Published in final edited form in:
Quiroga, R.-Q., Panzeri, S. eds. (2013)
Principles of Neural Coding. CRC Press, 449-469.

Gamma-band synchronization and information transmission

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The discovery of gamma-band synchronization in visual cortex (Gray et al., 1989) and the hippocampus (Bragin et al., 1995) has sparked intense research on its mechanistic underpinnings, and its function in cortical computation. After two decades, the emerging picture is that gamma-band synchronization plays an important role in both information encoding (König et al., 1995; Fries et al., 2007) and selective information transmission (Fries, 2005). Here, we review evidence showing that: (i) An exquisite machinery exists to generate cortical gamma-band oscillations (Section 1); (ii) Gamma-band synchronization is an ubiquitous phenomenon in the cortex (Section 2); (iii) Gamma-band synchronization likely bears strong network consequences, due to feedforward coincidence detection (Abeles, 1982) and coherent phase-coupling across structures (Fries, 2005) (Section 3); (iv) Gamma-band synchronization may serve as a mechanism for flexible signal routing (Fries, 2005), and attention strongly enhances both local gamma-band synchronization (Fries et al., 2001b) and cross-areal gamma-band coherence (Gregoriou et al., 2009); (v) Gamma-band oscillations serve as a temporal reference frame, allowing spike phases to convey stimulus information (Fries et al., 2007) (Section 5); (vi) Gamma-band synchronization may be an important determinant of the rate code itself (Section 5).

23.1 Generation of gamma-band oscillations

There is a broad consensus that PV+ (parvalbumin expressing), FS (fast spiking) basket cells play a pivotal role in generating cortical gamma-band synchronization (Bartos et al., 2007; Tiesinga et al., 2009; Cardin et al., 2009; Sohal et al., 2009; Gulyás et al., 2010; Wang, 2010; Whittington et al., 2011). The generation of gamma-band oscillations does not depend on remote pacemaker cell input, but is supported by the intrinsic components of the cortical microcircuit. Therefore, gamma-band oscillations may be a fundamental processing mode of cortical circuits (Fries, 2009). The gamma processing mode is triggered by sufficient excitatory input from pyramidal cells to FS basket cells, since the latter do not fire tonically without receiving recurrent excitatory inputs from pyramidal cells.

FS basket cells provide perisomatic inhibitory inputs to pyramidal cells, which puts them in an ideal position to gate excitatory inputs from all dendritic compartments (Freund and Katona, 2007), and FS basket cells can strongly entrain pyramidal spiking activity (Lytton and Sejnowski, 1991; Cobb et al., 1995; Hasenstaub et al., 2005). Furthermore, FS basket cells are resonators at gamma

frequencies and are capable of firing more than one spike per gamma cycle, given that sufficient excitatory drive is provided (Pike et al., 2000; Klausberger et al., 2003; Hasenstaub et al., 2005; Cardin et al., 2009; Gulyás et al., 2010;).

Pharmacological studies show that gamma-band oscillations in the hippocampus can be induced by the cholinergic agonist carbachol (Fisahn et al., 1998), by agonists of kainate receptors (Fisahn et al., 2004), or by metabotropic glutamate receptors (Whittington et al., 1995). In all cases, gamma-band oscillations are blocked by the GABAa receptor antagonist bicuculline. This supports a crucial role of inhibition in gamma rhythmogenesis, but does not exclude a potential role of other inhibitory interneuron classes. To directly test whether FS basket cells play a causal role in gamma rhythmogenesis, Cardin et al. (2009) and Sohal et al. (2009) used optogenetic tools to precisely control the firing of FS, PV+ interneurons. Activation of FS, PV+ interneurons through channelrhodopsin with broadband or gamma-rhythmic trains of light pulses strongly enhanced gamma-band oscillations in the LFP (Local Field Potential). Thus, upon activation, FS, PV+ interneurons rhythmically entrained pyramidal cells (Cardin et al., 2009), showing that their activation is sufficient for the emergence of gamma-band oscillations. When gamma-band oscillations were induced by activation of pyramidal cells, they were suppressed by the inhibition of FS, PV+ interneurons (Sohal et al., 2009), showing that their activation is not only sufficient, but also required for the emergence of gamma-band oscillations. However, these optogenetic studies do not exclude a potential role of FS, PV+ axo-axonic cells. To address this issue, Gulyás et al. (2010) used opiates to selectively reduce GABAa release from FS basket cell terminals, leaving GABAa release from axo-axonic cells unaffected. This strongly reduced the carbachol-induced in vitro gamma-band oscillations, suggesting that the activation of FS basket cells is required, whereas the activation of axo-axonic cells is not sufficient for the generation of gamma-band oscillations.

Although a pivotal role of FS basket cells is implied by these findings, it remains difficult to dissect the precise dynamics of the gamma rhythm, since the network dynamics are not easily separable into cause and consequence. In particular, there is substantial debate about whether the precise timing of pyramidal cell firing plays an essential role in gamma rhythmogenesis (Bartos et al., 2007; Morita et al., 2008; Tiesinga et al., 2009; Cardin et al., 2009; Wulff et al., 2009; Whittington et al., 2011). In the ING (Interneuron Network Gamma) model, the crucial factor producing gamma-band synchronization is the mutual inhibition between basket cells (Whittington et al., 1995; Wang and Buzsáki, 1996; Vida et al., 2006; Bartos et al., 2007): Upon activation, the FS basket cell network propels towards an attractor state where basket cells escape each other's mutual inhibition through synchronization (Whittington et al., 1995; Wang and Buzsáki, 1996; Bartos et al., 2007). The gamma-synchronized FS basket cell network activity then rhythmically entrains pyramidal cells. In this scheme, the timing of pyramidal cells is a mere consequence of rhythmic inhibition, and the critical parameter determining the gamma frequency is the decay of GABAa inhibition (Whittington et al., 1995). Conversely, the timing of pyramidal cell spiking plays a central role in the PING (Pyramidal Interneuron Network Gamma) model. When pyramidal cells recover from inhibition, they cause an increase in feedback inhibition. This causes a decrease in pyramidal cell activity in turn, leading to a decrease in inhibition, until the pyramidal cells recover (Wilson and Cowan, 1972; Leung, 1982; Eeckman and Freeman, 1990; Whittington et al., 2000; Hansel and Mato, 2003).

