted line was subtracted to obtain the power residuals.

464 **Pairwise phase consistency (PPC) and Phase-amplitude coupling (PAC).** Phase locking was
465 quantified with the pairwise phase consistency (PPC) metric (44). We used PPC both to
466 quantify the locking between LFPs recorded from separate sites, the locking between
467 microsaccades and LFP, and the locking between the LFP phase and its amplitude fluctuations,
468 that is, the PAC (phase-amplitude coupling) (45). PPC is not biased by the number of epochs,
469 whereas the more conventional coherence metric has that bias. Essentially, the PPC
470 calculation proceeds in two steps. First, the relative phases are calculated for the multiple
471 epochs of the two signals. The second step is the crucial step: In conventional coherence
472 calculation, those relative phases are averaged, which leads to the bias by epoch number; in
473 PPC calculation, all possible pairs of relative phases are formed, the cosines between those
474 relative phases are determined and those cosine values are averaged.

475 To quantify PAC, we computed the PPC between the LFP at lower frequencies, the “phase-
476 frequencies”, and the time-varying power at higher frequencies, the “amplitude-frequencies”.
477 One-second long epochs of the raw LFP and of its time-varying power were Fourier
478 transformed, and locking among the phase estimates at the phase-frequencies was quantified
479 as the PPC across all available epochs. PAC can in general only be estimated for pairs of phase-
480 and amplitude-frequencies, for which the amplitude frequency is higher than the phase
481 frequency. In addition, the estimation of time-varying power entails low-pass filtering, and
482 PAC can only be estimated for pairs of phase- and amplitude-frequencies, for which this low-
483 pass frequency is above the phase frequency. Power is estimated on the basis of epochs and
484 tapers of finite length. As described above, we chose epochs of ± 2.5 cycle length per
485 frequency. In order to assess the resulting low-pass filtering, we applied the power estimation
486 10000 times to a random Gaussian process of the same length as the data epochs, and
487 determined the frequency, at which this low-pass filtering reduced the average power to less
488 than 70% of the power in the passband. For example, for 50 Hz, this cutoff frequency was
489 7.7 Hz. This procedure was applied for each amplitude frequency, and the PAC for this
490 amplitude frequency was only considered up to the respective phase frequency. The excluded
491 combinations of phase-frequencies and amplitude-frequencies are masked with black in the
492 figures. The PAC results shown here use phase and power estimates from the same electrode.
493 We also calculated PAC by combining phase estimates from one electrode with power
494 estimates of neighboring electrodes, and this left the results essentially unchanged.

495
496 **Granger causality.** We used the non-parametric estimation of Granger causality (46). For this,
497 Fourier spectra were estimated as described above and entered into a non-parametric
498 spectral matrix factorization (NPSF) as implemented in the FieldTrip toolbox.

499 **Statistical testing.** The confidence intervals shown for power and PPC spectra in Figure 1 were
500 estimated with a bootstrap procedure (1000 bootstrap replications for power, 500 for PPC)
501 (47): Spectra were first averaged across electrodes (for power) or site pairs (for PPC), and
502 subsequently, the bootstrap was performed across epochs. All statistical comparisons were
503 based on non-parametric permutation and included corrections for the multiple comparisons
504 made across frequencies. We illustrate the procedure for the comparison of power between
505 the two attention conditions. The power difference between the attention conditions was first
506 averaged over all electrodes per monkey and then over the two animals, giving the observed
507 power difference per frequency. Subsequently, the following procedure was done 1000 times:
508 1) The attention conditions were randomly exchanged between epochs, keeping the original
509 number of epochs per attention conditions constant; 2) The average power difference was
510 calculated as described for the observed data; 3) The maximal (minimal) difference across all
511 frequencies was placed into the randomization distribution of maximal (minimal) values; 4)
512 The 2.5th percentile of the minimal values and the 97.5th percentile of the maximal values were
513 taken as statistical thresholds. The observed differences were compared to those thresholds.
514 This procedure implements a non-parametric version of a two-sided test with multiple
515 comparison correction (48). The same procedure was used for comparing power, PPC, GC and
516 PAC values between attention conditions; for power and PAC, we used 1000 permutations,
517 for PPC and GC 500 permutations.

518 The spatial correlation coefficients and the PAC values were tested in two ways: They were
519 compared between attention conditions as described, and they were additionally tested for
520 the presence of significant correlation or PAC. In the case of PAC, the comparison was done
521 between the observed values and a randomization distribution obtained by randomly pairing
522 raw LFP epochs and power time courses 1000 times. After each random pairing and
523 recalculation of PAC, maximal and minimal values across all frequency-frequency pairs were
524 placed into the respective randomization distribution, and further testing proceeded as
525 described. In the case of the spatial correlations, the comparison was done between the
526 observed values and zero, because the Spearman rank correlation has no bias; the
527 randomization was done by randomly pairing electrodes between the theta power residuals
528 and the stimulus induced gamma. After each randomization, maximal and minimal correlation
529 values across all tested frequencies were placed into the respective randomization
530 distribution, and further testing proceeded as described.

531
532 **Microsaccade detection.** Raw vertical and horizontal eye position signals were low-pass
533 filtered by replacing each value with the average over itself ± 15 samples (at 1 kHz sampling
534 rate). Signals were then differentiated in time to obtain the vertical and horizontal velocities.
535 Those are combined to obtain the eye speed irrespective of the direction of eye movement.
536 Per trial, the standard deviation of eye speed was determined, and any deviation larger than
537 5 SDs and lasting for at least 30 ms was considered a saccadic eye movement. Saccadic eye
538 movements that remained within the fixation window were considered microsaccades (MSs).

539 **Stratification.** We intended to test, whether some of the observed differences were due to
540 differences in the rate of MSs, which existed between attention conditions, or in the power of
541 theta, which existed between attention conditions or between areas. To this end, we used a
542 stratification approach, that is, we randomly subsampled the available data to equate as well
543 as possible the distributions of MS rates or theta power (49). For MS stratification, we first
544 calculated MS density by convolving the MS sequence with a Gaussian kernel with an SD of
545 150 ms (truncated at ± 500 ms). For each epoch, we calculated the average MS density, which
546 was then used for stratification. For theta power stratification, we estimated and removed the
547 $1/f^n$ component for each electrode, averaged over electrodes, and used the resulting average
548 residual theta (3-5 Hz) power for stratification. We describe the stratification procedure for a
549 given parameter (MS density or theta power) for the attention contrast: The parameter
550 distributions were compiled for the two attention conditions and binned into 40 equally
551 spaced bins. For each bin, the number of entries for the two attention conditions was equated
552 by random subsampling with a procedure that aims at equating the parameter averages
553 between the conditions as well as possible. This procedure is applied to the distributions per
554 bin: 1) The condition with more entries is defined as the larger condition, the other as the
555 smaller condition; 2) The mean of the parameter for the smaller condition is calculated and
556 taken as target value; 3) The larger condition is randomly subsampled, by first drawing one
557 entry at random, and then proceeding as follows: a) A further entry is randomly drawn; b) If
558 the mean of the current bin entries (or the starter entry) is smaller (larger) than the target
559 value, the new entry is added if it is larger (smaller), otherwise it is discarded and a new
560 random draw is performed. This latter step aims at equating means; if no such entry is present,
561 a randomly drawn entry is accepted. Stratification across areas proceeded accordingly.

