

# Feedback Suppression of Neural Synchrony in Two Interacting Populations by Vanishing Stimulation

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**Abstract** We discuss the suppression of collective synchrony in a system of two interacting oscillatory networks. It is assumed that the first network can be affected by the stimulation, whereas the activity of the second one can be monitored. The study is motivated by ongoing attempts to develop efficient techniques for the manipulation of pathological brain rhythms. The suppression mechanism we consider is related to the classical problem of interaction of active and passive systems. The main idea is to connect a specially designed linear oscillator to the active system to be controlled. We demonstrate that the feedback loop, organized in this way, provides an efficient suppression. We support the discussion of our approach by a theoretical treatment of model equations for the collective modes of both networks, as well as by the numerical simulation of two coupled populations of neurons. The main advantage of our approach is that it provides a vanishing-stimulation control, i.e., the stimulation reduces to the noise level as soon as the goal is achieved.

**Keywords** Neuronal synchrony · Global coupling · Hopf bifurcation

## 1 Introduction

Synchronization is believed to play a key role in the pathogenesis of several neurological diseases, such as Parkinson's disease and essential tremor (see, e.g., [1–3] and references therein). For example, it is hypothesized that Parkinsonian symptoms result from a synchronized pacemaker-like activity of a population of many thousands of neurons in the basal ganglia, whereas normal functioning of the basal ganglia is characterized by an uncorrelated firing of neurons. This hypothesis is supported by several experimental studies [4–7]. Thus, suppression of the abnormal neural activity, or, in physical terms, destruction

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of an undesired synchrony in neural populations, constitutes an important clinical problem. In severe cases, when the disease cannot be treated by a standard medication, this problem is currently being solved with the help of a neurosurgical procedure, called *deep brain stimulation (DBS)* [8–10]. DBS implies permanent electrical stimulation of the brain tissue via implanted microelectrodes. The electrodes deliver current pulses with frequency greater than 100 Hz from a subcutaneously implanted controller. As a result, the amplitude of the Parkinsonian tremor essentially decreases. In spite of the efficiency of such a stimulation, its usage is complicated by several side-effects like speech problems (dysarthria, dysphasia); abnormal, involuntary muscle contractions (dystonia, dyskinesia); facial and limb muscle weakness or partial paralysis (paresis); etc. For example, permanent stimulation requires frequent (about every 3 years) exchange of the battery of the implanted controller, which means another minor surgery. Next, it is important to note that the mechanisms of DBS are still being debated and the parameters of stimulation are being chosen empirically.

Recently, several methods for suppression of neural synchrony were introduced in theoretical studies, with the ultimate goal of substituting the standard DBS with a more mild and efficient technique. These methods can be roughly classified into two groups: nonfeedback (see [1, 11] and references therein) and feedback techniques [12–15]. A simple and efficient technique, which restores asynchronous dynamics in a network of oscillatory neurons, was presented in our previous publication [16]. The main idea of this approach is related to the classical problem of oscillation theory, namely to the problem of interaction of an active system (or medium) with a passive one.<sup>1</sup> Classical oscillation theory treats interaction between an active, self-sustained oscillator and a passive load (resonator). It is known (see, e.g., [17]) that, for certain parameters, the passive system, coupled to the active one, can quench the oscillations of the latter. In a more complex setting, one can analyze the dynamics of an ensemble of (infinitely) many interacting units for the case when some units exhibit self-sustained oscillations, whereas the other units are passive. Thus, one can speak of interaction between active and passive subpopulations. The dynamics of such mixed populations of oscillators has been investigated in [18, 19]. It was reported that the collective dynamics of the ensemble (mean field) depend on the ratio between the numbers of active and passive oscillators. In particular, for certain ratios and parameters, the mean field oscillation vanished.

In our approach, we exploit this idea by designing a passive unit and coupling it to the neuronal population to be controlled. From the control theory viewpoint, it means designing a linear feedback loop with a built-in, second-order filter. The destruction of an undesirable synchronous oscillation is accomplished as follows: the activity of a neural population is permanently measured and fed back after linear processing. The main advantage of the suggested technique is that the administered control input vanishes as soon as a desynchronized state is achieved. This feature is extremely important for therapeutic applications since it means significant reduction of intervention into a living tissue.

In the present paper, we extend our previous work on nondelayed feedback suppression [16] to treat a more complicated case of two interacting populations of neurons. This is motivated by the fact that stimulation and measurement electrodes can be implanted into two nonoverlapping, though interacting, populations: the first one is affected by the stimulation, while the collective activity is registered from the second one. Generally speaking, the second population can be, by itself, both active and passive; below, we

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<sup>1</sup>By active system, we mean a self-sustained oscillator capable of producing stable oscillations without external forces. On the contrary, a passive system oscillates only in response to external driving.

consider both cases. Next, we demonstrate that feedback loop parameters can be easily determined by a test stimulation.

### 1.1 Synchrony in Neural Populations

The most frequently used model, describing the collective dynamics in a large population of self-sustained oscillators, is the model of globally (all-to-all) coupled units. It is well known that if the coupling strength exceeds some threshold, which depends on the frequency distribution of elements, such a population becomes synchronized via the *Kuramoto transition* [20–22]. Synchronization is manifested by the appearance of nonzero mean field oscillation.