Both types of gamma-band oscillations can be induced in the cortex. Gamma-band oscillations that are induced in the CA1 and CA3 regions by kainate induction or metabotropic glutamate

receptor agonists are maintained in the presence of AMPA receptor antagonists (Traub et al., 1996; Whittington et al., 1996), consistent with ING-type models. Gamma oscillations induced by cholinergic agonist activation are inhibited by AMPA receptor antagonists in both hippocampus (Fisahn et al., 1998) and neocortex (Buhl et al., 1998), consistent with PING-type models. However, converging evidence tentatively supports the conclusion that the typical gamma-band oscillations that have been observed in for example the hippocampus (Bragin et al., 1995; Csicsvari et al., 2003) and sensory cortices (Gray et al., 1989; Fries et al., 2001b) arise from a precise interplay between excitation and inhibition: (i) PING-models predict a characteristic delay of several milliseconds between pyramidal cell activity and FS basket cell activity (Eeckman and Freeman, 1990). Consistent with this, extracellular in vivo recordings have shown that pyramidal cell activity has a gamma phase-lead over putative FS basket cell activity of a few milliseconds (Csicsvari et al., 2003; Hasenstaub et al., 2005; Tukker et al., 2007; Womelsdorf et al., 2008, van Wingerden et al., 2010). This phase-relation is an important motif of the cortical microcircuit that also exists in the absence of gamma-band synchronization (Okun and Lampl, 2008). ING models on the other hand predict that pyramidal cells fire in phase with FS basket cells, since for both cell types the probability of firing is governed by the timing of inhibition (Traub et al., 1996). (ii) A problem with ING models is the robustness against heterogeneity in excitatory drive (Wang and Buzsáki, 1996). Strong, shunting interneuron-interneuron inhibition can make ING networks robust against heterogeneities in excitatory drive (Vida et al., 2006; Bartos et al., 2007). However, as argued by (Freund and Katona, 2007), the required depolarization induced by GABAa inhibition may be found only in the dentate gyrus, where the GABAa reversal potential is particularly close to action potential threshold. The fast kinetics of the mutual FS basket cell inhibition (Bartos et al., 2002) may rather support the genesis of fast oscillations (>100 Hz) instead of gamma-band oscillations (Brunel and Wang, 2003; Geisler et al., 2005). (iii) Cardin et al. (2009) induced gamma-band oscillations in vivo through depolarization of FS basket cells by activating channelrhodopsin with light pulses. Blocking AMPA and NMDA receptors abolished gamma-band oscillations, even though the FS basket cells continued to receive external, channelrhodopsin mediated excitatory drive. Furthermore, pyramidal cells fired with a characteristic phase-lead with respect to FS basket cells (Cardin et al., 2009), as predicted by PING-models. (iv) Genetically impairing the GABAa receptor in hippocampal PV+ interneurons, which abolishes the mutual inhibition mechanism, did not significantly affect the strength and frequency of gamma-band synchronization in awake mice (Wulff et al., 2009).

23.2 Incidence of gamma-band synchronization in the nervous system

Since gamma-band oscillations emerge from an interplay between two basic components of the cortical microcircuit, pyramidal cells and FS basket cells, it is expected to be a widespread cortical phenomenon. Indeed, gamma-band oscillations have been documented in many areas and species, and under many behavioral conditions. Intense research on gamma-band oscillations commenced with the finding that neurons in primary visual cortex engage in strong gamma-band synchronization in response to visual stimulation (Gray et al., 1989). Since then, many labs have revealed gamma-band oscillations in anesthetized cat and monkey visual cortex (Gray et al., 1989; Livingstone, 1996; Yu and Ferster, 2010) and awake cat, monkey and human visual cortex (Fries et al., 1997, 2001b; Friedman-Hill et al., 2000; Maldonado et al., 2000; Rols et al., 2001; Hoogenboom et al., 2006; Womelsdorf et al., 2007; Gieselmann and Thiele, 2008; Chalk et al., 2010; Lima et al., 2010; Ray and Maunsell, 2010; Vinck et al., 2010). Gamma-band synchronization is typically induced through

moving bars or gratings, but has also been induced by viewing stationary squares (Rols et al., 2001), smoothly changing shapes (Taylor et al., 2005) and by the free-viewing exploration of a stationary array of objects (Bichot et al., 2005). Gamma-band synchronization is stronger for salient stimuli, increasing with stimulus size (Gieselmann and Thiele, 2008), contrast (Henrie and Shapley, 2005) and spatial integrity (Zhou et al., 2008; Lima et al., 2010). Also, gamma-band synchronization is especially strong during active, awake states (Munk et al., 1996; Herculano-Houzel et al., 1999; Fries et al., 2001b; Rodriguez et al., 2004; Taylor et al., 2005; Womelsdorf et al., 2006; Gregoriou et al., 2009). Thus, while visual activation is required for the emergence of gamma-band synchronization in visual cortex, it is not a sufficient condition for strong gamma-band oscillations to emerge. Further, gamma-band synchronization in visual cortex (Buffalo et al., 2004) and somatosensory cortex (Roopun et al., 2006) is particularly strong in the superficial layers, whereas beta-band synchronization is particularly strong in infragranular layers. The dependence of gamma-band oscillations on these variables may explain why a minority of studies has failed to demonstrate gamma-band synchronization in primary visual cortex (Lamme and Spekreijse, 1998; Nowak et al., 1999; Montemurro et al., 2008).

The gamma rhythm is very prominent in rat and mouse hippocampal formation (Bragin et al., 1995; Csicsvari et al., 2003; Colgin et al., 2009). Given appropriate inputs, it can also be induced in auditory cortex (Brosch et al., 2002), somatosensory cortex (Bauer et al., 2006), barrel cortex (Cardin et al., 2009), the olfactory system (Eeckman and Freeman, 1990; Wehr and Laurent, 1996), parietal cortex (Pesaran et al., 2002; Buschman and Miller, 2007; Medendorp et al., 2007), several nodes of the frontal cortex (Buschman and Miller, 2007; Gregoriou et al., 2009; Siegel et al., 2009; Sohal et al., 2009; Canolty et al., 2010; Sigurdsson et al., 2010; van Wingerden et al., 2010), ventral striatum (van der Meer and Redish, 2009) and amygdala (Popescu et al., 2009).

Long-range gamma-band synchronization has been documented between spinal cord and motor cortex (Brown et al., 1998; Schoffelen et al., 2005), between different nodes of the visual system (Engel et al., 1991a,b; Womelsdorf et al., 2007; Bosman et al., 2010), visual cortex and parietal cortex (Roelfsema et al., 1997; von Stein et al., 2000; Saalmann et al., 2007; Bosman et al., 2010), V4 and FEF (Gregoriou et al., 2009), LIP and FEF (Buschman and Miller, 2007), amygdala and striatum (Popescu et al., 2009), and hippocampus and prefrontal cortex (Sigurdsson et al., 2010).