562 **Acknowledgements:**

563 PF acknowledges grant support by DFG (SPP 1665, FOR 1847, FR2557/5-1-CORNET), EU
564 (HEALTH-F2-2008-200728-BrainSynch, FP7-604102-HBP, FP7-600730-Magnetodes), a
565 European Young Investigator Award, NIH (1U54MH091657-WU-Minn-Consortium-HCP), and
566 LOEWE (NeFF). The authors thank Jarrod Dowdall for help with microsaccade detection and
567 Martin Vinck for helpful comments on the manuscript.

568

References

569

- 570 1. Buzsáki G (2006) *Rhythms of the brain* (Oxford University Press, Oxford ; New York) pp xiv, 448 p.
- 571 2. Keitel A & Gross J (2016) Individual Human Brain Areas Can Be Identified from Their Characteristic
- 572 Spectral Activation Fingerprints. *PLoS biology* 14(6):e1002498.
- 573 3. O'Keefe J & Recce ML (1993) Phase relationship between hippocampal place units and the EEG theta
- 574 rhythm. *Hippocampus* 3(3):317-330.
- 575 4. Hafting T, Fyhn M, Bonnevie T, Moser MB, & Moser EI (2008) Hippocampus-independent phase
- 576 precession in entorhinal grid cells. *Nature* 453(7199):1248-1252.
- 577 5. Jezek K, Henriksen EJ, Treves A, Moser EI, & Moser MB (2011) Theta-paced flickering between place-cell
- 578 maps in the hippocampus. *Nature* 478(7368):246-249.
- 579 6. Skaggs WE, McNaughton BL, Wilson MA, & Barnes CA (1996) Theta phase precession in hippocampal
- 580 neuronal populations and the compression of temporal sequences. *Hippocampus* 6(2):149-172.
- 581 7. Dragoi G & Buzsaki G (2006) Temporal encoding of place sequences by hippocampal cell assemblies.
- 582 *Neuron* 50(1):145-157.
- 583 8. Kahana MJ, Sekuler R, Caplan JB, Kirschen M, & Madsen JR (1999) Human theta oscillations exhibit task
- 584 dependence during virtual maze navigation. *Nature* 399(6738):781-784.
- 585 9. Killian NJ, Jutras MJ, & Buffalo EA (2012) A map of visual space in the primate entorhinal cortex. *Nature*
- 586 491(7426):761-764.
- 587 10. Jutras MJ, Fries P, & Buffalo EA (2013) Oscillatory activity in the monkey hippocampus during visual
- 588 exploration and memory formation. *Proceedings of the National Academy of Sciences of the United*
- 589 *States of America* 110(32):13144-13149.
- 590 11. Rutishauser U, Ross IB, Mamelak AN, & Schuman EM (2010) Human memory strength is predicted by
- 591 theta-frequency phase-locking of single neurons. *Nature* 464(7290):903-907.
- 592 12. Lega BC, Jacobs J, & Kahana M (2012) Human hippocampal theta oscillations and the formation of
- 593 episodic memories. *Hippocampus* 22(4):748-761.
- 594 13. Axmacher N, *et al.* (2010) Cross-frequency coupling supports multi-item working memory in the human
- 595 hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*
- 596 107(7):3228-3233.
- 597 14. Raghavachari S, *et al.* (2001) Gating of human theta oscillations by a working memory task. *The Journal*
- 598 *of neuroscience : the official journal of the Society for Neuroscience* 21(9):3175-3183.
- 599 15. Siapas AG, Lubenov EV, & Wilson MA (2005) Prefrontal phase locking to hippocampal theta oscillations.
- 600 *Neuron* 46(1):141-151.
- 601 16. Sirota A, *et al.* (2008) Entrainment of neocortical neurons and gamma oscillations by the hippocampal
- 602 theta rhythm. *Neuron* 60(4):683-697.
- 603 17. Brincat SL & Miller EK (2015) Frequency-specific hippocampal-prefrontal interactions during associative
- 604 learning. *Nature neuroscience* 18(4):576-581.
- 605 18. Debener S, *et al.* (2005) Trial-by-trial coupling of concurrent electroencephalogram and functional
- 606 magnetic resonance imaging identifies the dynamics of performance monitoring. *The Journal of*
- 607 *neuroscience : the official journal of the Society for Neuroscience* 25(50):11730-11737.
- 608 19. Voloh B, Valiante TA, Everling S, & Womelsdorf T (2015) Theta-gamma coordination between anterior
- 609 cingulate and prefrontal cortex indexes correct attention shifts. *Proceedings of the National Academy*
- 610 *of Sciences of the United States of America* 112(27):8457-8462.
- 611 20. Babapoor-Farrokhran S, Vinck M, Womelsdorf T, & Everling S (2017) Theta and beta synchrony
- 612 coordinate frontal eye fields and anterior cingulate cortex during sensorimotor mapping. *Nature*
- 613 *communications* 8:13967.
- 614 21. Hawellek DJ, Wong YT, & Pesaran B (2016) Temporal coding of reward-guided choice in the posterior
- 615 parietal cortex. *Proceedings of the National Academy of Sciences of the United States of America*
- 616 113(47):13492-13497.
- 617 22. Phillips JM, Vinck M, Everling S, & Womelsdorf T (2014) A long-range fronto-parietal 5- to 10-Hz network
- 618 predicts "top-down" controlled guidance in a task-switch paradigm. *Cereb Cortex* 24(8):1996-2008.
- 619 23. Womelsdorf T, Johnston K, Vinck M, & Everling S (2010) Theta-activity in anterior cingulate cortex
- 620 predicts task rules and their adjustments following errors. *Proceedings of the National Academy of*
- 621 *Sciences of the United States of America* 107(11):5248-5253.
- 622 24. Liebe S, Hoerzer GM, Logothetis NK, & Rainer G (2012) Theta coupling between V4 and prefrontal cortex
- 623 predicts visual short-term memory performance. *Nature neuroscience* 15(3):456-462, S451-452.

