Time-delayed feedback in neurosystems

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The influence of time delay in systems of two coupled excitable neurons is studied in the framework of the FitzHugh–Nagumo model. A time delay can occur in the coupling between neurons or in a self-feedback loop. The stochastic synchronization of instantaneously coupled neurons under the influence of white noise can be deliberately controlled by local time-delayed feedback. By appropriate choice of the delay time, synchronization can be either enhanced or suppressed. In delay-coupled neurons, antiphase oscillations can be induced for sufficiently large delay and coupling strength. The additional application of time-delayed self-feedback leads to complex scenarios of synchronized in-phase or antiphase oscillations, bursting patterns or amplitude death.

Keywords: time-delayed feedback; stochastic synchronization; coupled neural systems

1. Introduction

The control of unstable or irregular states of nonlinear dynamic systems is a central issue of current research (Schöll & Schuster 2008). A particularly simple and efficient control scheme is the time-delayed feedback that occurs naturally in a number of biological systems, including neural networks, where both propagation delays of the electrical signals connecting different neurons and local neurovascular couplings lead to time delays (Wilson 1999; Gerstner & Kistler 2002; Haken 2006). Moreover, time-delayed feedback loops might be deliberately implemented to control neural disturbances, e.g. to suppress undesired synchrony of firing neurons in Parkinson’s disease or epilepsy (Schiff et al. 1994; Rosenblum & Pikovsky 2004; Popovych et al. 2005). Chaos control techniques were first applied experimentally in vitro in a spontaneously bursting neural network (Schiff et al. 1994), using a method proposed by Ott et al. (1990). In contrast to this method, the time-delayed feedback method of Pyragas (1992) and its extensions (Socolar et al. 1994) do not require detailed information on the system to be controlled, and they are non-invasive, i.e. once the target state is reached, the control force vanishes. However, one needs to tune the feedback gain and the delay time. Therefore, theoretical investigations help us to understand optimal choices of these parameters. Various global delayed feedback schemes have been proposed as effective and robust therapy.
of neurological diseases with pathological synchronization causing tremor (Rosenblum & Pikovsky 2004; Popovych et al. 2005). They have been contrasted with local delayed feedback methods (Gassel et al. 2007, 2008; Dahlem et al. 2008).

Neurons are excitable units that can emit spikes or bursts of electrical signals, i.e. the system rests in a stable steady state, but after it is excited beyond a threshold, it emits a pulse. In the following, we consider electrically coupled neurons. Such electrical synapses are less common than chemical synapses, but it has been shown in hippocampal slices that high-frequency synchronized oscillations are independent of chemical synaptic transmission (Jefferys & Haas 1982), and physiological, pharmacological and structural evidence has

Figure 1. (a) Scheme of two axo-axonally coupled neurons (pyramidal cells coupled by an electrical synapse; Schmitz et al. 2001). (b) Two mutually coupled neural populations (delay \( \tau \) and coupling constant \( C \)) with feedback control loop (delay \( \tau_K \) and coupling constant \( K \)) and noise input \( D_1 \) and \( D_2 \).

Figure 2. Excitable dynamics of a single FitzHugh–Nagumo system: (a) phase portrait \((x_1, y_1)\) (blue line, trajectories; black dashed line, nullclines); (b) time series of activator \( x_1(t) \) (red) and inhibitor \( y_1(t) \) (green). The coloured dots A (black), B (red), C (green) and D (blue) mark the corresponding points on (a) and (b). The inset in (b) shows a blow-up of the phase portrait near A. The parameters are \( \varepsilon_1 = 0.01, a = 1.05 \) and \( D_1 = 0 \).
shown (Schmitz et al. 2001) that the axons of hippocampal pyramidal cells are electrically coupled (figure 1a). Time delays in the coupling must be considered, particularly in the case of high-frequency oscillations.

The simplest model that displays the features of neural interaction consists of two coupled neural systems. A single electrical synapse can lead to synchronized cooperative behaviour between two axo-axonally coupled hippocampal pyramidal cells when only one of them is stimulated antidromically at high frequency (Traub et al. 1994, 1999). Moreover, such neurons have been shown to reflect antidromic spikes (propagating opposite to the normal direction) at the soma, but a continuous reverberating activity is not generated by axonal reflections in two axo-axonally coupled cells alone (Schmitz et al. 2001). In order to describe the complicated interaction between billions of neurons in large neural networks, the neurons are often lumped into highly connected subnetworks or synchronized subensembles. Such neural populations are usually localized spatially and contain both excitatory and inhibitory neurons (Wilson & Cowan 1972). In this sense, the model of two mutually coupled neurons may also serve as a paradigm of two coupled neural subensembles.