It is relatively unknown what mechanisms support long-range gamma-band coherence. Long-range gamma-band synchronization at a phase delay that mirrors the synaptic delay (Gregoriou et al., 2009) may be supported by simple rhythmic entrainment (Fries, 2005; Börgers and Kopell, 2008; Gielen et al., 2010), in which pyramidal cells reset the phase of FS basket cell activity through long-range excitatory connections. Such a scheme is akin to a PING-type dynamics, in which local pyramidal cells control the timing of local FS basket cells. A more difficult problem is the generation of long-range, zero-lag rhythmic synchronization in the presence of substantial synaptic delays, as in (Engel et al., 1991a). Computational models suggest that this type of long-range synchronization may be supported by mutual, long-range excitatory connections causing doublet spikes in FS basket cells (Traub et al., 1996; Kopell et al., 2000), a scheme which is stable up to conduction delays of 8-10 ms.

23.3 Consequences of rhythmic neuronal synchronization

Demonstrating that gamma-band synchronization plays a fundamental role in cortical computation rests on two pillars. Firstly, it needs to be demonstrated that rhythmic synchronization bears

consequences in terms of neuronal interactions. Secondly, it needs to be demonstrated that gamma-band synchronization varies across experimental conditions in a meaningful way, supporting the computations that the brain needs to perform (Salinas and Sejnowski, 2001; Fries, 2009). In the words of Gregory Bateson, for information to be contained in gamma-band synchronization, we need to show ”differences that make a difference”. In this section, we will address the question whether differences in rhythmic synchronization indeed make a difference in terms of neuronal interactions.

23.3.1 Feedforward coincidence detection

The mechanism of feedforward coincidence detection entails that spikes have more impact on a postsynaptic target neuron if they coincide within a narrow temporal window (Abeles, 1982; Bernander et al., 1991; Softky, 1994; König et al., 1996; Azouz and Gray, 2000; Galarreta and Hestrin, 2001; Salinas and Sejnowski, 2001). Coincident firing implies that there exists a peak around t = 0 in the cross-correlogram between spike-trains, i.e. zero-lag synchronization. If spiking activity is asynchronous, then the cross-correlogram between spike-trains will be flat. The concept of synchronization should be distinguished from the concept of rhythmic or oscillatory synchronization. Zero-lag synchronization merely implies coincident firing in the time domain, and can occur without any oscillatory preference. However, coincident firing typically arises as a consequence of coherent oscillatory activity, which focuses spikes within a narrow temporal window. Zero-lag synchronization can also be caused by common inputs or co-variation of stimulus-locked rate modulations (Brody, 1998).

The question whether neurons are coincidence detectors or temporal integrators should not be framed as an absolute one. Obviously, excessive temporal integration would limit the brain’s capacity to track fast changes in sensory inputs. Enhanced synchrony between presynaptic inputs may only increase the firing rate of a postsynaptic target up to a certain point (Murthy and Fetz, 1994; Bernander et al., 1994): if a packet of coincident spikes causes the post-synaptic neuron to fire, then the surplus spikes that were not needed for threshold potential crossing are lost in the post-synaptic neuron’s refractory period. Consequently, excessive coincident firing entails low firing rates.

Viewpoints on coincidence detection have changed substantially during the past decade, and effective temporal integration times may in fact be much shorter than was previously appreciated (Shadlen and Newsome, 1994; Koch et al., 1996). Firstly, the classic idea is that feedforward coincidence detection depends on the membrane time constant, which determines the decay rate of EPSPs (Excitatory Post-Synaptic Potentials). Shadlen and Newsome (1994) argued that integration times are effectively limited by membrane time-constants of 8-20 ms, values that are typically obtained from in vitro slice recordings. Thus, coincident firing on a faster time-scale would not significantly impact neuronal interactions, and cause many pre-synaptic inputs to be lost in the post-synaptic neuron’s refractory period (Shadlen and Newsome, 1994). Consequently, gamma- band synchronization of spiking activity with a cycle duration of 12-30 ms would not enhance impact on a postsynaptic target, since spikes occurring at preferred and non-preferred gamma phases would effectively be temporally integrated.

However, membrane time constants depend on both neuron type and cortical state, and are shorter when the slice is at physiological temperatures. When an animal is in an awake state, neurons are bombarded by synaptic background activity that is composed of balanced excitation and inhibition. This synaptic background activity causes the membrane potential to be closer to threshold

than the resting potential is, and induces a several fold increase in the membrane leak conductance. The membrane leak conductance is inversely proportional to the membrane time constant. It follows that the several fold increase in membrane conductance causes a proportional decrease in the membrane time constant in comparison to in vitro slice recordings. This decrease in the membrane time constant corresponds to a proportional decrease in the temporal window of integration (Bernander et al., 1991; Borg-Graham et al., 1998; Hirsch et al., 1998; Destexhe et al., 2003; Kuhn et al., 2004; Leger et al., 2005; Hasenstaub et al., 2007; Kumar et al., 2008). In addition, inhibitory interneurons operate more like coincidence detectors than pyramidal cells, since they have shorter membrane time constants, and respond with rapidly decaying EPSPs to pyramidal cell inputs (Galarreta and Hestrin, 2001; Geiger et al., 1997; Cardin et al., 2007, 2010).