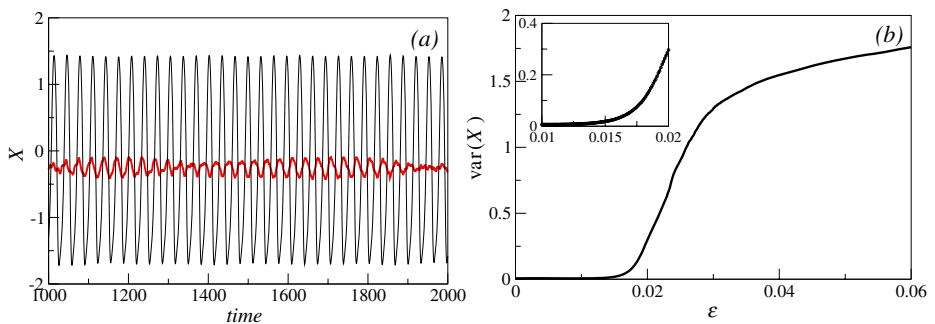
We illustrate the Kuramoto transition by considering an ensemble of  $N$  Bonhoeffer–van der Pol oscillators, coupled via the mean field in the  $x$  variable:

$$\begin{aligned} \dot{x}_i &= x_i - x_i^3/3 - y_i + I_i + \varepsilon X, \\ \dot{y}_i &= 0.1(x_i + 0.7 - 0.8y_i). \end{aligned} \tag{1}$$

Each unit is driven by the force  $\varepsilon X$ , where  $\varepsilon$  quantifies the strength of the mean field coupling and  $X = N^{-1} \sum_{i=1}^N x_i$  is the mean field. Parameter  $I_i$  has the meaning of the external current and directly influences the spiking frequency of elements of the ensemble. The elements are not identical: parameter  $I_i$  is taken as  $I_i = 0.6 + \sigma$ , where  $\sigma$  is a Gaussian distributed number with zero mean and 0.1 rms value. For coupling strength below the critical value,  $\varepsilon < \varepsilon_{cr} \approx 0.015$ , one observes small irregular fluctuations of the mean field  $X$  around  $X_0 \approx -0.25$  (see the bold line in Fig. 1a for an example computed for  $N = 500$  and  $\varepsilon = 0.01$ ); these fluctuations are due to the finite size of the ensemble. With the increase of  $\varepsilon$  beyond the critical value  $\varepsilon > \varepsilon_{cr} \approx 0.015$ , the oscillators of the ensemble synchronize (see the solid line in Fig. 1a computed for  $\varepsilon = 0.03$ ).

### 1.2 Desynchronization from the Control Theory Viewpoint

Desynchronization can be viewed as stabilization of an unstable asynchronous state of the population. For *low-dimensional systems*, stabilization is a standard problem of control theory [23]. A basic method used for this purpose is a feedback control. Typically, the feedback signal is proportional to the deviation of a coordinate of the system from the



**Fig. 1** **a** The evolution of the mean field of a population of 500 Bonhoeffer–van der Pol neurons (1) for subcritical coupling  $\varepsilon = 0.01$  (bold line) and supercritical coupling  $\varepsilon = 0.03$  (solid line). **b** Transition to the macroscopic mean field in the model (1)

desired state (proportional control), to the derivative of the coordinate (proportional-derivative control), to the integral of the coordinate over the past (proportional-integral control), or to a combination of these three values [23].

We remind the reader that, in view of a possible neuroscience application, it is important to provide a *vanishing-stimulation control*. Clearly, the control proportional to the deviation of a state variable  $x$  from the equilibrium state (or operating point)  $x_0$ , i.e.,  $\mathcal{C} \sim (x - x_0)$ , vanishes only if the equilibrium point of the system is accurately known. However, in many experimental situations, the locations of the operating point and the model equations are generally uncertain. This problem can be overcome by using a first-order filter (washout filter) in the feedback loop (see [24–26] and references therein) or a time-delayed feedback (see, e.g., [27–30] and references therein):  $\mathcal{C} \sim f(x(t - \tau))$ , where  $f$  is a feedback function and  $\tau > 0$  is the delay.

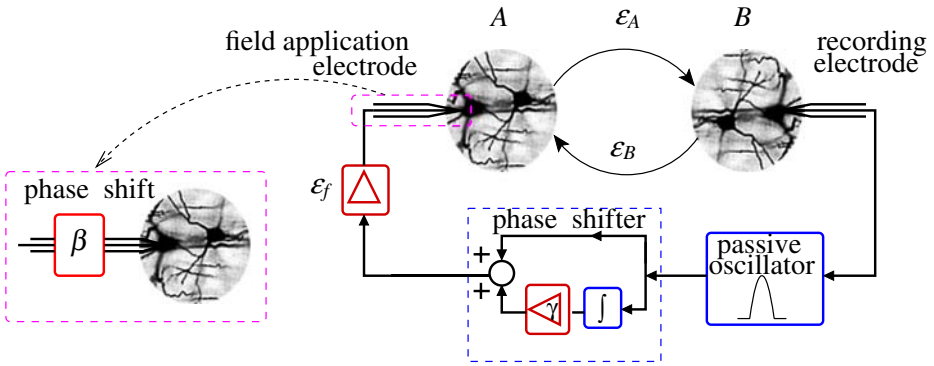
Stabilization of an unstable asynchronous state of a *high-dimensional system*, i.e., in an ensemble of globally coupled units by means of linear time-delayed feedback, was treated numerically and analytically in [13–15]. It has been demonstrated that feedback of the form  $\mathcal{C} \sim (X(t - \tau) - X(t))$ , where  $X(t)$  is the mean field of the population, provides a reliable suppression of collective synchrony, i.e.,  $\text{var}(X) \rightarrow 0$ , with vanishing stimulation,  $\mathcal{C} \rightarrow 0$ . Simulations show that this technique does not influence the activity of the individual units. On the other hand, if the feedback is proportional to the delayed mean field,  $\mathcal{C} \sim X(t - \tau)$  [13, 14] or to its power [12, 28, 29], then the stimulation is generally non-vanishing; i.e., a permanent stimulation with  $\mathcal{C} = \text{const}$  is required for the maintenance of the suppressed state,  $\text{var}(X) \rightarrow 0$ . Note that, in the context of chaos control, vanishing-stimulation techniques are called noninvasive. We do not use this expression here since, from the viewpoint of neuroscience, a technique using implanted electrodes is invasive.

