Review TRENDS in Neurosciences Vol.30 No.7

INMED/TINS special issue

The gamma cycle

Pascal Fries[1,2], Danko Nikolić[3,4] and Wolf Singer[3,4]

[1] F.C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, 6525 EN Nijmegen, the Netherlands
[2] Department of Biophysics, Radboud University Nijmegen, 6525 EZ Nijmegen, the Netherlands
[3] Department of Neurophysiology, Max Planck Institute for Brain Research, Frankfurt am Main, 60528, Germany
[4] Frankfurt Institute for Advanced Studies, Johann Wolfgang Goethe University, Frankfurt am Main, 60438, Germany

Activated neuronal groups typically engage in rhythmic synchronization in the gamma-frequency range (30–100 Hz). Experimental and modeling studies demonstrate that each gamma cycle is framed by synchronized spiking of inhibitory interneurons. Here, we review evidence suggesting that the resulting rhythmic network inhibition interacts with excitatory input to pyramidal cells such that the more excited cells fire earlier in the gamma cycle. Thus, the amplitude of excitatory drive is recoded into phase values of discharges relative to the gamma cycle. This recoding enables transmission and read out of amplitude information within a single gamma cycle without requiring rate integration. Furthermore, variation of phase relations can be exploited to facilitate or inhibit exchange of information between oscillating cell assemblies. The gamma cycle could thus serve as a fundamental computational mechanism for the implementation of a temporal coding scheme that enables fast processing and flexible routing of activity, supporting fast selection and binding of distributed responses. This review is part of the *INMED/TINS* special issue *Physiogenic and pathogenic oscillations: the beauty and the beast*, based on presentations at the annual *INMED/TINS* symposium (http://inmednet.com).

Introduction

Activated neuronal groups engage in rhythmic synchronization in the gamma-frequency band (30–100 Hz) [1–26]. This has by now been documented in many brain regions, including the visual [1–5,9,11,14,15,23–25], auditory [18,22], somatosensory [28], motor [6,12,21] and parietal cortex [17] and the hippocampus [7,19]. It has also been found in a variety of species, from insects [27] to mammals [1–6,9,14,15,17,18,25], including humans [11,12,20–24,26]; and during conditions ranging from simple sensory stimulation [2] to attentional selection [15,25,29,30], working memory maintenance [17] and beyond [26]. Thus, neuronal gamma-band synchronization appears to be a fundamental mode of neuronal activity.

The past two decades have seen enormous gains in insight into the mechanisms underlying gamma-band synchronization as well as its functional roles. Here, we link these results to better understand how neuronal gamma-band synchronization subserves the various cognitive functions. At the core of our considerations is the gamma cycle, that is, the sequence of neuronal processes that reoccur within each oscillation cycle. We suggest that, within the gamma cycle, the excitatory input to a pyramidal cell is converted into a temporal code whereby the amplitude of excitation is recoded in the time of occurrence of output spikes relative to the gamma cycle, stronger inputs leading to earlier responses. Thus, amplitude values are converted into phase values that indicate by how much a discharge precedes the peak of a gamma cycle. Furthermore, we argue that pyramidal cells receiving strong excitation and hence discharge early in the gamma cycle silence those that receive less excitation and thereby profit from a winner-take-all algorithm (strictly speaking, a few-winners-take-all algorithm, because it will always be a group of neurons). Such a coding strategy enables fast processing and readout because it is based on coincidence detection, rather than on rate integration.

Several previous studies contained aspects of the concept presented here [31–37] and the current work attempts a broadly accessible synthesis. We would like to note that the hypothesis put forward here is clearly distinct from the binding-by-synchronization hypothesis [38,39], which states that neurons forming a functional assembly are bound together by synchronization of their action potentials, a mechanism that is probably based, in part, on experience-dependent refinement of intra- and inter-areal connections. By contrast, the hypothesis explored here relies on basic biophysiological dynamics that unfolds primarily within a local neuronal group. Although the two hypotheses are distinct, they are fully compatible with each other. Rhythmic synchronization is a fundamental emergent property of neuronal interactions and no single theory will capture all of its functional consequences at once.

Mechanisms behind gamma-band synchronization

To assess the functional consequences of gamma-band synchronization, we briefly consider the mechanisms that underlie neuronal gamma-band synchronization. It is well established that inhibitory interneuron networks have a prominent role in the generation of gamma-band synchronization [8,40–45]. Experiments with pharmacologically isolated networks of inhibitory interneurons and model simulations have shown that these networks can generate synchronized gamma-band oscillations on their own [8,44,45], requiring only synaptic inhibition and gap junctional coupling to be intact [46–48]. The activation of these

Corresponding author: Fries, P. (pascal.fries@fcdonders.ru.nl).
Available online 6 June 2007.

 0166-2236/$ – see front matter doi:10.1016/j.tins.2007.05.005

interneuron networks is due to excitatory drive and, under physiological conditions, this is supplied through excitatory input from pyramidal cells. Interneuron networks generate rhythmic synchronization regardless of whether their excitatory drive is rhythmic; however, under physiological conditions, the rhythmic synchronization of the interneurons imposes synchronized rhythmic inhibition onto the pyramidal cells and, therefore, their discharges also engage in rhythmic synchronization.

