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# Reciprocal connectivity enhances frequency locking and phase coherence between gamma oscillations

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**Abstract**—The power spectrum of electrical signals recorded from the cortex shows distinct peaks at a variety of frequencies. In this work we study under which conditions two areas oscillating at initially different rhythms can lock their frequencies in the gamma band (30–90 Hz) by virtue of their synaptic interactions. To do so, we investigated the effect that the coupling topology, synaptic strength, and frequency detuning had on the emergence of locking and phase coherence between two conductance-based neuronal populations. Two measures of neuronal activity, local field potentials (LFP) and multi-unit activity (MUA) were extracted from the simulations to bridge the gap with experimental popular measures. Reciprocal topologies (bidirectional) favored the appearance of frequency locking and phase coherence, and thus offer a more robust connectivity for mechanisms exploiting the control of the coherence of neuronal oscillations as a flexible communication gating.

## 1. Introduction

During sleep and many behavioral states electrical signals recorded from the human cortex show local frequency peaks in their power spectra, which otherwise decrease with increasing frequency following a  $1/f^2$  power law [1]. In this study we focus on the gamma band (30–90 Hz), which is known to underlie many activated states. The mechanisms generating gamma-band oscillations rely on local recurrent inhibitory networks that modulate the excitability of neurons in a periodic manner [2]. Such fluctuating excitability makes the spiking probability of a neuron be correlated with the global oscillation phase [3]. The decay time constants of the inhibitory synapses determine the local gamma peak: slower synapses, i.e. longer time constants, give rise to slower oscillations.

Frequency locking of nonlinear oscillators to a periodic forcing depends on the strength of the coupling,

[4]: a sufficiently intense coupling is needed to bring two distant frequencies together. A similar behavior occurs between coupled autonomous oscillators. Coupling is usually assumed to be permanently active and a continuous function of the variables that are coupled. However, neurons are usually coupled by means of their chemical synapses, which are only effective when the membrane potential of the pre-synaptic neuron exceeds a certain excitability threshold. When the coupling is excitatory, it enhances the spiking activity of the postsynaptic neurons, and thus increases the frequency of the aforementioned recurrent excitatory-inhibitory cycle. Therefore, frequency locking between two neuronal areas does not behave as in the case of two coupled phase oscillators, because an excitatory synaptic coupling always triggers a decrease of the oscillatory period, larger for stronger couplings, and thus coupling can amplify the frequency difference.

As a result of the above-mentioned effect of coupling on the frequency, a specific connectivity between two areas is needed to achieve frequency synchronization. Under unidirectional coupling, the sending population must be faster than the receiving one and the bidirectional coupling must be asymmetric in such a way that the connections from the slower to the faster population must be weaker than in the opposite direction.

Brain activity can be measured by means of the local field potential (LFP), assumed to build up from the synaptic currents induced on well-aligned pyramidal (excitatory) neurons in the vicinity of the electrode, and the multi-unit activity (MUA), which reflects the spiking times of the neurons in the population. The fluctuating LFP reveals changes in the excitability of the local tissue: incoming action potentials arriving at the troughs of the signal have a higher probability of triggering spikes in comparison with those arriving within the low excitability state at the peaks of the signal. An efficient and dynamic gating of neuronal communication, known as the *communication through*

*coherence* hypothesis [5], can occur by modulating the phase difference and/or the phase coherence between oscillatory populations. Here we present simulations of oscillating neuronal populations and investigate the conditions for the appearance of locking and phase coherence. In particular, we tested which connectivity and synaptic strengths promote locking despite frequency mismatch in the isolated neuronal oscillators.

## 2. Model of neuronal populations

We have modeled two neuronal populations (representing cortical areas) each composed by 2000 neurons, with each neuron connecting randomly with 200 other neurons of the same area. 80% of the cells in each network are excitatory, [6]. Inter-areal connectivity is purely excitatory [7]. For those long-range connections, we assume an axonal conduction delay of 5 ms.