In summary, the delayed feedback scheme can provide suppression with a vanishing stimulation property. However, the delay term can bring a new, undesirable instability into the system, and thus, the scheme requires a careful parameter tuning. Below, we show that efficient suppression can be achieved by a feedback circuit without delay. The scheme we discuss is very simple and can be easily implemented in hardware.

### 1.3 Linear Feedback Control Scheme: Assumptions and Requirements

As already mentioned, in our previous publication [16], we introduced an efficient technique for control of collective synchrony in a large population of globally coupled elements; we suggested that this technique can be used for the suppression of pathological brain rhythms with the help of DBS. Our approach is based on several assumptions and requirements. We proceed with the assumption that the collective activity of many neurons is represented in the local field potential (LFP), which can be continuously monitored in an experiment and, subsequently, after a certain processing, used for stimulation of the brain tissue via a feedback loop. We also assumed that the signal from the whole network can be registered and that the whole network can be stimulated. However, for practical applications, it is important to consider the situation when the measurement and stimulation electrodes are implanted into different, but interacting, neural populations.

For this reason, in this paper, we treat a model of two interacting globally coupled ensembles (cf. [15, 31–33]), where one population is supposed to be affected by the stimulation derived from collective activity (LFP) of the second one (see Fig. 2). Next, we require that, as soon as the desired asynchronous state is achieved, the control signal should vanish, or, strictly speaking, should decrease to the noise level (vanishing-stimulation control).



**Fig. 2** Suggested suppression scheme. The LFP of the population *B* is measured by the recording electrode and is fed back via the field application electrode to the population *A*. The feedback loop contains a passive oscillator playing the role of a band pass filter, an integrator, a summator, and two amplifiers

Furthermore, the control scheme should be able to compensate an a priori unknown phase shift, inherent to stimulation. This phase shift  $\beta$  is determined by the way the stimulation is incorporated into the model equations (note that the exact electrophysiological mechanism by which stimulation improves motor symptoms is unknown) and by organization of internal coupling in the ensemble (see discussion in [14]).

The control technique should also be able to compensate for latency in measurements. Another requirement is that the controller should be able to extract the relevant signal from its mixture with the rhythms produced by neighboring neuronal populations and with the measurement noise.

## 2 Stability Analysis of Two Interacting Neuronal Ensembles

In this section, we analyze the controlled dynamics of two interacting ensembles of neurons. It is assumed that the elements within each population are globally coupled and the interaction between these populations is of the mean field type, i.e., the mean field *A* of one ensemble acts on all elements of the second ensemble *B* and, vice versa, the mean field *B* of the second influences all elements *A*.

### 2.1 Model Equations

First, we consider the stabilization problem at a macroscopic level, taking into account only the collective dynamics. Assuming that the collective oscillating mode is close to a Hopf bifurcation, we write two symmetrically coupled equations for the complex amplitudes *A*, *B*:

$$\begin{aligned} \dot{A} &= (\xi_1 + i\omega_1)A - |A|^2 A + \varepsilon(B - A) + C e^{i\beta}, \\ \dot{B} &= (\xi_2 + i\omega_2)B - |B|^2 B + \varepsilon(A - B). \end{aligned} \tag{2}$$

Here,  $\mathcal{C}$  is the control signal (stimulation) and the phase shift  $\beta$  describes the uncertainty of our action on the active oscillator. Let us include in the control loop a linear damped oscillator driven by the measured signal:

$$\ddot{u} + \alpha \dot{u} + \omega_0^2 u = X(t) = \text{Re}(B). \tag{3}$$

We set the oscillator frequency  $\omega_0$  equal to the frequency  $\omega$  of uncontrolled mean field oscillations; this frequency can be easily determined by a standard technique (see, e.g., [21]). Thus, the driven oscillator (3) is in resonance with the forcing (for a moment, we can consider it as a harmonic one with the frequency  $\omega = \omega_0$ ). This means that the phase of the output  $u$  is shifted by  $\pi/2$  with respect to the phase of the input  $X(t)$ , whereas the phase shift of the derivative of the output signal  $\dot{u}$  with respect to the input  $X(t)$  is zero. Hence, stimulation proportional to  $-\dot{u}$  is in antiphase with the collective mode  $X(t)$ , to be suppressed, and therefore, this stimulation will reduce collective synchrony. It is important to note that the variable  $\dot{u}$  does not contain a constant component,  $\langle \dot{u} \rangle = 0$ , even if the observed field does. Thus, a stimulation proportional to  $\dot{u}$  vanishes as soon as the goal of the control is achieved, and, hence, the main requirement to the control strategy is satisfied. It is of importance that the unit (3) offers an advantage of a band pass filter: it filters out noise and other components outside of the vicinity of the main oscillation mode.