During gamma-band synchronization, the discharges of interneurons and pyramidal cells exhibit a characteristic phase relation: the interneurons tend to fire a few milliseconds after the pyramidal cells. This has been first described for the CA1 and CA3 fields of the rodent hippocampus [19] and recently also for the ferret prefrontal cortex [43] (Figure 1). Simulations of networks with appropriately coupled pyramidal cells and interneurons replicated rhythmic synchronization with similar phase relationships

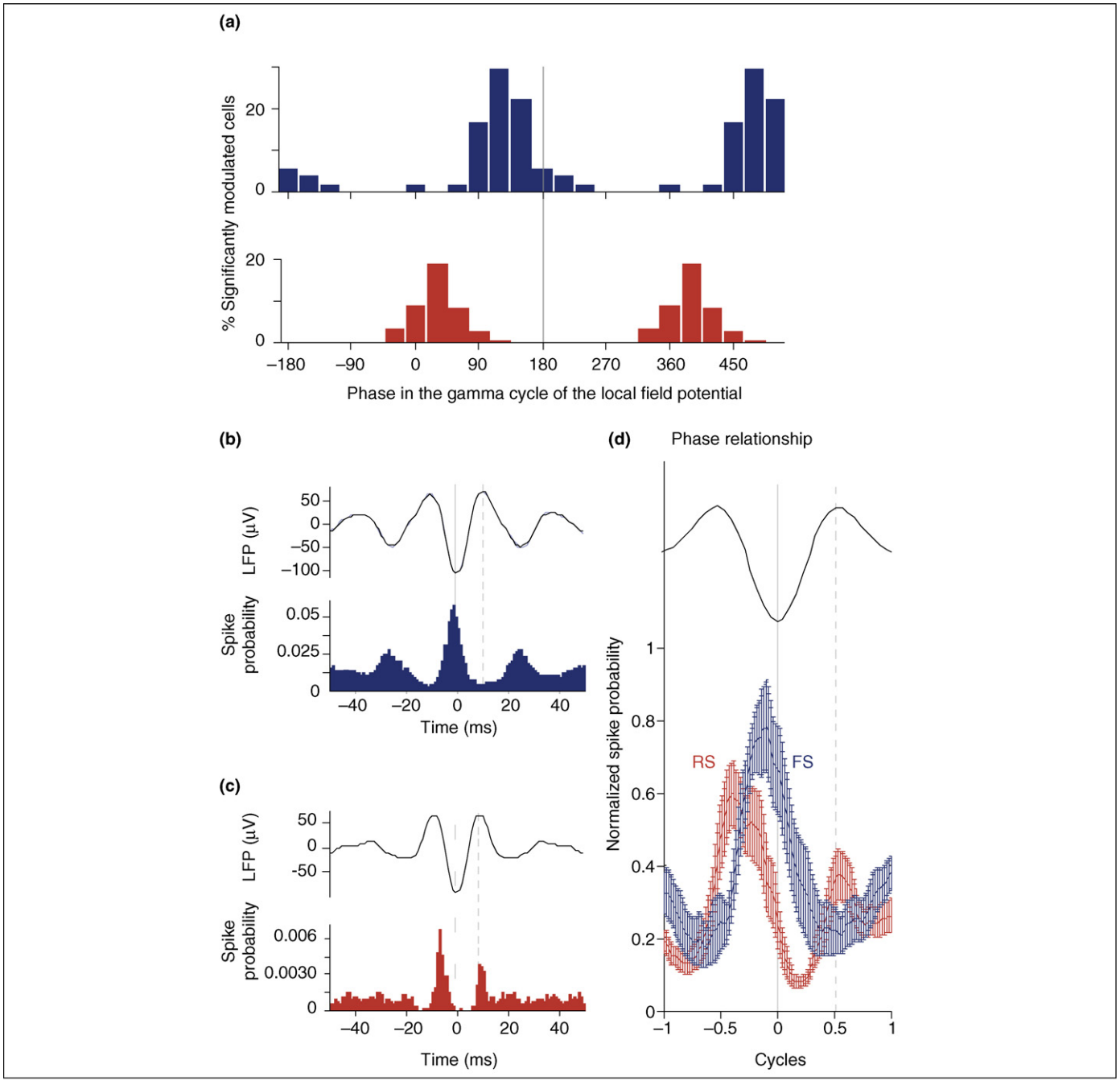

Figure 1. Pyramidal cell–interneuron firing in the gamma cycle. **(a)** Recordings from the hippocampus of behaving rats. The vertical line indicates the moment of peaks in the gamma band-filtered LFP recorded from the CA1 pyramidal layer. This gamma peak time served as a temporal alignment event. Simultaneously recorded spikes were sorted into interneuron spikes (blue histogram) and pyramidal cell spikes (red histogram) and were tested for locking to the gamma rhythm. For the significantly phase-locked cells, the distribution of mean phases is shown across interneurons and pyramidal cells. **(b–d)** Similar analysis in the prefrontal cortex of the anesthetized ferret. Here, the different cell types are characterized as either regular spiking (RS) or fast spiking (FS) with the RS neurons being putative pyramidal cells and the FS neurons being putative interneurons. (b) A putative interneuron whose spike probability was modulated by the phase of the simultaneously recorded gamma band LFP. (c) Same as (b), but for a putative pyramidal cell. (d) Average normalized spike probability for the two cell classes. For averaging, the widths were normalized to the period of the extracellular gamma oscillation and the peak probabilities to 1. Reproduced, with permission, from Ref. [19] (a) and Ref. [43] (c).

between the cell types and demonstrated the importance of this particular firing sequence [49].

Any simplifying description of these network dynamics will fall short of their real complexity, but simplifications are justified if they help to better understand the dynamics and their consequences. One way to describe the process is as follows: after excitatory input, the network of inhibitory interneurons generates rhythmic synchronized activity and imposes rhythmic inhibition onto the entire local network. Pyramidal cells will be able to respond to excitatory input only during the time window of fading inhibition. Because pyramidal cells provide the major excitatory drive to the interneurons, the interneurons will discharge with some phase delay relative to the pyramidal cells and the resulting network inhibition terminates the firing of both the pyramidal cells and the interneurons. The whole network is inhibited and the next gamma cycle starts anew.

Conversion of excitatory drive into relative spike timing

One aspect of this gamma cycle is particularly important for our further considerations: if one assumes that all pyramidal cells of a local, oscillating group of cells receive a similar amount of phasic inhibition, then those pyramidal cells receiving the strongest excitatory drive will fire first during the phase of the cycle when pyramidal cells can fire [31–33]. Consequently, the strength of pyramidal cell excitation is translated into a phase value that corresponds to the time of occurrence of the spikes relative to the cycle period.