16

- 624 25. Lee H, Simpson GV, Logothetis NK, & Rainer G (2005) Phase locking of single neuron activity to theta
625 oscillations during working memory in monkey extrastriate visual cortex. *Neuron* 45(1):147-156.
- 626 26. Rollenhagen JE & Olson CR (2005) Low-frequency oscillations arising from competitive interactions
627 between visual stimuli in macaque inferotemporal cortex. *Journal of neurophysiology* 94(5):3368-3387.
- 628 27. Esghaei M, Daliri MR, & Treue S (2015) Attention Decreases Phase-Amplitude Coupling, Enhancing
629 Stimulus Discriminability in Cortical Area MT. *Frontiers in neural circuits* 9:82.
- 630 28. Fries P, Womelsdorf T, Oostenveld R, & Desimone R (2008) The effects of visual stimulation and selective
631 visual attention on rhythmic neuronal synchronization in macaque area V4. *The Journal of neuroscience*
632 : the official journal of the Society for Neuroscience 28(18):4823-4835.
- 633 29. Bosman CA, et al. (2012) Attentional stimulus selection through selective synchronization between
634 monkey visual areas. *Neuron* 75(5):875-888.
- 635 30. Bastos AM, et al. (2015) Visual areas exert feedforward and feedback influences through distinct
636 frequency channels. *Neuron* 85(2):390-401.
- 637 31. Bosman CA, Womelsdorf T, Desimone R, & Fries P (2009) A microsaccadic rhythm modulates gamma-
638 band synchronization and behavior. *The Journal of neuroscience : the official journal of the Society for*
639 *Neuroscience* 29(30):9471-9480.
- 640 32. Lowet E, Roberts MJ, Bosman CA, Fries P, & De Weerd P (2016) Areas V1 and V2 show microsaccade-
641 related 3-4-Hz covariation in gamma power and frequency. *The European journal of neuroscience*
642 43(10):1286-1296.
- 643 33. Bastos AM, et al. (2015) A DCM study of spectral asymmetries in feedforward and feedback connections
644 between visual areas V1 and V4 in the monkey. *NeuroImage* 108:460-475.
- 645 34. Brunet N, et al. (2015) Visual cortical gamma-band activity during free viewing of natural images. *Cereb*
646 *Cortex* 25(4):918-926.
- 647 35. Brunet N, Vinck M, Bosman CA, Singer W, & Fries P (2014) Gamma or no gamma, that is the question.
648 *Trends in cognitive sciences* 18(10):507-509.
- 649 36. Brunet NM, et al. (2014) Stimulus repetition modulates gamma-band synchronization in primate visual
650 cortex. *Proceedings of the National Academy of Sciences of the United States of America* 111(9):3626-
651 3631.
- 652 37. Lewis CM, Bosman CA, Womelsdorf T, & Fries P (2016) Stimulus-induced visual cortical networks are
653 recapitulated by spontaneous local and interareal synchronization. *Proceedings of the National*
654 *Academy of Sciences of the United States of America* 113(5):E606-615.
- 655 38. Pinotsis DA, et al. (2014) Contrast gain control and horizontal interactions in V1: A DCM study.
656 *NeuroImage*.
- 657 39. Richter CG, Thompson WH, Bosman CA, & Fries P (2015) A jackknife approach to quantifying single-trial
658 correlation between covariance-based metrics undefined on a single-trial basis. *NeuroImage* 114:57-70.
- 659 40. Vinck M, et al. (2015) How to detect the Granger-causal flow direction in the presence of additive noise?
660 *NeuroImage* 108:301-318.
- 661 41. Rubehn B, Bosman C, Oostenveld R, Fries P, & Stieglitz T (2009) A MEMS-based flexible multichannel
662 ECoG-electrode array. *Journal of neural engineering* 6(3):036003.
- 663 42. Oostenveld R, Fries P, Maris E, & Schoffelen JM (2011) FieldTrip: Open source software for advanced
664 analysis of MEG, EEG, and invasive electrophysiological data. *Computational intelligence and*
665 *neuroscience* 2011:156869.
- 666 43. Mitra PP & Pesaran B (1999) Analysis of dynamic brain imaging data. *Biophysical journal* 76(2):691-708.
- 667 44. Vinck M, van Wingerden M, Womelsdorf T, Fries P, & Pennartz CM (2010) The pairwise phase
668 consistency: a bias-free measure of rhythmic neuronal synchronization. *NeuroImage* 51(1):112-122.
- 669 45. Scheffer-Teixeira R & Tort AB (2016) On cross-frequency phase-phase coupling between theta and
670 gamma oscillations in the hippocampus. *eLife* 5.
- 671 46. Dhamala M, Rangarajan G, & Ding M (2008) Estimating Granger causality from fourier and wavelet
672 transforms of time series data. *Physical review letters* 100(1):018701.
- 673 47. Efron B & Tibshirani RJ (1994) *An introduction to the bootstrap* (CRC Press).
- 674 48. Nichols TE & Holmes AP (2002) Nonparametric permutation tests for functional neuroimaging: a primer
675 with examples. *Hum Brain Mapp* 15(1):1-25.
- 676 49. Schoffelen JM, Oostenveld R, & Fries P (2005) Neuronal coherence as a mechanism of effective
677 corticospinal interaction. *Science* 308(5718):111-113.
- 678 50. Vinck M, Womelsdorf T, Buffalo EA, Desimone R, & Fries P (2013) Attentional modulation of cell-class-
679 specific gamma-band synchronization in awake monkey area V4. *Neuron* 80(4):1077-1089.

- 680 51. Fries P, Reynolds JH, Rorie AE, & Desimone R (2001) Modulation of oscillatory neuronal synchronization
681 by selective visual attention. *Science* 291(5508):1560-1563.
- 682 52. Manning JR, Jacobs J, Fried I, & Kahana MJ (2009) Broadband shifts in local field potential power spectra
683 are correlated with single-neuron spiking in humans. *The Journal of neuroscience : the official journal of*
684 *the Society for Neuroscience* 29(43):13613-13620.
- 685 53. Bragin A, et al. (1995) Gamma (40-100 Hz) oscillation in the hippocampus of the behaving rat. *The*
686 *Journal of neuroscience : the official journal of the Society for Neuroscience* 15(1 Pt 1):47-60.
- 687 54. Luck SJ, Chelazzi L, Hillyard SA, & Desimone R (1997) Neural mechanisms of spatial selective attention
688 in areas V1, V2, and V4 of macaque visual cortex. *Journal of neurophysiology* 77(1):24-42.
- 689 55. Lubenov EV & Siapas AG (2009) Hippocampal theta oscillations are travelling waves. *Nature*
690 459(7246):534-539.
- 691 56. Patel J, Fujisawa S, Berenyi A, Royer S, & Buzsaki G (2012) Traveling theta waves along the entire
692 septotemporal axis of the hippocampus. *Neuron* 75(3):410-417.
- 693 57. von Stein A & Sarnthein J (2000) Different frequencies for different scales of cortical integration: from
694 local gamma to long range alpha/theta synchronization. *International journal of psychophysiology :*
695 *official journal of the International Organization of Psychophysiology* 38(3):301-313.
- 696 58. Buzsaki G & Draguhn A (2004) Neuronal oscillations in cortical networks. *Science* 304(5679):1926-1929.
- 697 59. Buffalo EA, Fries P, Landman R, Liang H, & Desimone R (2010) A backward progression of attentional
698 effects in the ventral stream. *Proceedings of the National Academy of Sciences of the United States of*
699 *America* 107(1):361-365.
- 700 60. Buffalo EA, Fries P, Landman R, Buschman TJ, & Desimone R (2011) Laminar differences in gamma and
701 alpha coherence in the ventral stream. *Proceedings of the National Academy of Sciences of the United*
702 *States of America* 108(27):11262-11267.
- 703 61. Chalk M, et al. (2010) Attention reduces stimulus-driven gamma frequency oscillations and spike field
704 coherence in V1. *Neuron* 66(1):114-125.
- 705 62. Shin J & Talnov A (2001) A single trial analysis of hippocampal theta frequency during nonsteady wheel
706 running in rats. *Brain research* 897(1-2):217-221.
- 707 63. Geisler C, Robbe D, Zugaro M, Sirota A, & Buzsaki G (2007) Hippocampal place cell assemblies are speed-
708 controlled oscillators. *Proceedings of the National Academy of Sciences of the United States of America*
709 104(19):8149-8154.
- 710 64. Colgin LL (2013) Mechanisms and functions of theta rhythms. *Annual review of neuroscience* 36:295-
711 312.
- 712 65. Worden MS, Foxe JJ, Wang N, & Simpson GV (2000) Anticipatory biasing of visuospatial attention
713 indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex.
714 *The Journal of neuroscience : the official journal of the Society for Neuroscience* 20(6):RC63.
- 715 66. Busch NA & VanRullen R (2010) Spontaneous EEG oscillations reveal periodic sampling of visual
716 attention. *Proceedings of the National Academy of Sciences of the United States of America*
717 107(37):16048-16053.
- 718 67. Landau AN & Fries P (2012) Attention samples stimuli rhythmically. *Current biology : CB* 22(11):1000-
719 1004.
- 720 68. Landau AN, Schreyer HM, van Pelt S, & Fries P (2015) Distributed Attention Is Implemented through
721 Theta-Rhythmic Gamma Modulation. *Current biology : CB* 25(17):2332-2337.
- 722 69. Fiebelkorn IC, Saalmann YB, & Kastner S (2013) Rhythmic sampling within and between objects despite
723 sustained attention at a cued location. *Current biology : CB* 23(24):2553-2558.
- 724 70. Holcombe AO & Chen WY (2013) Splitting attention reduces temporal resolution from 7 Hz for tracking
725 one object to <3 Hz when tracking three. *Journal of vision* 13(1):12.