Each neuron is defined by its membrane potential and several channel gating variables, described by Hodgkin-Huxley equations. Excitatory and inhibitory synaptic currents are mediated by AMPA and GABA<sub>A</sub> receptors, respectively, with an elicited conductivity time-course in the shape of an alpha function. The rise and decay times of inhibitory synapses control the frequency of gamma oscillations. Afferent connections to each population from lower cortical or subcortical areas is represented by an external input in the form of an inhomogeneous Poisson train of incoming excitatory post-synaptic potentials (EPSPs). The instantaneous rate of this input is generated by an Ornstein-Uhlenbeck process, which fits the basic features of naturalistic stimuli driving the cortex. The inhomogeneous Poisson-train stimulation induces low frequency activity and contributes to the  $1/f^2$  power spectral profile of the simulated LFPs.

We calculate the LFP from the sum of the absolute value of the excitatory  $|I_{\text{AMPA}} + I_{\text{ext}}|$  and inhibitory  $|I_{\text{GABA}}|$  synaptic currents impinging on excitatory neurons [8]. A typical trial consisted of a 4-second realization of the dynamics of both networks. During the first second the two populations were driven by an external input (an inhomogeneous Poisson process with mean = 5000 Hz and variance = 400 Hz). For the next two seconds the rate of the external input is increased (mean = 7300 Hz), mimicking the arrival of excitatory drive possibly due to sensory stimulation. Concomitantly with the external rate increase, a peak appears in the gamma range on the LFP spectrum, as shown in Fig. 1 (b), at a frequency that we use as a measure of the rhythm of that area. This bump in the gamma-band of the LFP power spectrum is relatively broad and therefore, the associated oscillations are not harmonic. The MUA is assumed to be the histogram of spiking times of all neurons from a single population.

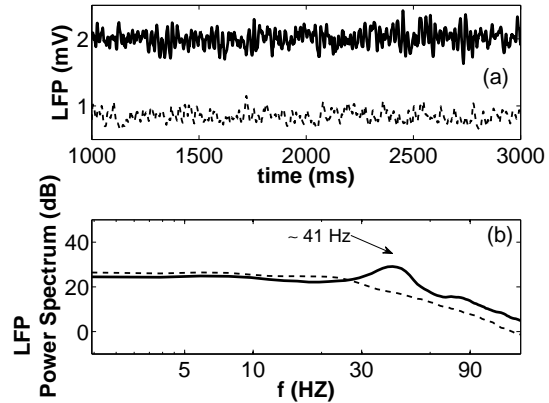


Figure 1: (a) Time trace of the LFP and (b) corresponding power spectrum for a decay time  $GABA_A = 5$  ms and an external mean rate of 7300 Hz (solid line) and 5000 Hz (dashed line).

We performed 400 simulations each representing a different experimental trial. From trial to trial the random connectivity and the realization of the Ornstein-Uhlenbeck process are varied.

## 3. Frequency locking

We have coupled two populations of neurons both unidirectionally and bidirectionally. We have considered three parameters to characterize this connectivity: *efferent parameter*  $E$ , defined as the percentage of excitatory neurons in a population projecting to the other area, *afferent parameter*  $A$  as the percentage of neurons in a population receiving input from a single excitatory neuron from the other area, and the *relative strength*  $F$  of AMPA intra-area synapses with respect to AMPA inter-area synapses. Increasing these values leads to an increase in the connectivity between areas.

The strength of the connectivity modifies the frequency content of the LFP power spectrum, since the discharge rates of neurons vary accordingly. Enhancing the spiking activity of the excitatory population can shorten the period of the cycle inhibition-excitation. In fact, lower stimulus intensities produce slower oscillations by inducing less suprathreshold activity (results not shown).

**Unidirectional coupling** In a unidirectional coupling, one of the neuronal populations is the sending area ( $s$ ) and the other the receiving area ( $r$ ). Due to the excitatory long-range connections, the average population firing rate of the receiving area increases and its local peak shifts towards higher frequencies when the coupling is turned on. We have varied the decay time of GABA<sub>A</sub> synapses of the receiving population from 3 ms to 8 ms in 1 ms intervals, leading

$GABA_A$ decay time (ms)	gamma local peak (Hz)
3	$51.85 \pm 0.42$
4	$45.85 \pm 0.37$
5	$41.01 \pm 0.00$
6	$37.01 \pm 0.42$
7	$33.20 \pm 0.00$
8	$31.25 \pm 0.00$

Table 1: Relation between the decay time of the  $GABA_A$  synapses and the local peak of the LFP power spectrum at the gamma range, for an isolated population. Mean frequency values are obtained from averaging over 20 peaks among the 400 total trials. The errors correspond to the standard deviation.

to oscillations in the range of 30–60 Hz (see Table 1), while the other population remained at 5 ms (its corresponding frequency of  $\sim 41.01$  Hz is shown as a solid vertical line in Figs. 2 and 3).