Now, we recall that the stimulation is characterized by an unknown phase shift  $\beta$  that should be compensated to ensure the required phase relations between the measured signal and the stimulation. For this purpose, we include in the feedback loop a phase-shifting unit, described by

$$\mu \dot{d} + d = \dot{u}. \tag{4}$$

For  $\mu\omega \gg 1$ , this unit operates as an integrator, with an additional multiplication by the factor  $1/\mu$ , whereas for  $\mu\omega \rightarrow 0$ , its transfer function is 1. Hence, the output of system (4) has the same average as the input, i.e.,  $\langle d \rangle = 0$ . We take the control signal  $\mathcal{C}$  to be proportional to the weighted sum of  $\dot{u}$  and  $d$ :  $\mathcal{C} \sim \varepsilon_f (\dot{u} + \gamma d)$ , where the parameter  $\gamma$  determines the desired phase shift. The units performing this summation and the integration according to (4) form the *phase shifter*. It is easy to show that the phase difference  $\theta$  between the output  $\dot{u} + \gamma d$  of the phase shifter and its input  $\dot{u}$  is

$$\theta = -\arctan\left(\frac{\gamma}{\omega\mu}\right), \tag{5}$$

and, therefore, can be arbitrarily varied in the interval  $-\pi/2 < \theta < \pi/2$ . The phase shift in the interval  $\pi/2 < \theta < 3\pi/2$  can be obtained by sign inversion:  $\varepsilon_f \rightarrow -\varepsilon_f$ . Summarizing, the control input  $\mathcal{C}$  to the system reads

$$\mathcal{C} = \pm \frac{\varepsilon_f}{\sqrt{1 + \gamma^2/\omega^2\mu^2}} (\dot{u} + \gamma d) = \varepsilon_f \cos \theta \cdot (\dot{u} - \omega\mu d \tan \theta), \tag{6}$$

where  $\sqrt{1 + \gamma^2/\omega^2\mu^2} = 1/\cos \theta$  is the normalization coefficient. It ensures an independence of the amplification in the feedback loop from the phase shift  $\theta$ , so that this amplification is completely determined by  $\varepsilon_f$ . At the points  $\theta = \pm\pi/2$ , the control term is calculated as  $\mathcal{C} = \varepsilon_f \omega\mu d$ .

Finally, we write the equations for the controlled system as

$$\begin{aligned}
 \dot{A} &= (\xi_1 + i\omega_1)A - |A|^2 A + \varepsilon(B - A) + C e^{i\beta}, \\
 \dot{B} &= (\xi_2 + i\omega_2)B - |B|^2 B + \varepsilon(A - B), \\
 \ddot{u} + \alpha \dot{u} + \omega_0^2 u &= \text{Re}(B), \\
 \mu \dot{d} + d &= \dot{u}.
 \end{aligned}
 \tag{7}$$

Choosing appropriate values of parameters (frequencies  $\omega_{1,2}$  and increments  $\xi_{1,2}$ ), we can implement different regimes. To analyze the stability of the asynchronous solution  $A = B = 0$ , we consider only the linear terms in (2) and substitute  $A = a_1 + ia_2$ ,  $B = b_1 + ib_2$ ,  $\dot{u} = v$  in (7). Writing separately the real and imaginary parts, we obtain:

$$\begin{aligned}
 \dot{a}_1 &= \xi_1 a_1 - \omega_1 a_2 + \varepsilon(b_1 - a_1) + \mathcal{E}(v + \gamma d) \cos \beta, \\
 \dot{a}_2 &= \xi_1 a_2 + \omega_1 a_1 + \varepsilon(b_2 - a_2) + \mathcal{E}(v + \gamma d) \sin \beta, \\
 \dot{b}_1 &= \xi_2 b_1 - \omega_2 b_2 + \varepsilon(a_1 - b_1), \\
 \dot{b}_2 &= \xi_2 b_2 + \omega_2 b_1 + \varepsilon(a_2 - b_2), \\
 \dot{u} &= v, \\
 \dot{v} + \alpha v + \omega_0^2 u &= b_1, \\
 \mu \dot{d} + d &= \dot{u}.
 \end{aligned}
 \tag{8}$$

Here, we denote  $\mathcal{E} = \varepsilon_f / \sqrt{1 + \gamma^2 / \mu^2 \omega_0^2} = \varepsilon_f \cos \theta$ . Seeking the solution in the form  $a_1 = A_1 e^{\lambda t}$ ,  $a_2 = A_2 e^{\lambda t}$ ,  $b_1 = B_1 e^{\lambda t}$ ,  $b_2 = B_2 e^{\lambda t}$ ,  $u = U e^{\lambda t}$ ,  $v = V e^{\lambda t}$ , and  $d = D e^{\lambda t}$ , we obtain the algebraic system of seven linear equations. This system has a nontrivial solution if its determinant is equal to 0; this condition provides the equation  $f(\lambda, \mathcal{E}, \gamma) = 0$ . The border of the stability domain is determined by the condition  $\text{Re}(\lambda) = 0$ . Therefore, taking  $\lambda = i\Omega$  on the stability border and separating real and imaginary parts, we obtain two real equations:

$$\begin{aligned}
 f_r(\Omega, \mathcal{E}, \gamma) &= 0, \\
 f_i(\Omega, \mathcal{E}, \gamma) &= 0.
 \end{aligned}
 \tag{9}$$