726

727

728 Legends

729 **Fig. 1.** Average power and phase locking spectra for the two macaques. (A) Average power
730 spectrum of the ECoG LFP in V1 and V4, for monkey K, during attentional monitoring of a
731 drifting grating. Data around the 50 Hz line-noise frequency and harmonics is not shown. (B)
732 Same as A, but for monkey P. (C) Average phase locking (PPC) spectrum across all possible site
733 pairs within and between V1 and V4, for monkey K. The shading (hardly visible behind the
734 lines) shows the 95% confidence interval based on a bootstrap procedure across trials. (D),
735 Same as C, but for monkey P.

736 **Fig. 2.** Average low-frequency LFP power spectra and their modulation by selective attention.
737 (A) Average LFP power spectra in area V1 with attention toward (red) and away (blue) from
738 the activating stimulus. The gray-shaded region indicates frequencies with a significant
739 difference between attention conditions ($p < 0.05$; non-parametric permutation test with
740 correction for multiple comparisons across frequencies). (B) Same as A, but for area V4. (C)
741 Same as A, but showing the power residuals after removing the $1/f^n$ component of the power
742 spectrum through robust regression (see Materials and Methods). (D) Same as C, but for
743 area V4.

744 **Fig. 3.** Average low-frequency LFP phase-locking (PPC) spectra and their modulation by
745 selective attention. (A) Average LFP phase locking between sites within area V1 with attention
746 toward (red) and away from (blue) the activating stimulus. The gray-shaded region indicates
747 frequencies with a significant difference between attention conditions ($p < 0.05$; non-
748 parametric permutation test with correction for multiple comparisons across frequencies). (B)
749 Same as A, but between sites within area V4. (C) Same as A, but between sites in area V1 and
750 sites in area V4.

751 **Fig. 4.** The theta rhythm coextends with the visually induced gamma rhythm. (A) Visually
752 induced LFP gamma-band power, as a function of spatial location in V1 (indicated by blue
753 outline) and V4 (indicated by green outline). (B) Same as A, but showing LFP theta-band power
754 after removing the $1/f^n$ component. (C) Correlation between 1) visually induced gamma-band
755 power and 2) the power ($1/f^n$ removed) at the frequency indicated on the x-axis, across
756 recording sites in area V1. Colored lines on the bottom indicate frequencies with significant
757 correlations with attention toward (red) or away from (blue) the activating stimulus ($p < 0.05$;
758 non-parametric permutation test with correction for multiple comparisons across
759 frequencies). The gray line on the bottom indicates frequencies with a significant difference
760 in correlation between the attention conditions (same test). (D) Same as C, but for area V4.

761 **Fig. 5.** Average low-frequency Granger causality (GC) spectra between V1 and V4 sites. (A)
762 Average GC-influence spectra between V1 and V4 in the feedforward (green) and feedback
763 directions (black). The gray-shaded regions indicate frequencies with a significant difference
764 between bottom-up and top-down ($p < 0.05$; non-parametric permutation test with correction
765 for multiple comparisons across frequencies). (B) Average GC-influence spectra between V1
766 and V4 in the feedforward direction, with attention toward (red) and away from (blue) the

767 activating stimulus. The gray-shaded regions indicate frequencies with a significant difference
768 between attention conditions ($p < 0.05$; non-parametric permutation test with correction for
769 multiple comparisons across frequencies). Frequency regions with significant positive and
770 negative attention effects were directly abutting to each other, and therefore the gray region
771 is continuous. (C) Same as B, but for the feedback direction.

772 **Fig. 6.** Theta-gamma phase-amplitude coupling (PAC) in visual cortex. (A) LFP power of one
773 example site in the 50-150 Hz range (y-axis) as a function of time relative to the theta trough
774 (x-axis). (B) Grand-average PAC as a function of the frequency defining the power (y-axis) and
775 the frequency defining the phase (x-axis). The semitransparent gray mask indicates frequency
776 pairs with non-significant PAC ($p < 0.05$; non-parametric permutation test with correction for
777 multiple comparisons across frequency pairs). The black area indicates frequency pairs
778 excluded from the analysis (see Materials and Methods).

779 **Fig. 7.** Modulation of PAC by selective attention. Average PAC in area V1 with attention
780 toward (A) and away from (B) the activating stimulus. (C) Average PAC difference in area V1
781 between the two attention conditions shown in A and B. The semitransparent gray mask
782 indicates frequency pairs with non-significant PAC ($p < 0.05$; non-parametric permutation test
783 with correction for multiple comparisons across frequency pairs). The black area indicates
784 frequency pairs excluded from the analysis (see Materials and Methods). (D), (E), (F), Same as
785 A, B, C, but for area V4.

786 **Fig. 8.** Visual theta remains after microsaccade removal. (A) MS-LFP PPC as a function of
787 frequency, showing a clear theta peak. The shading shows the 95% confidence interval based
788 on a bootstrap procedure across MSs. (B) V1-V1 PPC in the attend-away condition as a
789 sensitive metric of V1 theta rhythmicity, calculated for different sets of epochs, which remove
790 MSs with increasing stringency. Dark blue line: All available epochs ($N=1917$); Medium blue
791 line: Epochs excluding MSs, that exceeded the mean eye speed by 5 SD ($N=827$); Light blue
792 line: Epochs excluding MSs, that exceeded the mean eye speed by 3 SD ($N=446$).