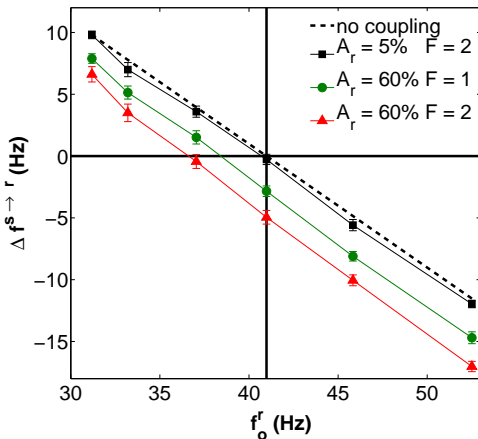


Figure 2: Frequency detuning,  $\Delta f^{s \rightarrow r}$ , in the gamma range between the unidirectionally coupled sending and receiving area with respect to the local frequency peak of the receiving area in the absence of coupling,  $f_o^r$ . Three value pairs of the afferent parameter  $A$  and relative strength  $F$  are considered.  $E_s=60\%$ .

As mentioned above, unidirectional coupling speeds up the rhythm of the receiving area. Naturally, in this case the two frequencies approach each other when the sending area is faster than the receiving area (left side of the solid vertical line in Fig. 2), otherwise they become more different due to the coupling. No frequency-locking range appears because the activity of the sending area is not modulated according to the spiking of the receiving area.

**Bidirectional coupling** When two neuronal populations are coupled bidirectionally, no distinction between receiving and sending area can be made.

Rather, the firing activity in each population is influenced by each other. Under bidirectional chemical coupling the output from one population has some fingerprints of the population receiving this input.

We have tuned the three connectivity parameters  $A$ ,  $E$ , and  $F$  in the two coupling directions, so that the pathway between the faster and the slower population is stronger than the reverse pathway. We will denote by 1 the neuronal population with a decay time of the  $GABA$  synapses equal to 5 ms, and by 2 the neuronal population with a varying decay time of the  $GABA$  synapses. Fig. 3 shows two regimes: one in which the local gamma frequency peak of 2 is faster than that of 1 (white area) and another one in which the local gamma frequency peak of 2 is slower than in 1 (shaded area). Both regimes are separated by a solid vertical line at the frequency of 1 ( $\sim 41.01$  Hz).

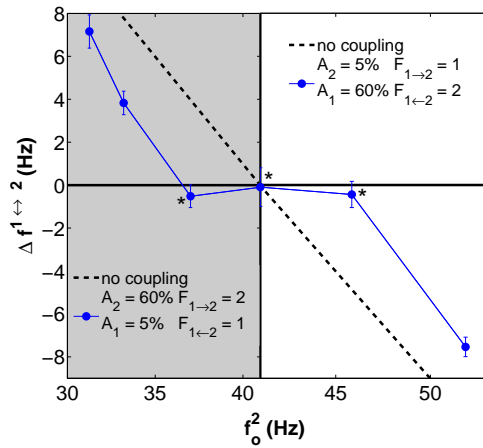


Figure 3: Frequency detuning,  $\Delta f^{1 \leftrightarrow 2}$ , in the gamma range between the bidirectionally coupled areas with respect to the frequency local peak of the area 2 when the coupling is turned off,  $f_o^2$ . The horizontal axis corresponds to the values shown in Table 1.  $E=60\%$ . The asterisks label the frequency locking range.

The frequency locking range (marked with asterisks in Fig. 3), defined as the region in which the frequency detuning  $\Delta f^{1 \leftrightarrow 2}$  approaches 0, arises only when the coupling is bidirectional and the strength of the connections from the faster to the slower neuronal area is stronger than the reverse connection.