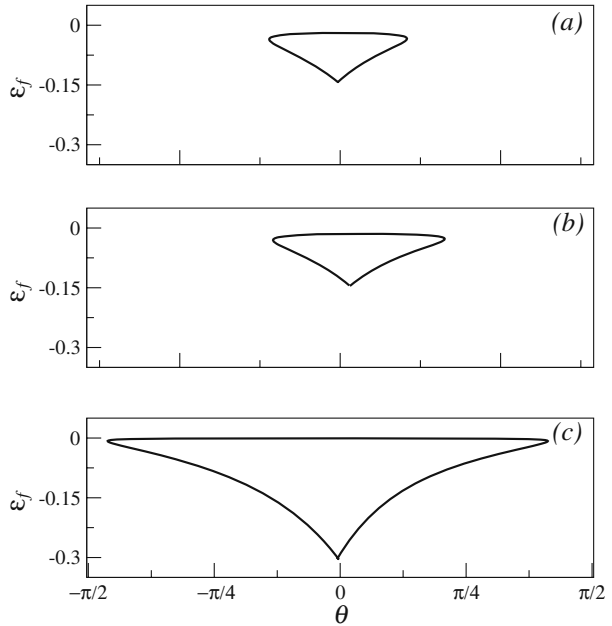
Both equations are linear with respect to  $\mathcal{E}$  and  $\gamma$ . Therefore, this system can be solved with respect to  $\gamma$  and  $\mathcal{E}$  and, taking into account of (5) and  $\varepsilon_f \cos \theta = \mathcal{E}$ , rewritten as

$$\begin{aligned}
 \theta &= \theta(\Omega), \\
 \varepsilon_f &= \varepsilon_f(\Omega).
 \end{aligned}
 \tag{10}$$

These are the equations of the stability border in the parameter plane  $(\theta, \varepsilon_f)$  in parametric form; these expressions are very lengthy and, therefore, not presented here.

Different regimes can be implemented by choosing appropriate values of frequencies  $\omega_{1,2}$  and increments  $\xi_{1,2}$ . Let us consider first the case of two interacting identical subsystems ( $\omega_1 = \omega_2 = \omega_0 = 1.0$ ,  $\xi_1 = \xi_2 = 0.02$ ). The stability domain in the parameter plane  $(\theta, \varepsilon)$ , i.e., the region where the control is efficient for this case, is presented in Fig. 3a. Second, we take two nonidentical populations,  $\omega_1 = 1.0$ ,  $\omega_2 = 1.04$ ,  $\omega_0 = 1.0$ . The results show (see Fig. 3b) that suppression can be achieved in this case as well. Finally, we model a situation when the population, from which LFP is measured, is, by itself, passive. This may reflect the case when the recording electrode is placed rather far from the region of pathological activity, e.g., on the surface of the scalp. We illustrate this case in Fig. 3c.

**Fig. 3** Stability domains (areas inside *closed curves*) for the controlled model system (7) for the case of identical (a) and nonidentical (b) subpopulations. c The case when the population B, where the measurement is performed, is stable ( $\xi_2 = -0.02$ ). The other parameters are:  $\varepsilon = 0.05$ ,  $\alpha = 0.3\omega_0$ ,  $\mu = 500$ , and  $\beta = 0$ . Note that stability of the fixed point  $A = B = 0$  corresponds to the asynchronous dynamics of the oscillator ensemble. Instability of the fixed point corresponds to synchronous ensemble dynamics with nonzero mean field



### 2.2 Numerical Example: Two Coupled Bonhoeffer–van der Pol Populations

To compare the above obtained results of theoretical analysis with results of numerical simulation, we consider two interacting ensembles of  $N$  globally coupled Bonhoeffer–van der Pol oscillators:

$$\begin{aligned}
 \dot{x}_{Ai} &= x_{Ai} - x_{Ai}^3/3 - y_{Ai} + I_{Ai} + \varepsilon_A X_A + \mathcal{K}(X_B - X_A) + \mathcal{C} \cos \psi, \\
 \dot{y}_{Ai} &= 0.1(x_{Ai} + 0.7 - 0.8y_{Ai}) + \mathcal{C} \sin \psi, \\
 \dot{x}_{Bi} &= x_{Bi} - x_{Bi}^3/3 - y_{Bi} + I_{Bi} + \varepsilon_B X_B + \mathcal{K}(X_A - X_B), \\
 \dot{y}_{Bi} &= 0.1(x_{Bi} + 0.7 - 0.8y_{Bi}), \\
 \ddot{u} + \alpha\dot{u} + \omega_0^2 u &= X_B, \\
 \mu\dot{d} + d &= \dot{u},
 \end{aligned}
 \tag{11}$$

where the two last equations describe the feedback loop, namely, the linear damped oscillator and integrator. Here,  $x$  and  $y$  correspond to the axon’s membrane potential and refractivity, respectively. The oscillators within each ensemble are globally coupled via the mean fields  $X_{A,B} = N^{-1} \sum_i x_{Ai,Bi}$ , with the internal coupling strengths  $\varepsilon_A$  and  $\varepsilon_B$ ;  $i = 1, \dots, N$  is the index of the neuron. Parameters  $I_{Ai,Bi}$  represent the external current and directly influence the spiking frequency of elements of both ensembles. In our case, the oscillators are not identical:  $I_{Ai} = 0.6 + \sigma$ ,  $I_{Bi} = 0.62 + \sigma$ , where  $\sigma$  is a Gaussian distributed number with zero mean and 0.1 rms value.<sup>2</sup> The external stimulus administered