In the hippocampus, this mechanism has been proposed to explain the phenomenon of theta-phase precession [50]: In the hippocampus, most pyramidal cells have so-called 'place fields'; that is, they fire preferentially when the animal moves through a certain region of its environment [51]. The discharges of place field neurons exhibit a prominent rhythmic synchronization in the theta-frequency band (~8 Hz in this structure) (see Ref. [52] and the corresponding special issue of *Hippocampus*). Similar to the above-described gamma-band synchronization, this theta-band synchronization entails rhythmic network inhibition at the theta frequency [53,54].

Theta-phase precession is a striking and well documented phenomenon that is likely to result from the interaction between excitatory drive onto pyramidal cells and rhythmically increasing and fading inhibition: when the animal moves through the place field of a particular cell, the cell discharges rhythmically and phase-locked to the theta-rhythm, whereby the discharges occur earlier and earlier in the theta phases as the animal moves into the place field. Several models of theta-phase precession explain this phenomenon as a consequence of the interaction between theta-modulated inhibition and place-field driven excitation [53,54]. When the animal moves towards the place field of a neuron, excitatory drive to this cell increases over the course of several theta cycles. At the same time, inhibition rhythmically increases and decreases within each theta cycle. At the periphery of the place field, the excitatory drive is weak and can elicit spikes only during the phase of the theta cycle when inhibition is minimal; that is, at the depolarizing peak of the theta-cycle. However when excitation increases, it can overcome inhibition earlier and elicit spikes earlier in the theta-cycle [53,54] (Figure 2). Interestingly, this phase-precession is unidirectional and does not reverse when the firing rate decreases toward the end of the place field and several mechanisms, such as spike frequency adaptation [53] and synaptic plasticity [54], have been proposed to account for this asymmetry.

This phase precession has been attributed great functional importance because the serial order of pyramidal cell firing in one single theta cycle contains all information

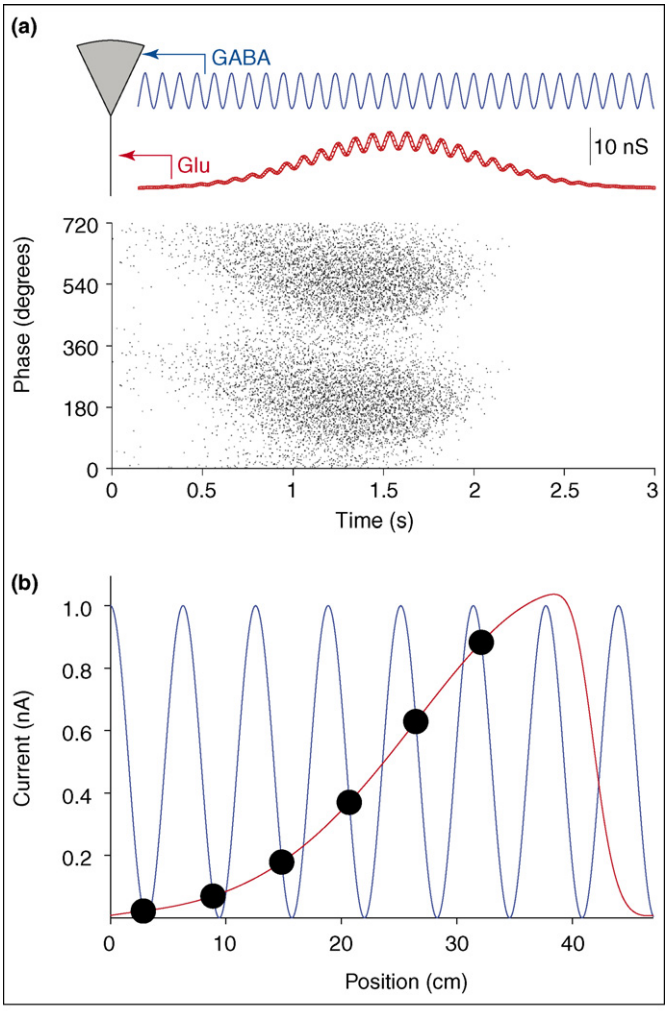

Figure 2. Hippocampal theta-phase precession modelled as an interaction between slowly changing excitation and theta-rhythmic inhibition. **(a)** and **(b)** illustrate two different models that explain hippocampal theta-phase precession. They agree in the assumption that the theta-phase of pyramidal cell spiking is modulated through an interaction between changing levels of excitation and theta-rhythmic inhibition. They differ in explaining why phase precession does not reverse when a rat leaves the place field of a pyramidal cell, which is not discussed further here. (a) The theta-rhythm entails rhythmic GABAergic perisomatic inhibition (blue input). The running of a rat through a place field of a pyramidal cell leads to slowly changing excitation (red input) that is slightly modulated by the ambient theta-rhythm. The scatter plot shows the theta-phases of spikes that occurred in a modelled neuron with those inputs. As (in the simulation) the rat takes three seconds to traverse the place field of the cell, spikes proceed from late to early theta-phases. In the second half of the place field, phase precession does not reverse, because, in this model, spike frequency adaptation silences the neuron. (b) Another model of hippocampal theta-phase precession. As in (a), excitation (red curve) interacts with inhibition (blue curve) to generate theta-phase precession. However, this model assumes that theta-phase precession does not reverse, because synaptic plasticity results in an asymmetric profile of excitation. Reproduced, with permission, from Ref. [53] (a) and Ref. [54] (b).

about the position and movement trajectory of the animal and, in addition, provides a code that links past with future positions [54]. We go on to review data that suggest that a similar conversion of amplitude to temporal codes is achieved by gamma-band synchronization.

Spike-phase encoding during cortical gamma-band synchronization

As reviewed above, neuronal gamma-band synchronization is associated with rhythmic inhibition of pyramidal cells. Therefore, pyramidal cells driven weakly will likely fire only late in the gamma cycle, whereas those driven strongly will fire earlier [31–33]. Although we are not aware of a published direct test of this prediction, which would involve a direct assessment of the gamma cycle itself, there is indirect supporting evidence: if the phase in the gamma cycle at which a neuron fires depends on its excitatory drive, then the relative phase at which two neurons fire should depend on the relation between their respective excitatory drives; the latter has been demonstrated in visual cortex of anesthetized cats [35–37,55] (Figure 3a).