793 **Fig. 9.** Attention contrast, excluding epochs with microsaccades. (A) Average LFP power
794 spectra in area V1 after removing the $1/f^n$ component, with attention toward (red) and away
795 (blue) from the activating stimulus. (B) Same as A, but for area V4. (C) Average LFP phase
796 locking between sites in area V1 and sites in area V4, with attention toward (red) and away
797 from (blue) the activating stimulus. (D), (E) Same as C, but for pairs of sites within area V1 (D)
798 and area V4 (E). (A-E) The gray-shaded region indicates frequencies with a significant
799 difference between attention conditions ($p < 0.05$; non-parametric permutation test with
800 correction for multiple comparisons across frequencies). (F), (G) Average PAC in area V1 with
801 attention toward (F) and away from (G) the activating stimulus. (H) Average PAC difference in
802 area V1 between the two attention conditions. (F-H) The semitransparent gray mask indicates
803 frequency pairs with non-significant PAC ($p < 0.05$; non-parametric permutation test with
804 correction for multiple comparisons across frequency pairs). The black area indicates
805 frequency pairs excluded from the analysis (see Materials and Methods).

806 **Fig. 10.** Attention contrast, controlled for microsaccade (MS) rate. Same analyses as shown in
807 Figure 8, but after equating the MS rate. (A) Cumulative distribution of MS rate with attention
808 toward (red) and away (blue) from the activating stimulus. Solid lines show data before
809 stratification; dashed lines show data after stratification. Note that after stratification, the
810 lines for the two attention conditions overlap essentially perfectly. (B) Average LFP power
811 spectra in area V1 after removing the $1/f^n$ component, with attention toward (red) and away
812 (blue) from the activating stimulus. (C) Same as B, but for area V4. (D) Average LFP phase
813 locking between sites in area V1 and sites in area V4, with attention toward (red) and away
814 from (blue) the activating stimulus. (E), (F) Same as D, but for pairs of sites within area V1 (E)
815 and area V4 (F). (B-F) The gray-shaded region indicates frequencies with a significant
816 difference between attention conditions ($p < 0.05$; non-parametric permutation test with
817 correction for multiple comparisons across frequencies). (G) Average PAC difference in
818 area V1 between the two attention conditions. The semitransparent gray mask indicates
819 frequency pairs with non-significant PAC ($p < 0.05$; non-parametric permutation test with
820 correction for multiple comparisons across frequency pairs). The black area indicates
821 frequency pairs excluded from the analysis (see Materials and Methods).

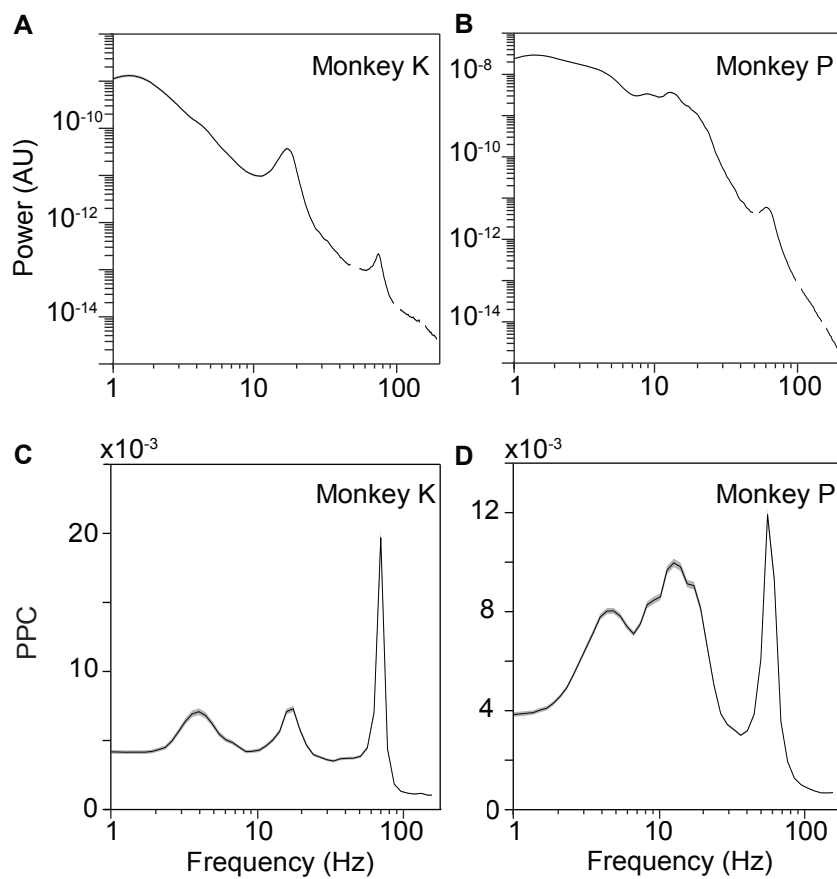


Figure 1
Spyropoulos et al.

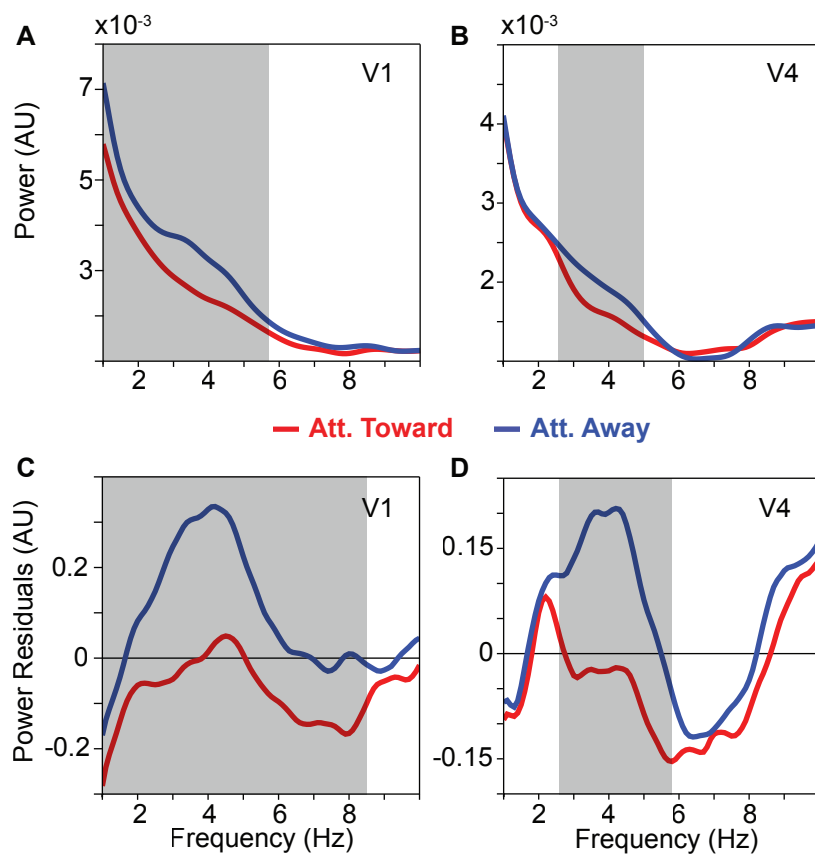


Figure 2
Spyropoulos et al.