<sup>2</sup>The following conclusions hold also for identical oscillators in the presence of noise.



to all elements of the first population is modeled by including an additional term on the right-hand side of the Bonhoeffer–van der Pol equations and has the same form as in (6). The parameter  $\psi$  describes the uncertainty of how the stimulation enters the equations, i.e., how the external force is distributed between the two equations. Note that the parameter  $\psi$  is related, but not equal, to the parameter  $\beta$  in (2).

The results of the simulation for  $N = 10000$  oscillators in each population are shown in Fig. 4 for the following set of parameters: internal coupling  $\varepsilon_A = \varepsilon_B = 0.03$ ,  $\mathcal{K} = 0.1$ , and  $\psi = 0$ ,  $\theta = 0.03$ . The parameters of the band pass filter and integrator are:  $\omega_0 = 2\pi/32.5$  and  $\mu = 500$ . The damping factor  $\alpha$  of the oscillator (3) determines the width of the band pass,  $\Delta f = \alpha/2\pi$ . Having in mind the application to Parkinsonian brain rhythms with realistic values for the band pass from 10 to 13 Hz (see, e.g., power spectrum of an MEG signal of a Parkinsonian patient in [34]), we choose  $\Delta f/f \approx 0.3$ , which gives  $\alpha = 0.3\omega_0$ .

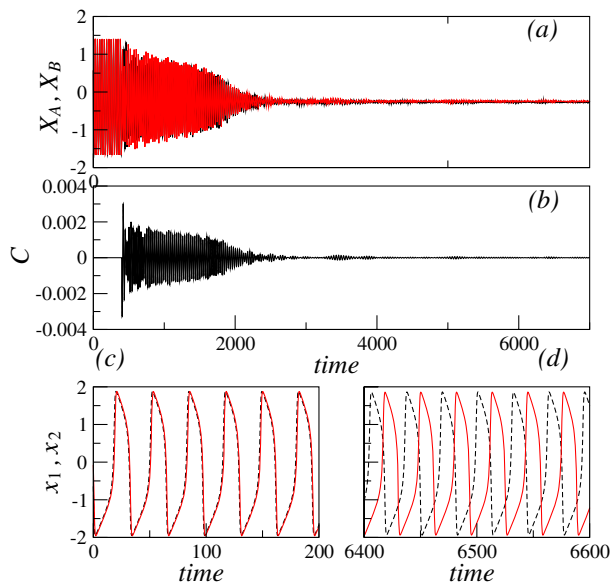
Figure 4a presents the mean field dynamics of the subsystems  $A$  and  $B$ . The control signal is switched on at  $t_0 = 400$ , i.e.,  $\varepsilon_f = 0$  for  $t < t_0$  and  $\varepsilon_f = -0.012$  for  $t \geq t_0$  (see Fig. 4b). Switching the stimulation on leads to the desynchronization in both subpopulations. We quantify the suppression of the mean field oscillation by introducing the suppression coefficient

$$S_{A,B} = \frac{\text{rms}(X_{A,B})}{\text{rms}(X_{A_f,B_f})},$$

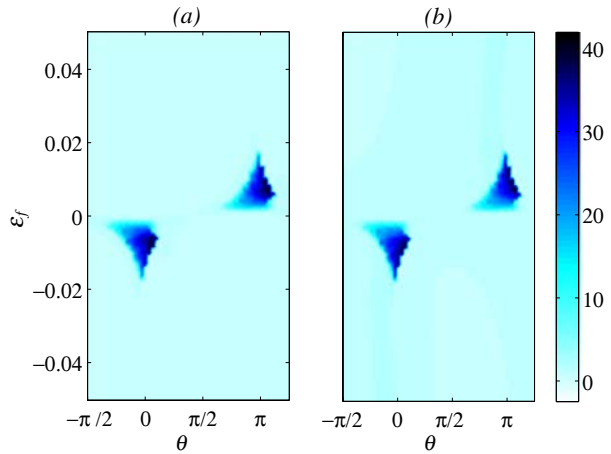
where  $X_{A,B}$  and  $X_{A_f,B_f}$  are the mean fields in the absence and presence of the feedback, respectively. For this particular example, we get  $S_A = 149$ ,  $S_B = 143$ . Figure 4 demonstrates two main properties of our feedback scheme: (1) as soon as desired suppression is achieved, the measured mean field  $X_B$  tends to zero, and thus, the feedback signal practically vanishes, i.e.,  $\langle C \rangle = 1.3 \cdot 10^{-7}$  and  $\text{rms}(C) = 0.001$ , and (2) the stimulation does not affect the natural oscillatory dynamics of individual neurons. This is seen in Fig. 4, where dynamics of two neurons are presented in the absence (Fig. 4c) and in the presence (Fig. 4d) of the