#### 4. Phase Coherence

When the networks are coupled, the EPSPs elicited at one population by the spikes coming from the other population can affect the timing of action potential generation. This, in turn, is reflected as a change of the LFP phase.

The relative phase between two areas modulates the response of neurons to the incoming EPSPs. The peaks of the LFP time series correspond to maximum

values of the inhibitory activity,  $I_{GABA}$ , and thus at those phases it is more difficult to trigger a spiking response. Phase coherence is a measure of how consistent a difference in phase is between two signals,  $x$  and  $y$ , across  $N$  different trials:

$$C_{yx}(f) = \frac{1}{N} \sum_n \frac{S_{yx}(f, n)}{|S_{yx}(f, n)|} \quad (1)$$

where  $S_{yx}(f, n)$  is the cross-spectral density estimate at frequency  $f$  of trial  $n$ , [9]. It ranges between 0 and 1, with 0 arising when the phase difference is randomly distributed.

We have calculated the level of phase coherence between the LFP signal of one area and the MUA of the other area. Under unidirectional coupling, phase coherence appears only when the sending area is faster than the receiving area, Fig. 4 (top) (results shown for the green circles in Fig. 2). This regime corresponds to the left area of the solid vertical line in Fig. 2, when the two frequency peaks in the gamma range approach due to the coupling. For bidirectional coupling phase coherences arises both between the LFP signal of area 1,  $LFP_1$ , and the MUA signal of area 2,  $MUA_2$  (Fig. 4, middle), and between the LFP signal of area 2,  $LFP_2$ , and the MUA signal of area 1,  $MUA_1$  (Fig. 4, bottom). When area 2 is slower than area 1 ( $f_o^2 < 41.01$  Hz), the phase coherence between  $LFP_1$  and  $MUA_2$  concentrates in the gamma range but is distributed across a wider frequency range for  $LFP_2$ - $MUA_1$  phase coherence. The contrary happens when area 2 is faster than area 1 ( $f_o^2 > 41.01$  Hz).

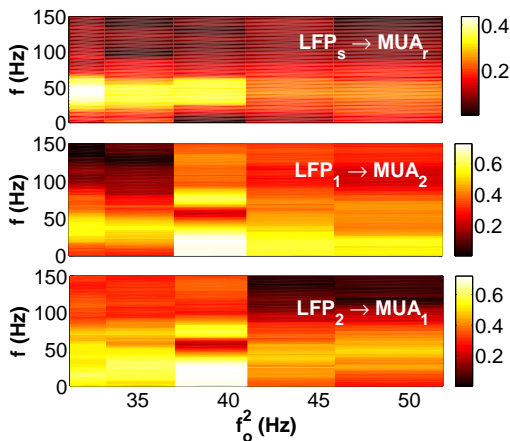


Figure 4: Phase coherence map between the LFP of one area and the MUA of the other, as a function of the frequency in the absence of coupling, for unidirectional (top) and bidirectional (middle and bottom) coupling.

## 5. Discussion

We have observed, for a simple coupling scheme between two neuronal populations, that frequency lock-

ing in the gamma range appears only when the connectivity is bidirectional. Moreover, locking requires the connectivity between the two populations to be asymmetric because the synapses connecting the faster population to the slower one must be stronger than the reverse pathway. This is a consequence of the fact that excitatory connections among areas produces a shift towards faster rhythms by increasing the firing rate activity of the postsynaptic area.

Phase coherence between the LFP and MUA signals is observed even in the absence of frequency locking. For unidirectional coupling, phase coherence is higher when the sending area is faster than the receiving area. This could be due to a larger effect of the presynaptic spikes on postsynaptic neurons when the latter fire at lower rates. For bidirectional coupling, phase coherence also appears, being concentrated in the gamma range in one direction (from the fast to the slow area), while the reverse direction (from the slow to the fast area) also shows high coherence at slower rhythms.

In a more physiological context, bidirectional coupling could represent, for instance, a combination of top-down and bottom-up connectivity. Our work suggest that asymmetries such as modulatory vs. driving connectivity, e.g. possibly occurring in the reciprocal connectivity between different hierarchical areas, might favor the establishment of common rhythmic oscillations via frequency locking. Although phase coherence appears for certain coupling architectures, further work has to show whether coherence can be used to effectively transmit spikes.

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