In these experiments [55], multiple electrodes were inserted into primary visual cortex. Each of these electrodes recorded the spiking activity of a small group of neurons around the electrode tip, the respective multi-unit activity (MUA). Such MUAs are likely to be dominated by pyramidal cells, because these cells outnumber interneurons approximately five times, are bigger and are equipped with asymmetric dendritic trees, leading to larger extracellular potentials that are more likely to be picked up by the electrode. The electrodes were sufficiently closely spaced that the receptive fields of the different MUAs overlapped and could be driven by a single stimulus. However, each MUA was driven to a different degree by different stimuli, depending on, for example, basic features such as orientation or spatial frequency. Accordingly, when different (single) stimuli were presented and pairs of MUA were analyzed, the two MUAs were driven to different activation strengths, probably because they received different excitatory drives.

In addition, as is found typically when neuronal groups in visual cortex are activated, different MUAs engaged in rhythmic synchronization, probably because they received correlated rhythmic inhibition [43]. The crucial experimental finding was that the relative phase at which two MUAs gamma synchronized depended on the relative strength with which they were activated: When a stimulus was presented that activated one neuronal group strongly and another weakly, then the more strongly activated group fired slightly earlier in the gamma cycle than did the more weakly activated group (Figure 3a). This is as predicted by the above considerations. Thus, gamma-band synchronization has the effect that the stronger a pyramidal cell is driven, the earlier it spikes in the gamma cycle, similar to hippocampal theta-phase precession.

The gamma cycle as a rapidly repeating winner-take-all algorithm

To date, and to the best of our knowledge, the functional significance of gamma-phase specific spike timing is not yet clear. It might be an irrelevant epiphenomenon given that the involved time differences are of the order of only a few milliseconds. However, in view of the increasing evidence that the precise timing of individual spikes matters, as, for example, in spike timing-dependent plasticity, gamma phase-dependent spike timing could be functionally relevant.

As mentioned above, pyramidal cells can only respond within a narrow temporal window when the network engages in gamma oscillations. Furthermore, pyramidal cell firing is a self-terminating process because pyramidal cells strongly excite interneurons and these feed back onto the pyramidal cells, curtailing their firing. Thus, if a pyramidal cell does not fire sufficiently early in the gamma cycle, it will not be able to fire at all in that cycle. In other words, in each gamma cycle, there is a race among the pyramidal cells during which the most excited pyramidal cells will compete against the less excited ones [32,33]. This timing-dependent suppression of weak responses could contribute to the improvement of signal-to-noise ratios.

Spike latency-based computation

Transforming an amplitude (rate) code into a temporal code could have a crucial role in object recognition: spike latency coding or spike rank order coding has been the core component in a class of computational models that perform object recognition with remarkable speed and computational efficiency [34,56–59]. The respective line of research began with an experiment in which human subjects were presented with images for just 20 ms and then had to report as quickly as possible whether the image contained an animal [60]. When event-related potentials were measured from the scalp of those human subjects, they differentiated between the presence and absence of an animal in the image as early as 150 ms after image presentation. Additional experiments made it highly unlikely that image classification could be based on elementary image properties such as color, but rather suggested that it depended on the detection of complex feature constellations [61]. Therefore, it probably required processing of the image by inferotemporal cortical areas where neurons show corresponding selectivities.

Given that it takes ~50 ms for the image to activate the primary visual cortex, and given that there are multiple synapses between primary visual and inferotemporal cortex, it is unlikely that the luminance distribution of the retinal image was assessed solely by evaluating the average firing rates because this would require integration over too-long time intervals. The complementary model hypothesized that brightness values are encoded by the latency of the first spikes in the responses, higher luminance causing shorter latencies and that further computations would be based on the relative spike latencies [56–59,62]. This algorithm is applied repeatedly in a hierarchy of layers and results in rapid image categorization. Surprisingly, these models demonstrate that most information in the output of a given layer is contained in the relative timing of the first 1–5% of the spikes fired after image onset, whereas the remaining 95% contribute only marginally (Figure 4).

Gamma-phase based computation

Importantly, in these models, spike timing is assessed relative to image onset and processing proceeds in a purely