Starting from such very simple network motifs, larger networks can be built, and their effects may be studied. For example, starting from two interconnected reticular thalamic neurons with oscillatory behaviour, it was shown by Destexhe et al. (1994) how more complex dynamics emerges in ring networks with nearest neighbours and fully reciprocal connectivity, or in networks organized in a two-dimensional array with proximal connectivity and ‘dense proximal’ coupling in which every neuron connects to all other neurons within some radius. In another example (Zhou et al. 2006), a neural population was itself modelled as a small subnetwork of excitable elements, to study the hierarchically clustered organization of excitable elements in a network of networks.

In the following, we consider two mutually coupled neurons modelled by the paradigmatic FitzHugh–Nagumo system (FitzHugh 1961; Nagumo et al. 1962;
Lindner et al. (2004) in the excitable regime:

\[
\begin{align*}
\dot{x}_1 &= x_1 - \frac{x_1^3}{3} - y_1 + C[y_1(t - \tau) - x_1(t)], \\
\dot{y}_1 &= x_1 + a + D_1 \xi_1(t), \\
\dot{x}_2 &= x_2 - \frac{x_2^3}{3} - y_2 + C[y_2(t - \tau) - x_2(t)], \\
\dot{y}_2 &= x_2 + a + D_2 \xi_2(t),
\end{align*}
\]

where \(x_1, y_1\) and \(x_2, y_2\) correspond to single neurons (or neuron populations), which are linearly coupled with coupling strength \(C\). The variables \(x_1\) and \(x_2\) are related to the transmembrane voltage, and \(y_1\) and \(y_2\) refer to various quantities connected to the electrical conductance of the relevant ion currents. Here, \(a\) is an excitability parameter whose value defines whether the system is excitable \((a > 1)\), or exhibits self-sustained periodic firing \((a < 1)\), and \(\varepsilon_1\) and \(\varepsilon_2\) are the time-scale parameters, which are usually chosen to be much smaller than unity, corresponding to fast activator variables \(x_1, x_2\), and slow inhibitor variables \(y_1, y_2\).

The synaptic coupling between two neurons is modelled as a diffusive coupling, considered for simplicity to be symmetric (Liley & Wright 1994; Pinto et al. 2000; De-Miguel et al. 2001). More general delayed couplings are considered in Buric & Todorovic (2003). The coupling strength \(C\) summarizes how information is distributed between neurons. The mutual delay \(\tau\) in the coupling is motivated by the propagation delay of action potentials between the two neurons \(x_1\) and \(x_2\).

Each neuron is driven by Gaussian white noise \(\xi_i(t)\) \((i = 1, 2)\) with zero mean and unit variance. The noise intensities are denoted by the parameters \(D_1\) and \(D_2\), respectively.

Besides delayed coupling, we will also consider delayed self-feedback in the form suggested by Pyragas (1992), where the difference \(s(t) - s(t - \tau_K)\) of a system variable \(s\) (e.g. activator or inhibitor) at time \(t\) and at a delayed time \(t - \tau_K\), multiplied by some control amplitude \(K\), is coupled back into the same system (figure 1b). Such feedback loops might arise naturally in neural systems, e.g. due to neurovascular couplings that have a characteristic latency, or due to finite propagation speed along cyclic connections within a neuron subpopulation, or they could be realized by external feedback loops as part of a therapeutic measure, as proposed in Popovych et al. (2005). This feedback scheme is simple to implement, is quite robust and has already been applied successfully in a real experiment with time-delayed neurofeedback from real-time magnetoencephalography (MEG) signals to humans via visual stimulation in order to suppress the alpha rhythm, which is observed due to strongly synchronized neural populations in the visual cortex in the brain (Hadamschek 2006). One distinct advantage of this method is its non-invasiveness, i.e. in the ideal deterministic limit the control force vanishes on the target orbit, which may be a steady state or a periodic oscillation of period \(\tau\). In the case of noisy dynamics, the control force, of course, does not vanish but still remains small, compared with other common control techniques using external periodic signals, for instance, in deep-brain stimulation to suppress neural synchrony in Parkinson’s disease (Tass 2002).