Secondly, several studies have shown that spiking activity is not merely determined by the level of depolarization of the membrane potential. In addition, a strong determinant of firing is the first derivative of the membrane potential (Azouz and Gray, 2000; Henze and Buzsáki, 2001). Rapid depolarizations of the membrane potential V_m lower the action potential threshold, likely due to the activation of sodium channels (Azouz and Gray, 2000; Cardin et al., 2010; Farries et al., 2010). On the other hand, while slow membrane potential depolarizations increase the probability that fast fluctuations cause threshold crossing, this effect is to some extent counteracted by the inactivation of sodium channels, which increases action potential threshold, and by an increase in membrane leak conductance, which decreases the amplitude and duration of incoming EPSPs (Petersen et al., 2003; Kuhn et al., 2004; Leger et al., 2005). In fact, a much stronger correlation of firing rate with the membrane potential derivative dV_m/dt than with the membrane potential V_m has been observed (Azouz and Gray, 2000, 2003). Consequently, orientation tuning in V1 is mainly driven by tuning of fast fluctuations of the membrane potential (20-80 Hz), rather than by tuning of the mean or slow fluctuations of the membrane potential V_m (Azouz and Gray, 2003). The integration times based on dV_m/dt are on the order of the time-course of the capacitive membrane current, which has a time-constant that is even faster than the excitatory post-synaptic current. The latter time-constant is on the order of a few milliseconds for the AMPA receptor on pyramidal cells (Hestrin, 1992) and there is a sub-millisecond decay constant for the AMPA receptor on FS basket cells (Geiger et al., 1997; Galarreta and Hestrin, 2001). Thus, temporal integration of synaptic inputs separated by a longer time delay occurs on the basis of V_m depolarization only: The positive rates of depolarization are not added across inputs separated by more than a few milliseconds, even though the levels of depolarization are. Given a neuronal refractory period of several milliseconds, it follows that multiple spikes from the same neuron do not give rise to larger rate of depolarization than single spikes. Consistent with the dV_m/dt spiking mechanism, cross-correlation peaks between pre- and post-synaptic neurons are very narrow (i.e. 2-3 ms) and typically precede the peak of the EPSP (Knox, 1974; Fetz and Gustafsson, 1983; Alonso et al., 1996; Matsumura et al., 1996; Bruno and Sakmann, 2006). During awake states, the integration period based on the V_m change induced by EPSPs may typically not be longer than 10 ms (Leger et al., 2005). Thus, spikes from opposite phases of the gamma cycle, which are separated by 6-15 ms, will not be integrated based on an adaptive threshold mechanism, and will only be weakly integrated based on the addition of their EPSP depolarizations.

Finally, neurons possess mechanisms that do not only render them sensitive to synchronous inputs, but also to specific temporal sequences of dendritic inputs. A series of sequential synaptic inputs that traverse from the dendritic branch towards the soma are more effective than a series of

inputs that traverse from the soma towards the dendritic branch (Branco et al., 2010). Further, the membrane potential is tuned to the velocity by which synaptic inputs traverse from dendritic branch to soma (Branco et al., 2010). Hence, dendrites do not act as linear integrators, but render neurons sensitive to the arrival order of synaptic inputs. Thus, neurons may detect regular sequences of synaptic inputs that are occurring across different phases of the gamma cycle (König et al., 1995; Vinck et al., 2010).

Based on the existence of these feedforward coincidence detection mechanisms that are based on biophsyical properties of the neuron, the prediction follows that increasing the amount of firing coincidences indeed increases the impact on a postsynaptic target. Several modeling and experimental studies directly support the notion that neurons are indeed highly sensitive to synchronous inputs. Salinas and Sejnowski (2000) investigated the effects of increasing the zero-lag synchrony between excitatory inputs in a simple conductance-based integrate-and-fire model with uncorrelated, yet balanced excitatory and inhibitory inputs (similar to Shadlen and Newsome (1994)). Enhanced synchrony between synaptic inputs did not cause a change in the mean membrane potential, but causes increased membrane potential fluctuations. This strongly increased the neurons output firing rate. Leger et al. (2005) have shown that during UP states, temporal integration times are twice as small as during DOWN states, likely due to an increase membrane leak conductance. EPSPs that were triggered through micro stimulation only summated when they arrived within a window of 10 ms (Leger et al., 2005). Interestingly, assuming that a neuron receives a large number of synaptic Poisson inputs (10000) with a high average firing rate (4.5 Hz), then the probability of obtaining the required coincidences to trigger spiking is very small (Leger et al., 2005). Thus, sparse, synchronous spiking activity may be required to cause threshold crossings of the membrane potential. Similarly, Stevens and Zador (1998) found that sparse, synchronous events are needed to produce the typical statistics of neuronal spike-trains. Alonso et al. (1996) have shown that LGN spiking activity is often synchronized within 1 ms precision. These synchronized spikes have supralinear effects on V1 cells, showing that not only coincidence detection takes place, but also supra-linear integration. The temporal integration of LGN input spikes by V1 neurons decays at a fast rate of 1/e, with e = 2.5 ms (Usrey et al., 2000).

In sum, there is abundant evidence that synchrony substantially increases the impact of synaptic inputs, and that neurons are particularly sensitive to synaptic inputs coinciding in a window of few milliseconds. Thus, observed differences in synchronization between experimental conditions likely bear strong network consequences.

23.3.2 Balanced excitation and feedback inhibition shape synaptic integration

We have reviewed several biophysical mechanisms that enable neurons to detect coincident synaptic inputs. In this section, we review another factor that shapes the integration of synaptic inputs, namely the temporal interplay between excitation and inhibition. Excitatory and inhibitory synaptic inputs are not only balanced in terms of amplitude, as in Shadlen and Newsome (1994), but are also tightly coordinated in time (Csicsvari et al., 2003; Wehr and Zador, 2003; Hasenstaub et al., 2005; Fries et al., 2007; Okun and Lampl, 2008; Atallah and Scanziani, 2009; Cafaro and Rieke, 2010; Cardin et al., 2010; Zhou et al., 2010). A balance and temporal coordination of excitation and inhibition may serve several functions. A critical function of fast inhibitory feedback is to prevent run-away excitation of the network (Abeles, 1982; Buzsáki, 2006; Pouille et al., 2009; Moore et al., 2010), allowing strong recurrent connections that facilitate fast responses to external network input (van

Vreeswijk and Sompolinsky, 1996). Further, balancing excitation by global inhibitory feedback has been proposed as a mechanism to remove output noise correlations (Renart et al., 2010). Such a mechanism would explain why noise correlations are very weak in auditory and primary visual cortex, despite the existence of common inputs (Ecker et al., 2010; Renart et al., 2010). An enhancement of gamma-band synchronization may correspond to a reduction in slow noise correlations through an up-regulation of the temporal coordination between excitation and inhibition. Attention enhances V4 gamma-band synchronization, and decreases low-frequency synchronization (Fries et al., 2001b, 2008), effectively equating a reduction in noise-correlations (Mitchell et al., 2009). Balancing excitation and inhibition can also sharpen neuronal selectivity by canceling out noisy fluctuations in excitatory inputs (Cafaro and Rieke, 2010).

A delay of inhibitory activity relative to excitatory activity is a fundamental motif of network activity, and has been shown in extracellular in vivo recordings in hippocampus (Csicsvari et al., 2003; Tukker et al., 2007) and orbitofrontal cortex (van Wingerden et al., 2010) from awake rats, and awake monkey (Womelsdorf et al., 2008). In addition, the delay has been demonstrated by intracellular recordings from anesthesized animals in several areas, including the ferret prefrontal cortex (Hasenstaub et al., 2005), the CA3 field of the rat hippocampus (Atallah and Scanziani, 2009), the rat barrel cortex (Wilent and Contreras, 2005; Okun and Lampl, 2008), the rat primary auditory cortex (Wehr and Zador, 2003), and the cat primary visual cortex (Cardin et al., 2010). The delay between excitation and inhibition can be expressed in the frequency domain as a phase lag in the gamma cycle (Csicsvari et al., 2003; Hasenstaub et al., 2005) or in the time domain as a temporal delay (Okun and Lampl, 2008), and is thought to arise from recurrent feedback inhibition or feedforward inhibition (Eeckman and Freeman, 1990; Pouille and Scanziani, 2001; Wehr and Zador, 2003; Wilent and Contreras, 2005).