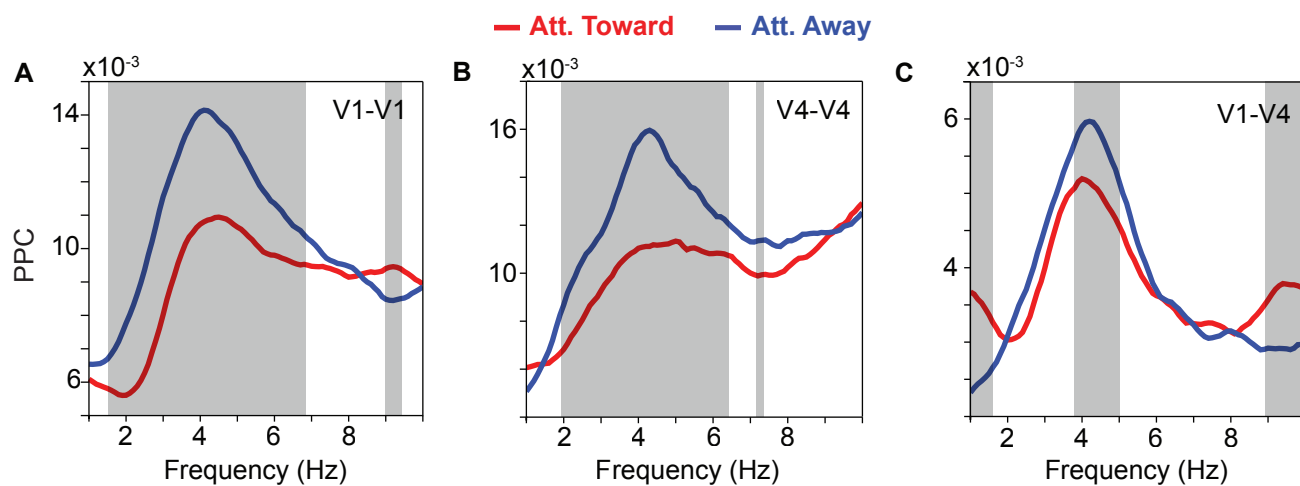


Figure 3
Spyropoulos et al.

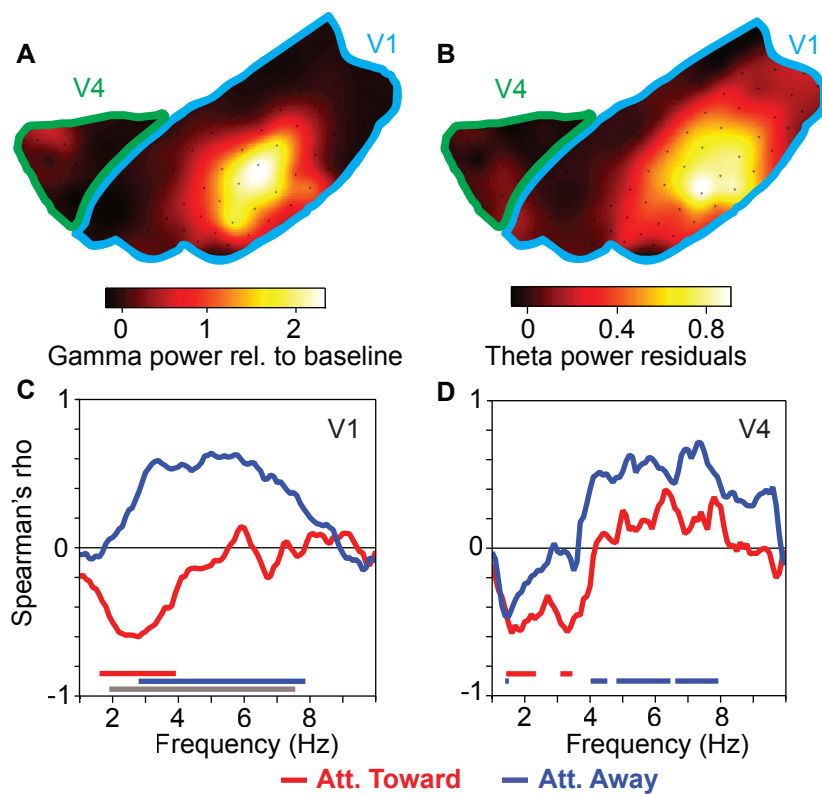


Figure 4
Spyropoulos et al.

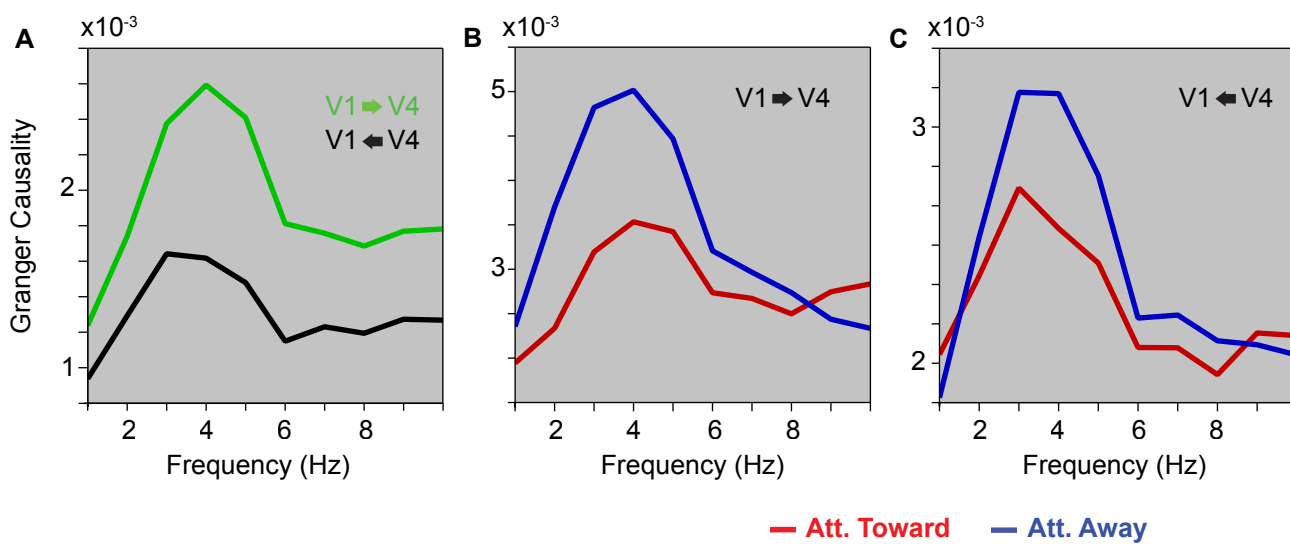


Figure 5
Spyropoulos et al.