The phase portrait and the nullclines of a single FitzHugh–Nagumo system without noise and feedback are shown in figure 2a. The fixed point \(A\) is a stable
focus or node for $a>1$ (excitable regime). If the system is perturbed well beyond point $A'$ (see inset), it performs a large excursion $A \rightarrow B \rightarrow C \rightarrow D \rightarrow A$ in the phase space corresponding to the emission of a spike (figure 2b). At $a=1$, the system exhibits a Hopf bifurcation of a limit cycle, and the fixed point $A$ becomes an unstable focus for $a<1$ (oscillatory regime).

In the following, we choose the excitability parameter $a=1.05$ in the excitable regime close to threshold. If noise is present, it will occasionally kick the system beyond $A_0$, resulting in noise-induced oscillations (spiking).

2. Stochastic synchronization of instantaneously coupled neurons

We shall first consider two coupled FitzHugh–Nagumo systems as in equation (1.1) albeit without delay in the coupling ($\tau=0$). Noise can induce oscillations even though the fixed point is stable (Hauschildt et al. 2006; Hövel et al. 2007). The noise sources then play the role of stimulating the excitable subsystems. Even if only one subsystem is driven by noise, it induces oscillations of the whole system through the coupling. In the following, we consider two non-identical neurons, described by different time scales $\varepsilon_1=0.005$ and $\varepsilon_2=0.1$, and set the noise intensity $D_2$ in the second subsystem equal to a small value, $D_2=0.09$, in order to model some background noise level. Depending on the coupling strength $C$ and the noise intensity $D_1$ in the first subsystem, the two neurons show cooperative dynamics.

Figure 3a depicts the temporal dynamics of a single FitzHugh–Nagumo system ($C=0$) due to stochastic input. One can see that the system is excitable because it performs large excursions in the phase space. Figure 3b shows the temporal dynamics of two instantaneously coupled neural systems for increasing noise intensities $D_1$, where the green, red and black curves correspond to $x_1$, $x_2$ and their sum $x_2=x_1+x_2$, respectively. For $D_1=0$, the first subsystem is enslaved and emits a spike every time the second unit does. For increasing $D_1$, however, this synchronization is weakened, and for large noise intensities $D_1$ the dynamics of the first subsystem is independently dominated by its own stochastic input.

There are various measures of the synchronization of coupled systems (Rosenblum et al. 2001). For instance, one can consider the average interspike intervals (ISIs) of each subsystem, i.e. $\langle T_1 \rangle$ and $\langle T_2 \rangle$, calculated from the $x$ variable of the respective subsystem. Their ratio $\langle T_1 \rangle/\langle T_2 \rangle$ is a measure of frequency synchronization, as depicted in figure 4. Figure 4a displays the ratio of the average ISIs as a function of the noise intensity $D_1$ (green dots) for fixed coupling strength $C=0.07$. One can see that for increasing $D_1$ the ratio $\langle T_1 \rangle/\langle T_2 \rangle$ decreases. Thus, the two subsystems become less synchronized. Figure 4b shows the dependence on the coupling strength $C$ for fixed noise intensity $D_1=0.25$. Without coupling ($C=0$), the two subsystems operate on their own time scale. For increasing $C$, however, they synchronize as the ratio of the average ISIs approaches unity. Figure 4c shows the result as a function of $D_1$ and $C$, where the bright (yellow) regions indicate a strongly synchronized behaviour of the two subsystems. For small $D_1$ and large coupling strength $C$, the two subsystems display synchronized behaviour, $\langle T_1 \rangle/\langle T_2 \rangle \approx 1$. On average, they show the same number of spikes indicated by bright (yellow) colour. In §3, we consider three different regimes of synchronization: moderately, weakly and strongly synchronized systems as marked by black dots in figure 4c.
Other measures for stochastic synchronization are given by the phase synchronization index (Hauschildt et al. 2006), or the mean phase synchronization intervals (Hövel et al. submitted), but they exhibit qualitatively similar behaviour.