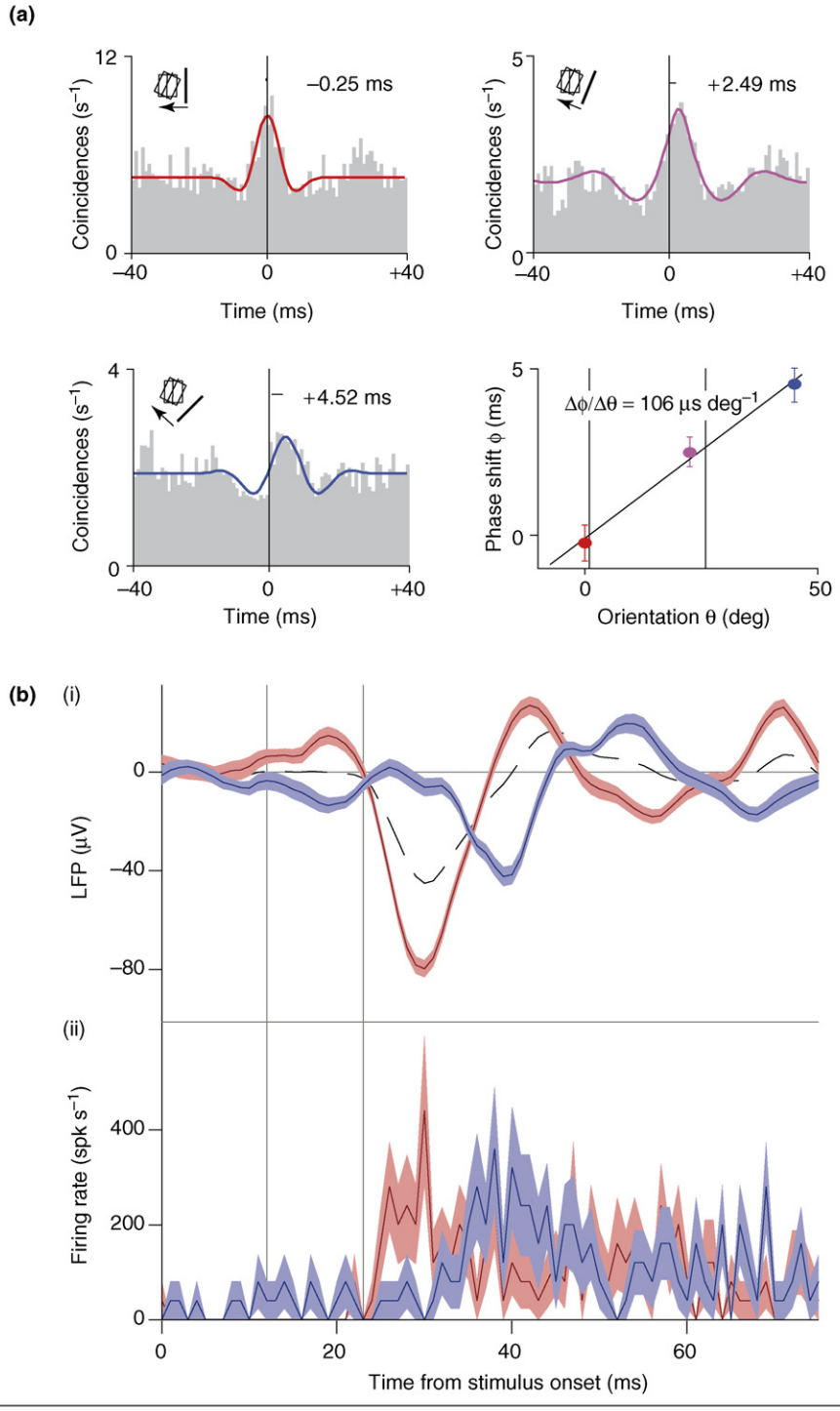

Figure 3. Evidence for an interaction between excitation and rhythmic inhibition in the visual cortex. **(a)** Gamma-band synchronization among visual cortical spike train recordings entails phase leads and lags that depend on relative excitation levels. A pair of multi-unit activity (MUA1 and MUA2) was recorded under three different visual stimulation conditions. For each condition, the cross-correlation histogram (CCH) between the two MUAs was calculated and fitted with a Gabor function (red, pink and blue lines for the three stimulation conditions). A CCH peak with negative (positive) time offset indicates that MUA1 was leading (lagging) MUA2. In condition 1 (red Gabor fit), MUA1 received more optimal visual stimulation than did MUA2. In condition 2 (pink fit), MUA2 received more optimal stimulation than did MUA1. In condition 3 (blue fit), the relative activation advantage of MUA2 was further increased. The results demonstrate that relative activation (and thereby excitation) strengths are translated into relative spiking phases within the gamma cycle. **(b)** Ongoing gamma-band oscillations co-determine the timing of first spiking in primary visual cortex after stimulus onset. LFPs and MUA were recorded from corresponding positions in primary visual cortex of the two hemispheres of an anesthetized cat. The average stimulus-related LFP is shown as a dashed line, defining response onset at 23 ms. Two subsets of trials were then chosen in which the LFP just before response onset was falling (rising), corresponding to spontaneous neuronal depolarization (hyperpolarization). The corresponding average LFPs are shown as red and blue curves in (i). (ii) shows the MUA responses averaged separately for these two groups of trials. When the LFPs indicated spontaneous depolarization (hyperpolarization), the MUA response was particularly early (late). Reproduced, with permission, from Ref. [55] (a) and Ref. [64] (b).

Figure 4. Efficiency of spike time coding. In spike timing-based computation, the first 1–5% of the spikes carry most of the information. The five images are reconstructions of the image presented to a model retina. The reconstruction is based on the latency of firing of the retinal ganglion cells, with higher retinal image contrast leading to shorter latencies. The percentage of ganglion cells that have generated a single spike is indicated for each reconstruction. It appears that 1% or less is already sufficient to obtain a clear idea of the contents of the input image. Reproduced, with permission, from Ref. [59].

feed-forward cascade (but *cf.* Ref. [59] for corresponding modifications). However, real-world sensory input is a temporal continuum and the human nervous system usually has no independent information about the absolute timing of its sensory input. Under these conditions, the latency or rank ordering of spikes can only be evaluated if there is an additional mechanism that provides temporal frames. We propose that the gamma cycle serves as such a reference frame. It repeats rapidly and it assures that pyramidal cells spike the earlier in the gamma cycle, the stronger they are driven. Thus, a neuronal computation scheme based on spike timing relative to the gamma cycle is physiologically plausible and might be efficient. As in the above mentioned models, it might operate exclusively on the basis of spike timing and avoid firing rate codes throughout. Furthermore, such a scheme might be metabolically cheap and therefore ecologically advantageous: early information-rich spikes are transmitted with high signal-to-noise ratio, whereas late information-poor spikes are avoided owing to rising inhibition. Because interneuron–pyramidal cell inhibition is powerful, a few interneuron spikes might prevent many unnecessary pyramidal cell spikes. Nevertheless, if fast processing within a single gamma cycle fails to yield unambiguous results, further processing, based on multiple gamma cycles, re-entrant loops and continuing sensory input, is likely to occur.

It is important to note that in this concept, gamma-rhythmic inhibition provides only the temporal reference frame [31,42]. The timing of each pyramidal cell's spike(s) in the gamma cycle depends on the level of excitation of the cell. The level of excitation, in turn, depends on the interplay between stimulus properties and the functional architecture in which the pyramidal cells are embedded. This architecture redefines at each processing level, which aspects of the output from previous levels are deemed 'exciting' for a given neuron.