An important consequence of the delay between balanced excitation and inhibition is that it can strongly reduce the temporal window of integration (König et al.,1996; Pouille and Scanziani, 2001; Thorpe et al., 2001; Fries et al., 2007). Balanced, delayed inhibition can effectively quench slow fluctuations in excitatory inputs (Cafaro and Rieke, 2010; Renart et al., 2010). Consequently, only strongly synchronized excitatory inputs may effectively trigger spiking. For example, in Pouille and Scanziani (2001), blocking the GABAa receptor on pyramidal cells increased maximum temporal integration times from a few milliseconds to about 30 ms.

The delay between excitation and inhibition is not a fixed quantity, but may be an important gating device to flexibly modulate the gain of excitation (Wehr and Zador, 2003; Wilent and Contreras, 2005; Fries et al., 2007; Kremkow et al., 2010; Zhou et al., 2010). An extreme example of such gating is the case of feedforward inhibition that precedes feedforward excitation, which occurs in so called ”silent” neurons in L6 of primary auditory cortex. The temporal lead of feedforward inhibition causes these neurons to be suppressed by sensory stimulation (Zhou et al., 2010). Conversely, "normal" regular spiking neurons, for which inhibition lags excitation, are activated upon sensory stimulation (Wehr and Zador, 2003; Zhou et al., 2010).

23.3.3 Rhythmic gain modulation

The impact of excitatory synaptic inputs onto a postsynaptic target neuron is modulated by inhibitory inputs. Gamma-band oscillations entail rhythmic fluctuations in inhibitory inputs. Synaptic inputs may have a larger effect on the firing rate of a postsynaptic target during gamma-phases of low inhibition (Burchell et al., 1998; Fries, 2005). Neuronal interactions between rhythmically active

groups should therefore depend on the phase-relationship between their gamma cycles (Fries, 2005). This mechanism makes selective coherence between sender's and receiver's gamma-band activity a potentially very powerful mechanism for the flexible routing of signals in the nervous system (Fries, 2005) ("Communication-Through-Coherence" hypothesis).

During gamma-band activity, pyramidal cells are entrained by gamma-rhythmic inhibition (Hasenstaub et al., 2005). Inhibition has two effects. Firstly, it drives the membrane potential towards the reversal potential of the GABAa receptor, which lies well below action potential threshold. Consequently, more EPSPs are needed to breach action potential threshold. Secondly, perisomatic inhibition increases membrane conductance, which decreases the amplitude and duration of incoming EPSPs, i.e. perisomatic inhibition results in shunting inhibition. Thus, excitatory synaptic inputs will be less likely to cause the post-synaptic neuron to fire when it receives strong inhibitory inputs. Consequently, spikes are often preceded by a drop in inhibition (Softky, 1994; Hasenstaub et al., 2005; Azouz and Gray, 2008). Thus, the gamma cycle represents a repetitive transition between a window of opportunity and a window of depression for communication (Fries, 2005). An advantage of sparse windows of opportunity may be to spare the energy of being in an excitable state all the time (Buzsáki, 2006), at the same time preventing noise from impacting neurons all the time (König et al., 1996; Buzsáki, 2006).

The core prediction of the Communication-Through-Coherence hypothesis is that a good gamma-phase relationship between sender and receiver improves their interactions. To directly test this hypothesis, Womelsdorf et al. (2007) recorded simultaneously from spatially separate sites in the visual cortex from awake cat and monkey. Upon visual activation, sites engaged in sustained gamma-band synchronization. Consistent gamma phase relationships were observed between different sites. Phase-relationships were not completely consistent however, because there was some variation around the mean phase-relationship. The mean phase-relationship was hypothesized to be the 'good' gamma-phase relationship, subserving strongest interactions. As predicted by the principle of rhythmic gain modulation, the gamma-rhythm strengths at the separate recording sites co-fluctuated strongly when there was a good gamma-phase relationship, and only weakly when there was a 'bad' phase relationship. Cross-correlation analysis revealed that 'good' gamma-phase relationships preceded strong interactions by about 5 ms, supporting a causal relationship between the two variables. Importantly, the dependence of interactions on gamma-phase held true for both short and long-range interactions, and also for the gamma-band cortico-muscular coherence as observed by (Schoffelen et al., 2005).

A direct test of the causal relationship between phase-relationship and neuronal interactions was performed by van Elswijk et al. (2010). During isometric contractions, there exists beta-band synchronization between the motor cortex and the spinal cord. The authors delivered TMS pulses to stimulate the motor cortex, while measuring spinal EMG. The post-TMS MEP amplitude was strongly dependent on the pre-TMS phase of the spinal beta rhythm.

Not only the effectiveness of neuronal inputs, but also the effectiveness of stimulus inputs depends on the ongoing phase of the gamma rhythm. Cardin et al. (2009) showed that the magnitude of evoked responses to whisker deflections depends on the ongoing phase of the pre-stimulus gamma-rhythm. Azouy and Gray demonstrated that visually evoked membrane potentials depend strongly on the depolarization of pre-stimulus membrane potentials (Azouz and Gray, 1999). Fries et al. (2001a) showed that there exist strong latency co-variations between separate LFP sites in visual cortex. Latencies were especially early if the LFP was in a falling phase (i.e., depolarization) before

the stimulus onset. Further, latencies were especially correlated if the LFPs engaged in high-frequency oscillations before the stimulus onset. Thus, the ongoing gamma-phase of a neuronal group modulates the impact of a sensory stimulus.

23.4 Attentional selection by selective gamma-band synchronization

The brain needs to achieve two important tasks in sensory processing. Firstly, it needs to reliably encode sensory stimuli. It is commonly accepted that neurons represent much information through reliable firing rate changes, although temporal codes may play an important role as well (see Section 26.5). Neurons can represent information because the weights of specific synaptic inputs are slowly adjusted over time through long-term potentiation (Hebb, 1949; Bliss and Lomo, 1973; Markram et al., 1997). Secondly, the brain needs to select a subset of available information for further processing and for action selection. The selection of information requires that routing of signals between neuronal groups is flexibly adjusted on a timescale much faster than the timescale at which synaptic potentiation takes place. Selective routing of signals between neuronal groups may be implemented through selective coherence between their ongoing rhythms (Fries, 2005).