3. Control of synchronization by time-delayed feedback

In this section, we consider the control of global cooperative dynamics by local application of a stimulus to a single system. This stimulus is realized by time-
delayed feedback, which was initially introduced by Pyragas in order to stabilize periodic orbits in deterministic systems (Pyragas 1992):

\[
\begin{align*}
\dot{x}_1 &= x_1 - \frac{x_1^3}{3} - y_1 + C[x_2(t) - x_1(t)], \\
\dot{y}_1 &= x_1 + a + K[y_1(t - \tau_K) - y_1(t)] + D_1 \xi_1(t), \\
\dot{x}_2 &= x_2 - \frac{x_2^3}{3} - y_2 + C[x_1(t) - x_2(t)], \\
\dot{y}_2 &= x_2 + a + D_2 \xi_2(t).
\end{align*}
\]

The parameters of the time-delayed feedback scheme are the feedback gain \(K\) and the time delay \(\tau_K\). With this method, a control force is constructed from the differences of the states of the system that are one time unit \(\tau_K\) apart. One could also consider the application of the feedback scheme to both subsystems and the effects of different values of the control parameters for each subsystem, but these investigations are beyond the scope of this work. Previously, time-delayed feedback has also been used to influence noise-induced oscillations of a single excitable system (Balanov et al. 2004; Janson et al. 2004; Prager et al. 2007), of systems below a Hopf bifurcation (Pomplun et al. 2005; Schöll et al. 2005; Flunkert & Schöll 2007; Pototsky & Janson 2007) or below a global bifurcation (Hizanidis et al. 2006; Hizanidis & Schöll 2008) and of spatially extended reaction–diffusion systems (Balanov et al. 2006; Stegemann et al. 2006; Dahlem et al. 2008). Extensions to multiple time-delay control schemes have also been considered (Hövel et al. 2007, submitted; Pomplun et al. 2007; Schöll et al. 2008).

Since we are interested in the effects of a control force on synchronization, in the following we consider three different cases: moderately, weakly and strongly synchronized systems, given by the specific choices of the coupling strength

\[
\begin{align*}
\text{(a)} & \quad \langle T_1 \rangle / \langle T_2 \rangle \quad \text{(b)} & \quad \langle T_1 \rangle / \langle T_2 \rangle \\
\text{(c)} & \quad \langle T_1 \rangle / \langle T_2 \rangle
\end{align*}
\]
and noise intensity in the first subsystem. These different cases of stochastic synchronization are marked as black circles in figure 4.

As a measure to quantify changes in the synchronization due to the control force, we consider the ratio of average ISIs. In the presence of a control force, i.e. $K \neq 0$, the cooperativity can be influenced by varying the feedback gain $K$ and the time delay $\tau_K$.

For fixed feedback gain $K=1.5$, figure 5 depicts the average ISIs of the subsystems, shown as solid black and dashed red curves for $\langle T_1 \rangle$ and $\langle T_2 \rangle$, and their ratio (green dots) for the case of moderately (figure 5a), weakly (figure 5b) and strongly (figure 5c) synchronized systems, respectively, as a function of the time delay $\tau_K$. In all three cases, the stochastic synchronization can be strongly modulated by changing the delay time, i.e. one can either enhance or suppress the synchronization by appropriate choice of the local feedback delay.

The overall dependence of the frequency synchronization, measured by the ratio of $\langle h_1 \rangle / \langle h_2 \rangle$, is displayed as a function of the control parameters $K$ and $\tau_K$ in figure 6a–c for moderate, weak and strong synchronization, respectively. Thus, figure 5 can be understood as a horizontal cut for $K=1.5$ through figure 6. One can see a modulation of the ratio of average ISI by $\tau_K$ for a large range of feedback gain. In view of applications, where neural synchronization is often pathological, e.g. in Parkinson’s disease or epilepsy, it is interesting to note that there are cases where a proper choice of the local feedback control parameters leads to desynchronization of the coupled system (dark regions in figure 6).