If a given neuronal processing stage does encode information in the precise spike timing during its gamma cycle, then the next processing stage can decode this information best when it receives a copy of the temporal frame; that is, the gamma cycle. Long-range gamma-band synchronization has been described [5,21,63] and probably synchronizes rhythmic inhibition across separate local networks, thereby enabling distributed spike-phase based computations to operate on the same reference frame.

Gamma-phase dependent spike timing in primary visual cortex

However, at the earliest levels of sensory processing, such a scheme cannot be operational, because visual input can arrive at any phase within an ongoing gamma-band oscillation. It is a strong prediction of the outlined concept that the neuronal response onset latencies in this case should be determined not only by stimulus onset, but also by the phase of ongoing rhythmic activity. This has been confirmed with recordings in primary visual cortex of anesthetized cats [64] (Figure 3b).

Multi-unit and local field potential activities were recorded from multiple electrodes while neurons were activated with light bars presented repeatedly with long intertrial intervals. The crucial finding was that, across trials, neuronal responses had variable onset latencies with respect to stimulus presentation and part of this variability could be explained by the phase of the ongoing gamma-band activity at which visual stimulation was delivered (Figure 3b). When visual stimulation provided thalamic input to cortex during moments when inhibition faded, latencies were short. By contrast, when input occurred during moments of strong inhibition, latencies were prolonged, such that the timing of the first spikes were shifted relative to stimulation, but remained roughly constant relative to the gamma-cycle reference frame. Also in this case, the relative timing of spikes contained important information. The data showed that columns coding for related features (same or co-linear orientation of contours) that tend to be grouped perceptually, oscillate with zero phase lag [64]. This has the effect that the latencies of the first spikes of cells responding to groupable features co-vary and are similar. Hence, these discharges are synchronized from the beginning. Following the indications that synchronous firing serves to establish relations among distributed responses (reviewed in Ref. [39]), it has been proposed that this rapid synchronization of first spikes supports rapid feature binding and perceptual grouping.

Such a coding strategy might not apply for all processing streams. It has been demonstrated that spikes can be tightly locked to stimulus transients, as for example in visual area MT [65], an area of the dorsal visual stream, whereas the above mentioned response latency fluctuations were observed in recordings from cat area 17 and monkey area V4, two areas that belong to the ventral stream.

Putative mechanisms of gamma-phase decoding

One important remaining issue is whether spike timing within the gamma cycle affects neuronal interactions, because only then could it have a functional role [66]. As mentioned above, gamma oscillations are a ubiquitous phenomenon and if distributed but connected groups of neurons engage in gamma oscillations, precise spike timing

matters: excitatory inputs that coincide with the period of fastest fall-off of the inhibition in the target group will be particularly effective because reduction of inhibition is by itself a potent trigger [43] and incoming excitation that coincides with falling inhibition will result in particularly steep membrane potential slopes. It has been shown that the membrane potential threshold for eliciting spikes is inversely correlated to the membrane potential slope [67,68]. By contrast, excitatory inputs arriving at the beginning of the inhibitory period will have particularly little effect because they will be exposed to the shunting and the hyperpolarizing effect of IPSPs.

Thus, the impact that an EPSP has on an oscillating target cell will depend on the time of arrival relative to the gamma cycle [69–71]. This time depends essentially on three variables: (i) the time of spike generation in the sending cell relative to its oscillation cycle; (ii) the conduction delay between the sending and receiving cell; and (iii) the phase relation between the oscillations of the sending and receiving network. Assuming fixed conduction delays, the effective gain of a given connection in oscillating networks can be modulated over a wide range by adjusting the phase relations between the oscillating cell groups, the oscillation frequencies and the phase at which spikes are emitted. As outlined above, the latter depends, in turn, on the strength of the excitatory drive impinging on the sending cell.

Conclusion

The evidence reviewed here and the numerous studies on phase and frequency relations among oscillating cortical networks suggest the existence of mechanisms for the adjustment of oscillation frequencies and of phase relations among oscillating cell populations (reviewed in Ref. [39]). Thus, the oscillatory patterning of neuronal activity offers a range of options to exploit the temporal domain for the dynamic routing of signals within the rigid network of fixed anatomical connections. This, in turn, can be used to support a variety of functions such as feature binding [1,2], polysensory integration [72,73], sensory-motor coordination [6,21], attention-dependent selection of signals [15,25,29,30,33,74], dynamic association of the ever-changing contents of working memory [17] and, through spike timing-dependent plasticity, the formation of long-term memories [16,75].

All of these functions are associated with oscillatory activity, in most cases in the high-frequency range of the beta- and gamma-bands. These high-frequency oscillations appear to be particularly well suited for these functions because there is a direct relation between the selectivity with which dynamic routing can be accomplished and the oscillation frequency: as the frequency increases, the precision of spike timing increases and, at the same time, the network becomes more sensitive to small variations in spike timing. These considerations suggest that the adjustment of spike timing by the gamma cycle is not an epiphenomenon but a fundamental mechanism in cortical information processing [66,71].

Acknowledgements

This research was supported by grants from the Human Frontier Science Program Organization, The Netherlands Organization for Scientific Research, The Volkswagen Foundation, and the European Science Foundation's European Young Investigator Award Program (to P.F.), as well as by the Max-Planck Society (to W.S.).