In the visual hierarchy, connectivity patterns are highly convergent, with many upstream neurons providing convergent input into a given downstream neuron. Accordingly, receptive field sizes strongly increase along the visual hierarchy. This design principle has several advantages: First, having large receptive fields allows for the invariant representation of objects, independent of e.g. object position. Second, it is economical, since higher order representations are capable of covering large portions of the visual field. The disadvantage of this design is that multiple objects can populate the large receptive field of downstream visual neurons, which confuses information from different objects. However, this problem may be solvable by using attention to select and process single objects from the multitude of available objects, effectively shrinking the receptive field size of higher visual neurons (Moran and Desimone, 1985). When attention is directed to one of the stimuli, then the neurons in higher visual areas respond as if only the behaviorally relevant stimulus was presented (Moran and Desimone, 1985; Desimone and Duncan, 1995; Reynolds et al., 1999; Reynolds and Chelazzi, 2004). That is, there is competition between converging inputs, which can be biased by attention (Desimone and Duncan, 1995).

Fries (2005) proposed that synaptic inputs that are strongly gamma-rhythmic and coherent with the gamma-rhythm of the downstream receiver have an advantage over competing synaptic inputs, a mechanism that could be employed to implement biased competition. In support of this hypothesis, several studies have shown a strong enhancement of gamma-band synchronization with attentional modulation in V4 (Fries et al., 2001b, 2008; Bichot et al., 2005; Taylor et al., 2005; Gregoriou et al., 2009; Chalk et al., 2010). An enhancement of visual gamma-band synchronization has strong behavioral consequences, since it corresponds to reduced reaction times or more accurate responses (Taylor et al., 2005; Womelsdorf et al., 2006; Hoogenboom et al., 2010). Importantly, induced gamma- band oscillations in V4 emerge before top-down modulations on firing rate arise (>50 ms) (Fries et al., 2001b), and attentional enhancement of gamma-band oscillations occurs as soon as an attentional cue is given, already before stimulus onset (Fries et al., 2008). Enhanced gamma-band synchronization in V4 may enhance impact onto IT neurons through feedforward coincidence detection, or may reflect increased coupling of oscillatory rhythms across visual areas. Consistent with the CTC-hypothesis, attentional modulation corresponds to increased gamma-band synchronization between V4 and FEF Gregoriou et al. (2009), LIP and FEF (Buschman and Miller,

2007), V1 and V4 (Bosman et al., 2010) and MT and LIP (Saalmann et al., 2007). Interestingly, attention does not increase gamma-band synchronization in V1 but often even mildly decreases it (Fries et al., 2003; Chalk et al., 2010), suggesting that neurons in V1 might not enhance their synaptic gain onto V4 target neurons by increased gamma-band synchronization among the V1 neurons.

23.5 Coding and gamma-band synchronization

23.5.1 Coding by phase-of-firing

It is well established that much information about sensory data is encoded by the firing rate. Yet, it is highly debated to what extent the temporal structure of spiking activity serves as a coding space. Temporal codes can, in theory, carry much more information than the firing rate (MacKay and McCulloch, 1952). A fundamental problem with temporal coding is that spike times can carry information only in relation to other neuronal events, i.e. the brain needs to measure spike times relative to a temporal reference frame. Using the onset of sensory stimuli as a reference frame is problematic, since the brain cannot obtain independent information about the timing of stimulus onsets, and sensory input typically forms a temporal continuum where distinct stimulus onsets are absent (VanRullen et al., 2005; Fries et al., 2007; Panzeri et al., 2010). Using the onset of saccades or microsaccades as a temporal reference frame would effectively limit the temporal resolution of sensory systems to the saccade or microsaccade rates, which are only about 3-4 Hz (Maldonado et al., 2008; Otero-Milan, 2008; Bosman et al., 2009). A more plausible solution is that the brain defines the timing of a spike relative to the activity of a group of neurons. Endogenously generated oscillations can serve as a reliable, internal clock to define the timing of spikes, constituting a phase coding space for sensory data (O'Keefe and Recce, 1993; Hopfield, 1995; Wehr and Laurent, 1996; Fries et al., 2007; Nádasdy, 2009; Panzeri et al., 2010, Tiesinga et al., 2010) and assembly formation (Singer, 1999; Buzsáki, 2010). In such a coding scheme, a group of neurons is entrained by one rhythm, while the spike times of individual neurons are phase-shifting within the rhythm's cycle as a function of the neuron-specific inputs.

The first experimental evidence for the existence of phase coding in the nervous system was obtained in the rat hippocampus. When a rodent moves through a place field of a given place cell, then the cell's phase of firing advances in a monotonic fashion relative to the hippocampal theta rhythm, a phenomenon called phase- precession (O'Keefe and Recce, 1993; Harris et al., 2002; Mehta et al., 2002; Huxter et al., 2003; Harvey et al., 2009; Schmidt et al., 2009). Phase-precession relative to the hippocampal theta rhythm also occurs in prefrontal cortex (Jones and Wilson, 2005) and ventral striatum (van der Meer and Redish, 2011). The mechanisms behind phase precession are still highly debated (Harris et al., 2002; Mehta et al., 2002; Huxter et al., 2003; O'Keefe and Burgess, 2005; Harvey et al., 2009; Romani et al., 2010). An elegant proposal is that phase precession arises from an interaction between somatic inhibition and dendritic excitation. Stronger dendritic excitation would allow a neuron to overcome inhibition earlier in the theta cycle. Corresponding, a theta-phase advance would be observed concurrently with higher firing rates. Indeed, earlier theta-phases correspond to higher firing rates when a rat moves through the first half of a place field (Harris et al., 2002; Mehta et al., 2002). Importantly, the same relationship between phase and rate holds during other behavioral states, namely wheel running and REM sleep (Harris et al., 2002). One problem with this model however is that firing rates start to decrease when a rat has moved beyond the center of the place field, while the spike theta-phase continues to advance (Huxter et al., 2003; O'Keefe and

Burgess, 2005). This discrepancy has lead others to the proposal that the theta-phase of firing advances because an activated place field is driven by theta-rhythmic inputs that have a slightly higher frequency than the LFP population theta-rhythm (O'Keefe and Burgess, 2005). However, intracellular recordings revealed that membrane potential depolarization is asymmetric, i.e., continues to rise when a rat moves beyond the center of a place field (Harvey et al., 2009). This asymmetric tuning of the membrane potential may explain why the phase continues to advance beyond the center of the place field (Mehta et al., 2002). However, the observed intracellular profile does not necessarily rule out interference (O'Keefe and Burgess, 2005) or network models (Romani et al., 2010). Nevertheless, the soma-dendritic model offers the simplest explanation of rate-to-phase conversion under different behavioral states (Harris et al., 2002).