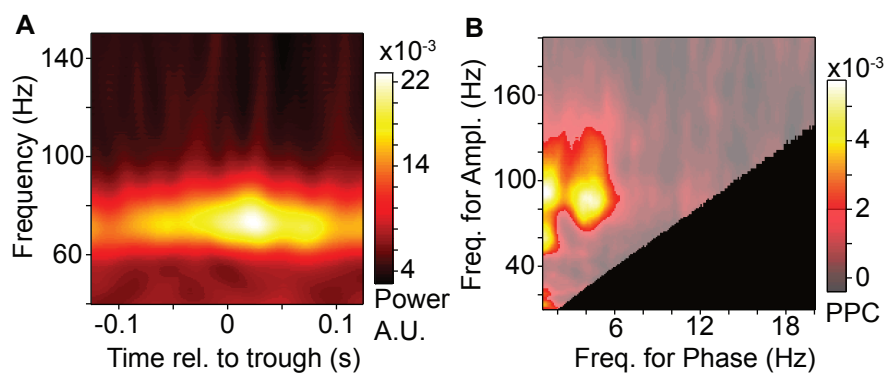


Figure 6
Spyropoulos et al.

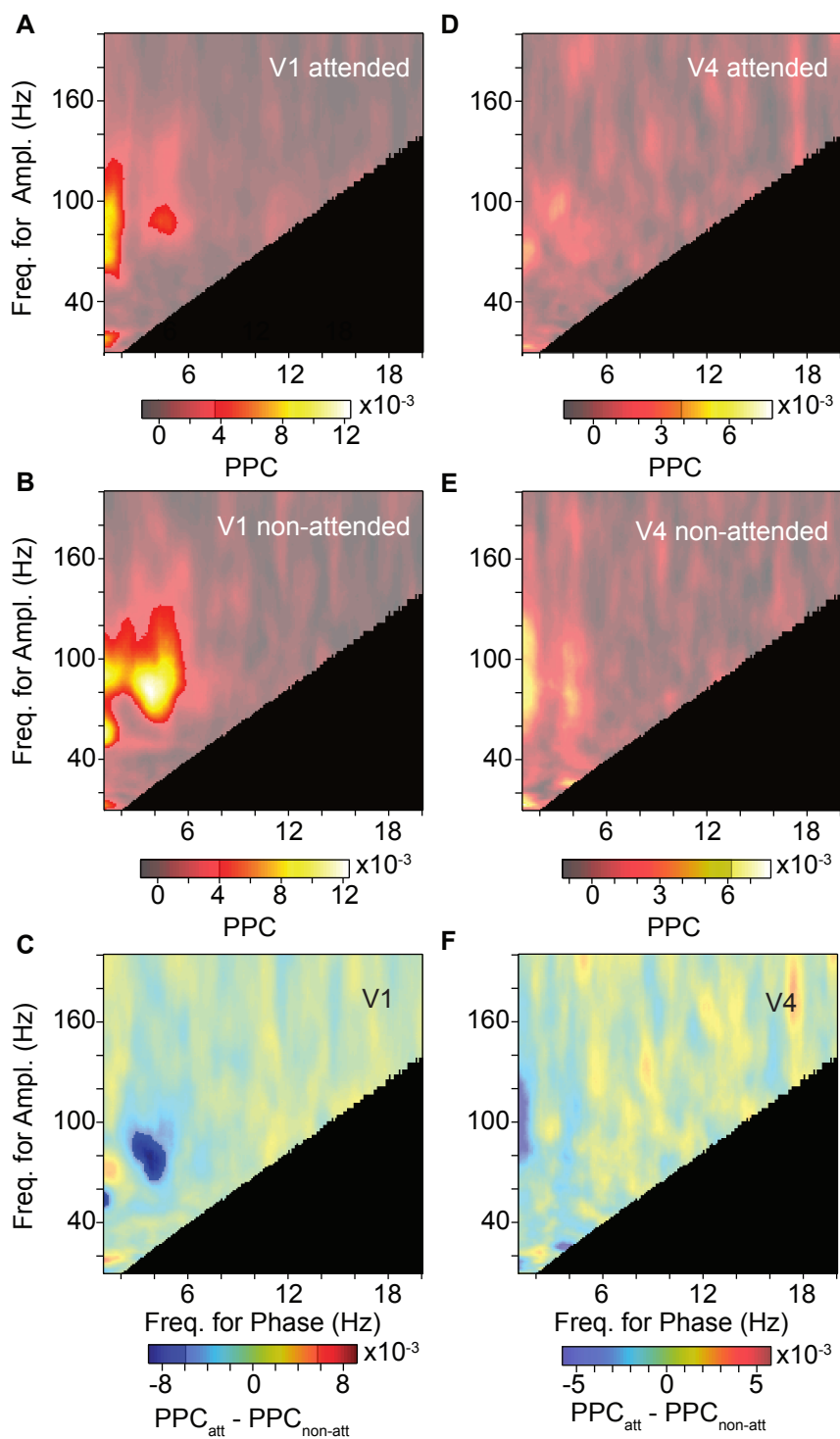


Figure 7
Spyropoulos et al.

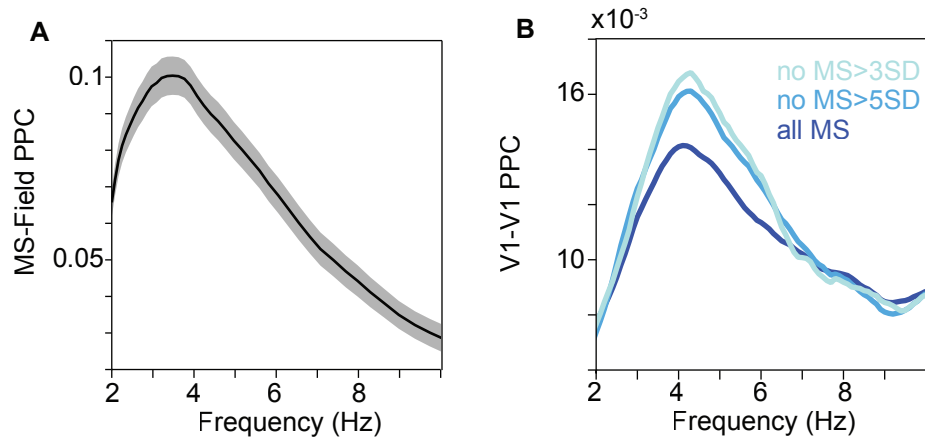


Figure 8
Spyropoulos et al.