**Fig. 4** Suppression of synchrony in two coupled Bonhoeffer–van der Pol subpopulations (11).

**a** The mean fields of these subpopulations ( $X_A, X_B$ ) without ( $t < 500$ ) and with ( $t > 500$ ) an external feedback. **b** The control signal  $C$  vs time. Synchronous **(c)** and asynchronous **(d)** dynamics of two neurons in the absence and in the presence of the stimulation, respectively



**Fig. 5** Domains of suppression for two coupled Bonhoeffer–van der Pol ensembles (11). Each population consists of  $N = 500$  oscillators. The suppression factor is shown in a color scale coding: for population *A* (a) and *B* (b)



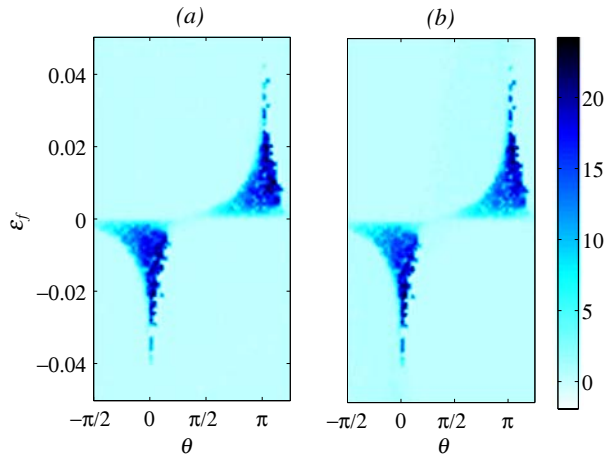
control. Individual neurons continue oscillating as before, but not coherently. In biological terms, this would mean the suppression of the tremor-related brain activity<sup>3</sup> with a minimal intervention into the neural tissue that does not destroy individual units.

For a quantitative comparison of the theoretical description within the framework of the model equation (2) with the numerics, we simulate  $N = 500$  Bonhoeffer–van der Pol oscillators (11) in each population and plot, in a color scale coding, the suppression coefficients  $S_A$  (Fig. 5a) and  $S_B$  (Fig. 5b) as a function of the phase shift  $\theta$  and the feedback strength  $\varepsilon_f$ . In this case, each ensemble in the absence of control produces a macroscopic mean field ( $\varepsilon_{A_f, B_f} > \varepsilon_{cr}$ ), or in other words, both ensembles are active. The parameters of ensembles and feedback control are chosen as in the previous example (Fig. 4). These domains of suppression have to be compared with theoretically obtained stability regions in the case of two nonidentical populations (see Fig. 3b). The case where the stimulated population produces non-zero macroscopic mean field, i.e., the population is active,  $\varepsilon_{A_f} > \varepsilon_{cr}$ , whereas the monitored population is passive,  $\varepsilon_{B_f} < \varepsilon_{cr}$ , is presented in Fig. 6. As is seen from this picture, the obtained suppression domains are larger than in the previous case (Fig. 5), which quantitatively corresponds to the theoretical results illustrated in Fig. 3c.

Another way to compare the theoretical analysis with the numerics is presented in Figs. 7 and 8. Here, we first compute the variance of the mean field for  $N = 500$  elements in both subpopulations. Then, we estimate the variance of the mean field for subcritical coupling to be 0.0075; this value corresponds to the level of noise in the system. We use this value as a cutoff level: if the variance of the mean field is larger than this value, the system is considered to be unstable. The obtained stability domains are shown in Fig. 7 for the case when both systems are active and in Fig. 8 for the case when one system is active and another one is passive. Comparing the stability domains in Figs. 7 and 8 with the suppression domains in Figs. 5 and 6, one can see a good correspondence between the theory and numerics.

<sup>3</sup>Here, we mean brain activity that manifests itself as a rather narrow spectral peak in the power spectrum of EEG or MEG signals.

**Fig. 6** Domains of suppression for two coupled Bonhoeffer–van der Pol ensembles (11). Each population consists of  $N = 500$  oscillators. The suppression factor is shown in color coding: **a** the suppression factor  $S_A$  of the stimulated population  $A$ , **b** the suppression factor  $S_B$  of the measured population  $B$