The short duration of the gamma cycle makes it especially suited to organize the encoding of sensory information. The alpha, theta and delta rhythm also imply synchrony of spike discharges, but their peaks of synchronized activity only repeat itself every 100-1000 ms. If sensory representations are built up and broken down along the oscillatory cycle, then these rhythms are too slow to be matched to typical sensory reaction times. The decoding of spike phase requires a waiting or updating time on the order of the cycle duration. For slower rhythms, this means that the system has to wait for 100-1000 ms before it can update its representations again. This updating time may be sufficient for representing the low-frequency characteristics of stimuli (Montemurro et al., 2008; Kayser et al., 2009; Panzeri et al., 2010). However, the visual system can represent separate objects at a high sampling rate (<100 ms) (Thorpe et al., 1996; VanRullen and Koch, 2003). The gamma cycle (40-80 Hz) allows for sensory updates every 12-20 milliseconds, which is well matched to these processing requirements.

First evidence for gamma-phase coding of visual stimuli was obtained by König et al. (1995). Primary visual cortex of anesthetized cat was activated by a drifting bar stimulus. A single stimulus activated separate MUAs (Multi Unit Activities) recorded on separate electrodes. Upon visual activation, the MUAs displayed synchronous firing, i.e., there was a peak in the cross-correlogram between their spike-trains. The extent to which a MUA was driven by the bar stimulus depended on the stimulus' orientation and spatial frequency. If a stimulus was driving two MUAs equally strong, then zero-lag synchrony was observed. When a stimulus activated one MUA more strongly than another MUA, the firing of the strongly activated MUA preceded the firing of the weakly activated MUA. While these results suggest that the relative timing of spikes can code for stimulus features, they do not demonstrate directly that spikes shift relative to the LFP gamma-band oscillation, since the effects were not studied in the frequency-domain.

We tested directly whether gamma phase-shifting exists in area V1 (Vinck et al., 2010). Awake monkeys were passively viewing drifting gratings, which elicited strong locking of spiking activity to the ongoing LFP gamma-band oscillations. When an isolated single unit was stimulated by its preferred grating orientation, spikes were on average advanced in the gamma cycle. In general, when the local spike-density was high around the time of spiking, then the gamma-phase of firing was also advanced. The phase-difference between high and low spike densities was on average 2-3 ms, a difference that should be detectable by a feedforward coincidence detection mechanism (Section 26.3).

We hypothesized that gamma phase-shifting is especially strong when spiking activity is weakly constrained by the gamma rhythm. This hypothesis follows from a Hopfield-type model (Hopfield, 1995), in which higher excitation allows the neuron to overcome gamma-rhythmic

inhibition earlier in the gamma cycle, leading to a phase advance. If gamma-rhythmic inhibition is strongly constraining spike timing, then an equal increase in excitation should lead to a smaller phase advance. Indeed, neurons whose firing was strongly constrained by the gamma-rhythm displayed smaller gamma-phase shifts (Vinck et al., 2010). In addition, we found gamma-phase shifts to be larger when LFP gamma-band power was weaker, and during the fixation baseline condition. These findings may explain why phase shifts were larger in (König et al., 1995) than in (Vinck et al., 2010): The former experiment used anesthesized cats, while the latter experiment used awake monkeys and large stimuli, causing spikes to be strongly constrained by the gamma rhythm. However, smaller yet reliable gamma-phase shifts may be more informative than larger yet unreliable gamma phase shifts.

The relationship between local firing rate and phase points to a shared mechanism between theta-phase precession and gamma phase-shifting. However, if stronger excitation allows a neuron to overcome inhibition earlier in the gamma cycle, then it should also allow the neuron to overcome inhibition for a longer period in the gamma cycle. This would not cause a phase-shift, but a decrease in phase-locking. However, neurons are more strongly locking to the gamma rhythm when they are activated by their preferred stimulus orientation (Friedman-Hill et al., 2000; Volgushev et al., 2002). Thus, a negative feedback mechanism, such as local inhibitory feedback or a refractory period, is required in addition to the interaction between excitation and global gamma-rhythmic inhibition.

Gamma phase-coding has also been demonstrated outside visual cortex, for a two-object short-term working memory task in lateral prefrontal cortex (Siegel et al., 2009). Monkeys were trained to remember the presentation order of two serially presented visual stimuli. Spikes were strongly locked to the ongoing LFP gamma-band oscillation at around 32 Hz, especially during the delay periods following the visual stimuli. These gamma-band oscillations were not phase-locked to trial events. During the second delay period, when monkeys had to represent both objects in working-memory, firing rates carried information about the identity of both visual stimuli. Astonishingly, information about the two objects was carried at separate gamma phases. Information about the first object was maximal at a gamma phase that was about 60 degree angles (i.e., about 5 ms) earlier than the gamma-phase at which information about the second object was maximal. These results suggest that the gamma cycle allows for the representation of different objects to be segregated by phase, thereby linking the activity of members of the same neuronal assembly by firing at the same gamma-phase (Singer, 1999; Buzsáki, 2010).

There are two main requirements for the phenomenon of gamma phase-shifting to occur. Firstly, the critical variable that determines gamma phase-shifts and theta phase-precession are the heterogeneous, neuron-specific inputs (O'Keefe and Recce, 1993; Vinck et al. 2010). The LFP is thought to primarily reflect recurrent, excitatory synaptic activity (Mitzdorf, 1985). Therefore, it is unlikely that the firing of all pyramidal cells in a local cortical volume shifts relative to the LFP gamma-band oscillation. Thus, increasing the contrast of a visual stimulus should not lead to gamma phase-shifting across the whole pyramidal cell population. Indeed, increasing the contrast of a visual stimulus does not cause an average advance of spike gamma-phase in V1 (Ray and Maunsell, 2010). Secondly, the detection of gamma phase-shifting requires that spike waveform energy does not bleed into the LFP. Trivially, spikes cannot shift relative to themselves. Ray et al. (2008) recorded from somatosensory cortex of the awake monkey, and failed to detect gamma phase-shifts as a function of stimulus intensity. However, they measured the relative phase between spikes and LFPs from the same electrode, which likely prevented the detection of gamma phase-shifting.