References

1 Eckhorn, R. *et al.* (1988) Coherent oscillations: a mechanism of feature linking in the visual cortex? Multiple electrode and correlation analyses in the cat. *Biol. Cybern.* 60, 121–130
2 Gray, C.M. *et al.* (1989) Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. *Nature* 338, 334–337
3 Engel, A.K. *et al.* (1991) Interhemispheric synchronization of oscillatory neuronal responses in cat visual cortex. *Science* 252, 1177–1179
4 Engel, A.K. *et al.* (1991) Direct physiological evidence for scene segmentation by temporal coding. *Proc. Natl. Acad. Sci. U. S. A.* 88, 9136–9140
5 Engel, A.K. *et al.* (1991) Synchronization of oscillatory neuronal responses between striate and extrastriate visual cortical areas of the cat. *Proc. Natl. Acad. Sci. U. S. A.* 88, 6048–6052
6 Murthy, V.N. and Fetz, E.E. (1992) Coherent 25- to 35-Hz oscillations in the sensorimotor cortex of awake behaving monkeys. *Proc. Natl. Acad. Sci. U. S. A.* 89, 5670–5674
7 Bragin, A. *et al.* (1995) Gamma (40–100 Hz) oscillation in the hippocampus of the behaving rat. *J. Neurosci.* 15, 47–60
8 Whittington, M.A. *et al.* (1995) Synchronized oscillations in interneuron networks driven by metabotropic glutamate receptor activation. *Nature* 373, 612–615
9 Kreiter, A.K. and Singer, W. (1996) Stimulus-dependent synchronization of neuronal responses in the visual cortex of the awake macaque monkey. *J. Neurosci.* 16, 2381–2396
10 Wehr, M. and Laurent, G. (1996) Odour encoding by temporal sequences of firing in oscillating neural assemblies. *Nature* 384, 162–166
11 Tallon-Baudry, C. *et al.* (1996) Stimulus specificity of phase-locked and non-phase-locked 40 Hz visual responses in human. *J. Neurosci.* 16, 4240–4249
12 Brown, P. *et al.* (1998) Cortical correlate of the Piper rhythm in humans. *J. Neurophysiol.* 80, 2911–2917
13 Fellous, J.M. and Sejnowski, T.J. (2000) Cholinergic induction of oscillations in the hippocampal slice in the slow (0.5–2 Hz), theta (5–12 Hz), and gamma (35–70 Hz) bands. *Hippocampus* 10, 187–197
14 Gail, A. *et al.* (2000) Contour decouples gamma activity across texture representation in monkey striate cortex. *Cereb. Cortex* 10, 840–850
15 Fries, P. *et al.* (2001) Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* 291, 1560–1563
16 Fell, J. *et al.* (2001) Human memory formation is accompanied by rhinal–hippocampal coupling and decoupling. *Nat. Neurosci.* 4, 1259–1264
17 Pesaran, B. *et al.* (2002) Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat. Neurosci.* 5, 805–811
18 Brosch, M. *et al.* (2002) Stimulus-related gamma oscillations in primate auditory cortex. *J. Neurophysiol.* 87, 2715–2725
19 Csicsvari, J. *et al.* (2003) Mechanisms of gamma oscillations in the hippocampus of the behaving rat. *Neuron* 37, 311–322
20 Howard, M.W. *et al.* (2003) Gamma oscillations correlate with working memory load in humans. *Cereb. Cortex* 13, 1369–1374
21 Schoffelen, J.M. *et al.* (2005) Neuronal coherence as a mechanism of effective corticospinal interaction. *Science* 308, 111–113
22 Edwards, E. *et al.* (2005) High gamma activity in response to deviant auditory stimuli recorded directly from human cortex. *J. Neurophysiol.* 94, 4269–4280
23 Hoogenboom, N. *et al.* (2006) Localizing human visual gamma-band activity in frequency, time and space. *Neuroimage* 29, 764–773
24 Siegel, M. *et al.* (2007) High-frequency activity in human visual cortex is modulated by visual motion strength. *Cereb. Cortex* 17, 732–741
25 Womelsdorf, T. *et al.* (2006) Gamma-band synchronization in visual cortex predicts speed of change detection. *Nature* 439, 733–736
26 Canolty, R.T. *et al.* (2006) High gamma power is phase-locked to theta oscillations in human neocortex. *Science* 313, 1626–1628
27 Stopfer, M. *et al.* (1997) Impaired odour discrimination on desynchronization of odour-encoding neural assemblies. *Nature* 390, 70–74