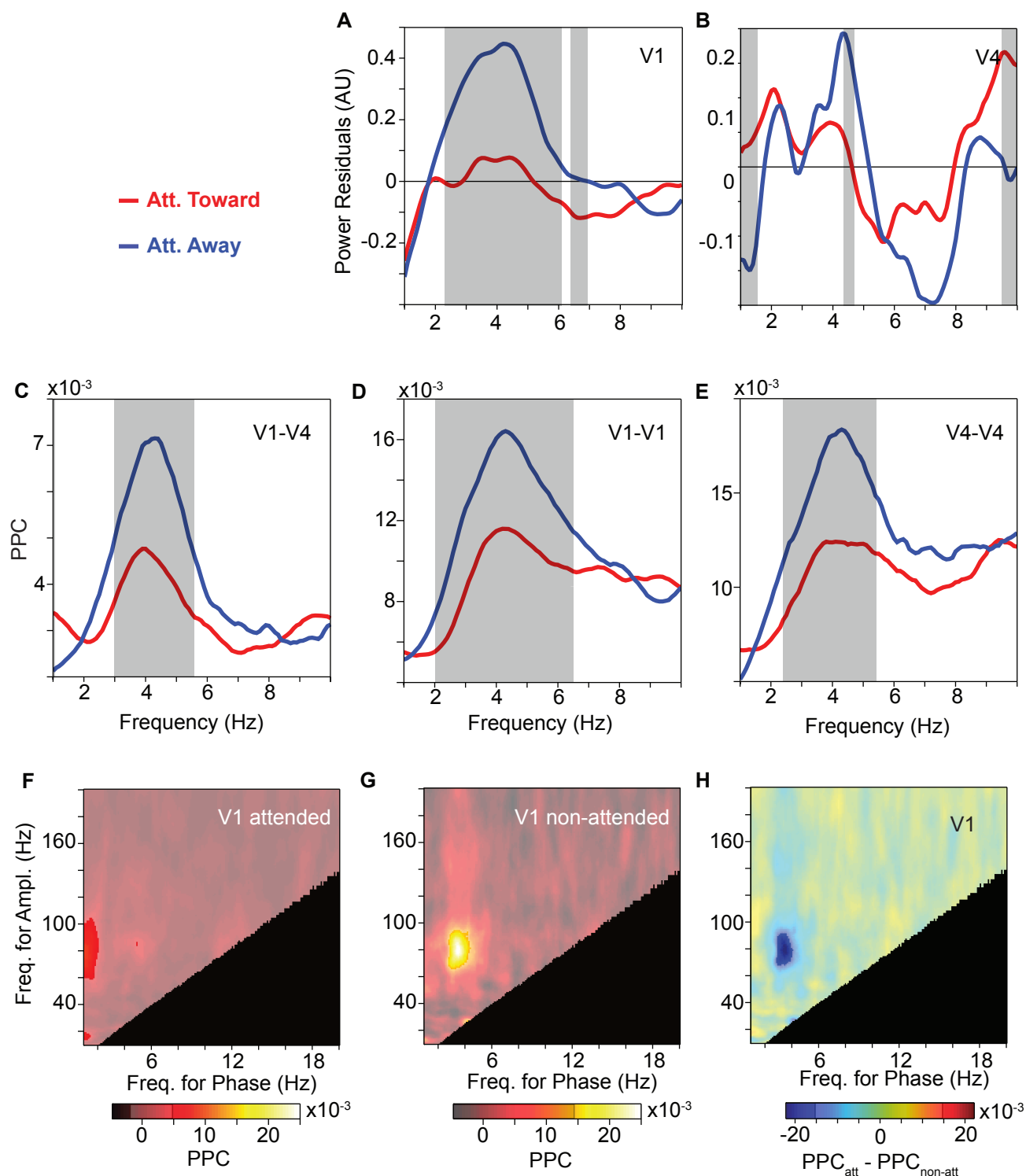


Figure 9
Spyropoulos et al.

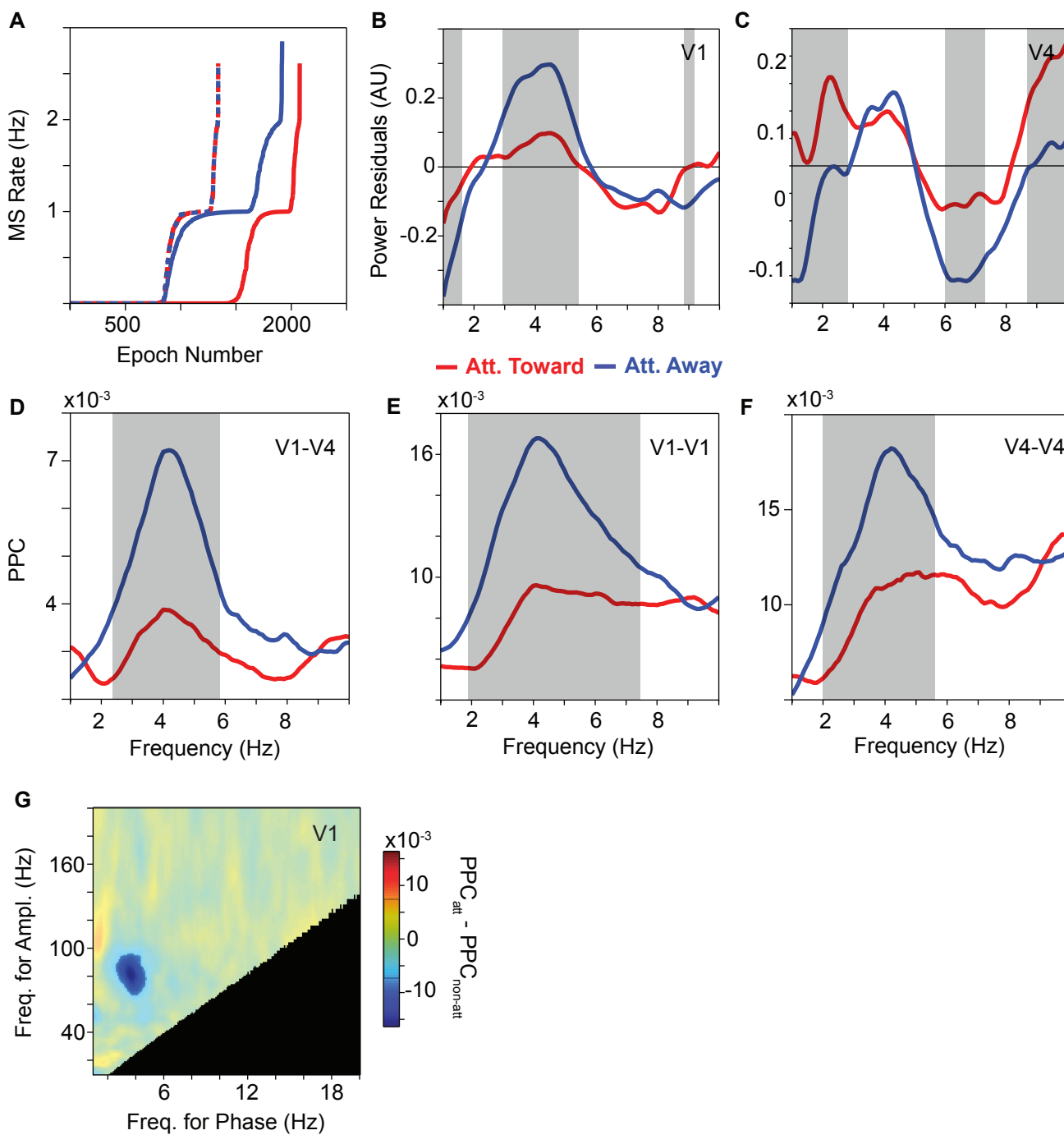


Figure 10
Spyropoulos et al.