Spike theta-phases and firing rate provide more information about the rodent's position and

heading trajectory than firing rate alone (Jensen and Lisman, 2000; Huxter et al., 2008). Vinck et al. (2010) and Siegel et al. (2009) did not demonstrate directly that spike gamma phase carries additional stimulus information above the firing rate. Spike gamma-phase and firing rate seem to provide redundant stimulus information, since they are statistically dependent (König et al., 1995; Vinck et al., 2010). Nevertheless, we believe that spike gamma phase adds significantly to the information carried by firing rate. Firstly, gamma phase-shifts are not caused by differences in firing rate, but by differences in synaptic inputs. A gamma phase-shift implies an increased probability of firing at a particular phase. However, a pyramidal cell typically fails to spike in a given gamma cycle. Thus, variation in spike phase and firing rate may be highly uncorrelated across trials, allowing both information sources to be effectively combined. Secondly, during sensory processing, every processing stage is offered only a limited amount of time for temporal integration (Thorpe et al., 1996). Moreover, because spikes are integrated over short temporal windows, every neuron will effectively contribute maximally one spike to a given cortical computation. This binary spike-count will carry only very limited information about the preferred spike gamma-phase and the firing rate. Thus, spike gamma-phase can provide additional information about the firing rate, and likewise the sensory stimulus. Thirdly, spike phase information is especially important in sensory tasks where the information carried by firing rates reaches a ceiling, e.g., in fine discrimination tasks. Information in spike phase can then be employed to further increase the resolution of the sensory system. Fourthly, sensory systems already contain a large degree of redundancy, e.g. because different neurons have highly overlapping receptive fields and sensory tuning curves. This redundancy is required because the firing rates of individual neurons are not sufficiently reliable. Fifthly, even if spike phase did not add information to the firing rate, then the spike phase information could still be used differentially, e.g. through feedforward coincidence detection, spike time dependent plasticity, and rhythmic gain modulation. Spiking activity that is advanced in the gamma cycle will on average precede the spiking activity of other neurons. Thus, the early spikes are in an ideal position to potentiate synapses through the spike time dependent plasticity mechanism (Markram et al., 1997).

23.5.2 Dependence of firing rate coding on rhythmic-synchronization

Rate coding and rhythmic synchronization have traditionally been described as two separate processes that may serve complementary functions (Singer, 1999; Fries, 2005). However, changes in the rate code itself may be a consequence of changes in rhythmic synchronization. Differences in rhythmic synchronization at the pre-synaptic side may be converted into differences in rhythmic synchronization at the post-synaptic side through feedforward coincidence detection (Abeles, 1991; Aertsen et al., 1996, Fries et al., 1997; Fries et al., 2002) or rhythmic entrainment (Fries, 2005). However, rhythmic synchronization of pre-synaptic neuronal activity likely affects post-synaptic firing rates as well. Azouz and Gray (2000) showed that the output firing rate of V1 neurons can be better predicted by the amplitude of membrane potential gamma-band fluctuations than by the average or the slow component of the membrane potential. Consequently, gamma-synchronized spiking activity has a prominent role in shaping V1 orientation tuning (Azouz and Gray, 2003). In concordance, the most gamma-synchronized spikes are also the most orientation tuned (Womelsdorf et al., 2012), and the gamma-band LFP power is more tuned to orientation than the power of the low-frequency LFP components (Frien et al., 2000). A similar relationship between firing rate selectivity and gamma-band synchronization likely holds for other stimulus features as well. In V1, the gamma-band component of the LFP is most strongly tuned to contrast (Henrie and Shapley, 2005; Ray and

Maunsell, 2010). In MT, the LFP gamma-band power is more strongly tuned to speed and direction than low-frequency power is (Liu and Newsome, 2006). Rotermund et al. (2009) showed that the gamma-band power spectrum of V4 electrodes provides much more information about stimulus shape than was contained in low-frequency LFP oscillations. Finally, a positive attentional modulation of V4 firing rates corresponds to an increase in LFP gamma-band power, but a decrease in the power of low-frequency LFP oscillations (Fries et al., 2008), suggesting that the attentional modulations in firing rate are partially driven by changes in gamma-band synchronization.

Not only the strength of rhythmic synchronization, but also its phase may affect rate coding substantially. V1 neurons that are strongly driven by a visual stimulus, spike early in the gamma cycle (König et al., 1995; Vinck et al., 2010). These early spikes may, through feedback inhibition, suppress the firing rates of neurons that are less strongly driven by the same stimulus (Fries et al., 2007; de Almeida et al., 2009). This could serve to suppress firing rates for non-preferred stimuli, thereby sharpening firing rate selectivity. The critical parameter in such a scenario is the delay between excitation and inhibition. If a neuron fires early in the gamma cycle, then it may have either received excitatory inputs that fall relatively early in the gamma cycle, or it may trigger early excitatory inputs in co-tuned neurons, thereby escaping the rise of FS basket cell inhibition. Small changes in the delay between excitation and inhibition strongly affect output firing rates (Wehr and Zador, 2003; Wilent and Contreras, 2005; Kremkow et al., 2010). In auditory and barrel cortex, the delay between monosynaptic feedforward excitation and disynaptic feedforward inhibition is the crucial parameter that shapes the resulting rate code (Wehr and Zador, 2003; Wilent and Contreras, 2005).

An important function of gamma-band synchronization may be to act as a mechanism to filter out irrelevant information (König et al., 1996; Buzsáki, 2006). Noisy background activity that is not synchronized to the gamma rhythm will typically fail to impact output firing rates, since it is likely quenched by gamma-rhythmic inhibition. At the same time, the nervous system may focus the most information rich cortical computations at the phase in the gamma cycle where pyramidal cells escape inhibition. Indeed, in V1, there is enhanced orientation tuning at this gamma phase, independent of the number of spikes (Womelsdorf et al., 2012). Similarly, synchronous LGN spikes carry more stimulus information (Dan et al., 1998) and also have more impact on V1 cells (Alonso et al., 1996; Usrey et al., 2000). Thus, the gamma cycle may act as a filter that focuses information rich processes at the phase of low inhibition, at the same time quenching the majority of noise background inputs.

23.6 Conclusion

We have reviewed extensive evidence that gamma-band synchronization plays a fundamental role both in neural coding and in shaping neuronal interactions. The role of gamma-band oscillations in coding and information transmission is likely complementary: Local gamma-band synchronization can boost information processing by phase coding, and by focusing information-rich neuronal activity in narrow temporal windows with high excitability. Gamma phase-coupling between structures may serve a complementary function of boosting the reliability and speed of information transmission, and resolving the competition between converging inputs (Fries, 2005).

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