28 Bauer, M. *et al.* (2006) Tactile spatial attention enhances gamma-band activity in somatosensory cortex and reduces low-frequency activity in parieto-occipital areas. *J. Neurosci.* 26, 490–501
29 Bichot, N.P. *et al.* (2005) Parallel and serial neural mechanisms for visual search in macaque area V4. *Science* 308, 529–534
30 Taylor, K. *et al.* (2005) Coherent oscillatory activity in monkey area v4 predicts successful allocation of attention. *Cereb. Cortex* 15, 1424–1437
31 Buzsáki, G. and Chrobak, J.J. (1995) Temporal structure in spatially organized neuronal ensembles: a role for interneuronal networks. *Curr. Opin. Neurobiol.* 5, 504–510
32 Olufsen, M.S. *et al.* (2003) New roles for the gamma rhythm: population tuning and preprocessing for the beta rhythm. *J. Comput. Neurosci.* 14, 33–54
33 Börgers, C. *et al.* (2005) Background gamma rhythmicity and attention in cortical local circuits: a computational study. *Proc. Natl. Acad. Sci. U. S. A.* 102, 7002–7007
34 Maass, W. and Natschläger, T. (1997) Networks of spiking neurons can emulate arbitrary Hopfield nets in temporal coding. *Network: Comput. Neural Syst.* 8, 355–372
35 Nikolic, D. (2007) Non-parametric detection of temporal order across pairwise measurements of time delays. *J. Comput. Neurosci.* 22, 5–19
36 Schneider, G. *et al.* (2006) Spatiotemporal structure in large neuronal networks detected from cross-correlation. *Neural Comput.* 18, 2387–2413
37 Schneider, G. and Nikolic, D. (2006) Detection and assessment of near-zero delays in neuronal spiking activity. *J. Neurosci. Methods* 152, 97–106
38 Singer, W. and Gray, C.M. (1995) Visual feature integration and the temporal correlation hypothesis. *Annu. Rev. Neurosci.* 18, 555–586
39 Singer, W. (1999) Neuronal synchrony: a versatile code for the definition of relations? *Neuron* 24, 49–25
40 White, J.A. *et al.* (1998) Synchronization and oscillatory dynamics in heterogeneous, mutually inhibited neurons. *J. Comput. Neurosci.* 5, 5–16
41 Jefferys, J.G. *et al.* (1996) Neuronal networks for induced '40 Hz' rhythms. *Trends Neurosci.* 19, 202–208
42 Singer, W. (1996) Neurophysiology: the changing face of inhibition. *Curr. Biol.* 6, 395–397
43 Hasenstaub, A. *et al.* (2005) Inhibitory postsynaptic potentials carry synchronized frequency information in active cortical networks. *Neuron* 47, 423–435
44 Vida, I. *et al.* (2006) Shunting inhibition improves robustness of gamma oscillations in hippocampal interneuron networks by homogenizing firing rates. *Neuron* 49, 107–117
45 Bartos, M. *et al.* (2007) Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. *Nat. Rev. Neurosci.* 8, 45–56
46 Hormuzdi, S.G. *et al.* (2001) Impaired electrical signaling disrupts gamma frequency oscillations in connexin 36-deficient mice. *Neuron* 31, 487–495
47 Deans, M.R. *et al.* (2001) Synchronous activity of inhibitory networks in neocortex requires electrical synapses containing connexin 36. *Neuron* 31, 477–485
48 Traub, R.D. *et al.* (2003) Contrasting roles of axonal (pyramidal cell) and dendritic (interneuron) electrical coupling in the generation of neuronal network oscillations. *Proc. Natl. Acad. Sci. U. S. A.* 100, 1370–1374
49 Börgers, C. and Kopell, N. (2005) Effects of noisy drive on rhythms in networks of excitatory and inhibitory neurons. *Neural Comput.* 17, 557–608
50 O'Keefe, J. and Recce, M.L. (1993) Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus* 3, 317–330
51 O'Keefe, J. (1976) Place units in the hippocampus of the freely moving rat. *Exp. Neurol.* 51, 78–109
52 Burgess, N. and O'Keefe, J. (2005) The theta rhythm. *Hippocampus* 15, 825–826
53 Harris, K.D. *et al.* (2002) Spike train dynamics predicts theta-related phase precession in hippocampal pyramidal cells. *Nature* 417, 738–741
54 Mehta, M.R. *et al.* (2002) Role of experience and oscillations in transforming a rate code into a temporal code. *Nature* 417, 741–746
55 König, P. *et al.* (1995) How precise is neuronal synchronization? *Neural Comput.* 7, 469–485
56 Delorme, A. and Thorpe, S.J. (2003) SpikeNET: an event-driven simulation package for modelling large networks of spiking neurons. *Network.* 14, 613–627
57 Delorme, A. and Thorpe, S.J. (2001) Face identification using one spike per neuron: resistance to image degradations. *Neural Netw.* 14, 795–803
58 VanRullen, R. and Thorpe, S.J. (2001) Rate coding versus temporal order coding: what the retinal ganglion cells tell the visual cortex. *Neural Comput.* 13, 1255–1283
59 VanRullen, R. and Thorpe, S.J. (2002) Surfing a spike wave down the ventral stream. *Vision Res.* 42, 2593–2615
60 Thorpe, S. *et al.* (1996) Speed of processing in the human visual system. *Nature* 381, 520–522
61 VanRullen, R. and Thorpe, S.J. (2001) The time course of visual processing: from early perception to decision-making. *J. Cogn Neurosci.* 13, 454–461
62 Hopfield, J.J. and Herz, A.V. (1995) Rapid local synchronization of action potentials: toward computation with coupled integrate-and-fire neurons. *Proc. Natl. Acad. Sci. U. S. A* 92, 6655–6662
63 Frien, A. *et al.* (1994) Stimulus-specific fast oscillations at zero phase between visual areas V1 and V2 of awake monkey. *Neuroreport* 5, 2273–2277
64 Fries, P. *et al.* (2001) Rapid feature selective neuronal synchronization through correlated latency shifting. *Nat. Neurosci.* 4, 194–200
65 Buracas, G.T. *et al.* (1998) Efficient discrimination of temporal patterns by motion-sensitive neurons in primate visual cortex. *Neuron* 20, 959–969
66 Buzsáki, G. (2006) *Rhythms of the Brain,* Oxford University Press
67 Azouz, R. and Gray, C.M. (2000) Dynamic spike threshold reveals a mechanism for synaptic coincidence detection in cortical neurons *in vivo*. *Proc. Natl. Acad. Sci. U. S. A.* 97, 8110–8115
68 Azouz, R. and Gray, C.M. (2003) Adaptive coincidence detection and dynamic gain control in visual cortical neurons *in vivo*. *Neuron* 37, 513–523
69 Burchell, T.R. *et al.* (1998) Gamma frequency oscillations gate temporally coded afferent inputs in the rat hippocampal slice. *Neurosci. Lett.* 255, 151–154
70 Volgushev, M. *et al.* (1998) Modification of discharge patterns of neocortical neurons by induced oscillations of the membrane potential. *Neuroscience* 83, 15–25
71 Fries, P. (2005) A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends Cogn. Sci.* 9, 474–480
72 Yuval-Greenberg, S. and Deouell, L.Y. (2007) What you see is not (always) what you hear: induced gamma band responses reflect cross-modal interactions in familiar object recognition. *J. Neurosci.* 27, 1090–1096
73 Mishra, J. *et al.* (2007) Early cross-modal interactions in auditory and visual cortex underlie a sound-induced visual illusion. *J. Neurosci.* 27, 4120–4131
74 Mishra, J. *et al.* (2006) Selective attention through phase relationship of excitatory and inhibitory input synchrony in a model cortical neuron. *Neural Netw.* 19, 1329–1346
75 Wespatat, V. *et al.* (2004) Phase sensitivity of synaptic modifications in oscillating cells of rat visual cortex. *J. Neurosci.* 24, 9067–9075