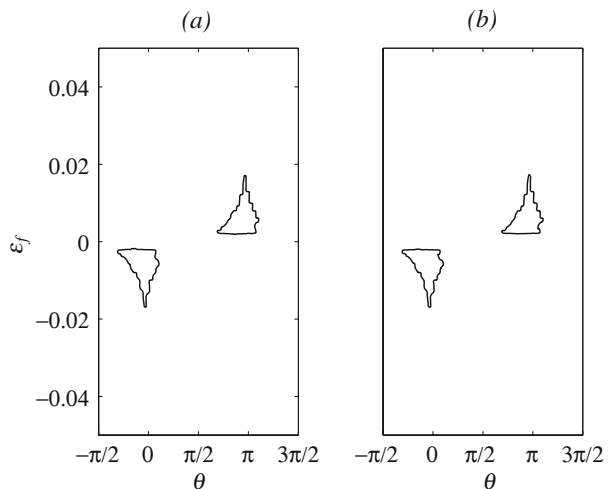


### 3 Determination of Stimulation Parameters by a Test Stimulation

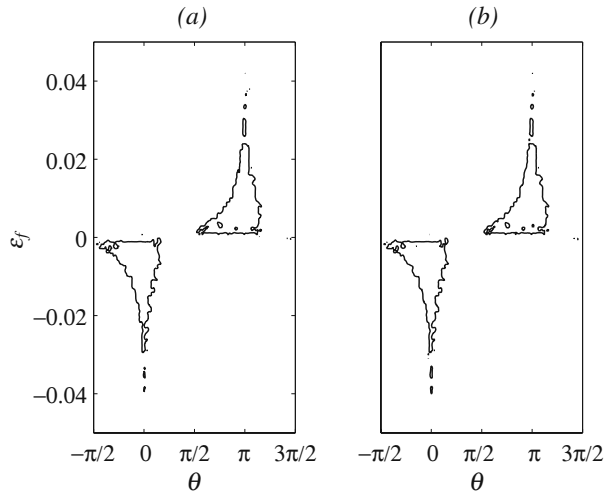
The presented suppression scheme has two parameters to be determined, namely, the feedback strength  $\epsilon_f$  and the phase shift  $\theta$ . The parameter  $\theta$  is related to the phase shift  $\beta$ , which is inherent to stimulation. We recall that the phase shift  $\theta$  is a free parameter of our control scheme, and it has been introduced with the purpose of compensating for the unknown phase shift  $\beta$  inherent to the stimulation. To find the appropriate parameters for an efficient stimulation, one has to estimate the phase shift  $\beta$ . Here, we introduce a simple way in which this can be done in an experiment.

Suppose first that we deal with one population only. For the determination of the unknown parameter  $\beta$ , we make use of a general property of oscillators, namely, of their ability to be synchronized by a weak external forcing. Considering the population as one oscillator, we stimulate it by a harmonic force with the same frequency as its collective

**Fig. 7** Results of numerical analysis of the stability domains of the two coupled Bonhoeffer–van der Pol ensembles (11). The case of two coupled active populations is presented here: **a** the stimulated population  $A$ , **b** the monitored population  $B$



**Fig. 8** Results of numerical analysis of the stability domains of the two coupled Bonhoeffer–van der Pol ensembles (11). **a** The stimulated population *A* is active, **b** the monitored population *B* is passive



oscillation, i.e.,  $C = \varepsilon_f \cos(\omega t)$ , and examine the entrained oscillation. (Note that, in this setup, we deal with an open loop system.) If the phase shift  $\beta$  were zero, the oscillator and the force would be in phase. Otherwise, the difference of the oscillator phase and phase of the force will be  $\phi_{osc} - \phi_{force} = \beta$ . Accordingly, at first, the frequency of the uncontrolled oscillation  $\omega$  has to be measured, and then the proper test signal  $C = \varepsilon_f \cos(\omega t)$  has to be applied. The unknown parameter  $\beta$  can be calculated by virtue of Fourier transformation for this frequency, i.e.,

$$\tilde{\beta} = -\arg \left( T_s^{-1} \int_0^{T_s} X(t) e^{i\omega t} dt \right), \tag{12}$$

where  $T_s$  is the time of stimulation.

To validate this method for the case of two coupled ensembles, we simulated (2) and as an output we took  $X(t) = \text{Re}(B)$ . In order to compare the obtained results with the results of stability analysis of Section 2, we consider three different cases. First, we take two identical ensembles ( $\omega_1 = \omega_2 = 1.0, \xi_1 = \xi_2 = 0.02$ ) with the parameters  $\varepsilon = 0.05, \varepsilon_f = 0.07, \beta = 0$ ; as a result, we obtain  $\tilde{\beta} = -6 \cdot 10^{-5}$ . In the case of nonidentical ensembles,  $\omega_1 = 1.0, \omega_2 = 1.04$ , we obtain  $\tilde{\beta} = 0.11$ . Finally, in the case when one system is active and the second one is passive,  $\xi_1 = 0.02, \xi_2 = -0.02$ , we obtain  $\tilde{\beta} = 0.08$ . Thus, in all cases, the estimated values are very close to the true value  $\beta = 0$  and are in good correspondence with the optimal value of the phase shift (see Fig. 3).

### 4 Conclusions

We have extended our nondelayed feedback approach for control of synchrony in a population of globally coupled elements to a more complex setting of two interacting populations, where the first one is affected by the stimulation, whereas the measurement is performed from the second one. The considered situation can model the suppression of pathological rhythm when recording and stimulation of the brain tissue cannot be carried out by the same or closely placed electrode(s). We have considered the cases where the second

population is either active or passive. We have shown that our control technique provides a vanishing-stimulation suppression and, thus, reduces the invasion into the system. That is a crucial property for possible applications in neuroscience. The theoretical analysis of suppression in a system of two interacting ensembles has been done in the framework of the model amplitude equations, and the results are in good agreement with numerical simulations.

Important advantages of our linear feedback control are the simplicity of its implementation, the ability to compensate for the phase shift inherent to stimulation as well as for latency in measurements, and presence of a built-in band pass filter. The latter allows one to extract the relevant signal from its mixture with other rhythms and noise; the central frequency and the bandwidth of the filter are governed by parameters  $\omega_0$  and  $\alpha$  [see (3)]. With this method, we also overcome the main disadvantage of the time-delayed method, namely, that a new instability can arise if the delay is large enough. The parameters of the control scheme can be easily tuned by means of a test stimulation by a harmonic force. We expect that our technique can contribute significantly to the development of mild and efficient techniques for suppression of pathological brain activity.

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