4. Delay-coupled neurons

In this section, we study the influence of a delay in the coupling of two neurons, rather than a delayed self-feedback. We set the noise terms in equation (1.1) equal to zero, $D_1=D_2=0$, but consider a time delay $\tau$ in the coupling. In the deterministic system, delayed coupling plays the role of a stimulus that can induce self-sustained oscillations in the coupled system even if the fixed point is stable. In this sense, delayed coupling has a similar effect as the noise term in the previous sections. Here, the bifurcation parameters for delay-induced bifurcations are the coupling parameters $C$ and $\tau$.

(a) Linear stability of fixed point

In the following, we shall choose symmetric time scales $\epsilon_1=\epsilon_2=\epsilon=0.01$ and fix $a=1.05$, where each of the two subsystems has a stable fixed point and exhibits excitability.

The unique fixed point of the system is symmetric and is given by $\mathbf{x}^* = (x^*_1, y^*_1, x^*_2, y^*_2)$, where $x^*_i = -a$ and $y^*_i = a^3/3-a$. Linearizing equation (1.1) around the fixed point $\mathbf{x}^*$ by setting $\mathbf{x}(t) = \mathbf{x}^* + \delta \mathbf{x}(t)$, one obtains

$$
\delta \dot{\mathbf{x}} = \frac{1}{\epsilon} \begin{pmatrix}
\xi & -1 & 0 & 0 \\
\epsilon & 0 & 0 & 0 \\
0 & 0 & \xi & -1 \\
0 & 0 & \epsilon & 0 \\
\end{pmatrix} \delta \mathbf{x}(t) + \frac{1}{\epsilon} \begin{pmatrix}
0 & 0 & C & 0 \\
0 & 0 & 0 & 0 \\
C & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\end{pmatrix} \delta \mathbf{x}(t-\tau),
$$

(4.1)
Figure 7. Real parts Re(\(\lambda\)) of the eigenvalues of the fixed point versus time delay \(\tau\) for \(a=1.05\) and \(\epsilon=0.01\), and (a) \(C=0.1\), (b) \(C=0.4\), (c) \(C=1\) and (d) \(C=2\).

where \(\xi=1-a^2-C\). The ansatz

\[
\delta x(t) = e^{\lambda t} u,
\]

where \(u\) is an eigenvector of the Jacobian matrix, leads to the characteristic equation for the eigenvalues \(\lambda\),

\[
(1-\xi \lambda + \epsilon \lambda^2)^2 - (\lambda C e^{-\lambda \tau})^2 = 0,
\]

which can be factorized to give

\[
1-\xi \lambda + \epsilon \lambda^2 \pm \lambda C e^{-\lambda \tau} = 0.
\]

This transcendental equation has infinitely many complex solutions \(\lambda\). Figure 7 shows the real parts of \(\lambda\) for various values of \(C\).

As can be seen in figure 7 the real parts of all the eigenvalues are negative throughout, i.e. the fixed point of the coupled system remains stable for all \(C\). This can be shown analytically for \(a>1\) by demonstrating that no delay-induced Hopf bifurcation can occur. Substituting the ansatz \(\lambda=i\omega\) into equation (4.4) and separating into real and imaginary parts yields for the imaginary part

\[
\xi = \pm C \cos(\omega \tau).
\]

This equation has no solution for \(a>1\) since \(|\xi|=a^2-1+C>C\), which proves that a Hopf bifurcation cannot occur.
Delay-induced antiphase oscillations

Delay-induced oscillations in excitable systems are inherently different from noise-induced oscillations. The noise term continuously kicks the subsystems out of their respective rest states, and thus induces sustained oscillations. Instantaneous coupling without delay then produces synchronization effects between the individual oscillators (Hauschildt et al. 2006; Hövel et al. 2007, submitted). For delayed coupling, the case is entirely different. Here, the impulse of one neuron triggers the other neuron to emit a spike, which in turn, after some delay, triggers the first neuron to emit a spike. Hence, self-sustained periodic oscillations can be induced without the presence of noise (figure 8). It is evident that the oscillations of the two neurons have a phase lag of $\pi$. The period of the oscillations is given by $T = 2(\tau + \delta)$, with a small quantity $\delta > 0$.

In order to understand this additional phase shift $\delta$, we shall now consider in detail the different stages of the oscillation as marked in figure 2. Owing to the small value of $\varepsilon \ll 1$, there is a distinct time-scale separation between the fast activators and the slow inhibitors, and a single FitzHugh–Nagumo system performs a fast horizontal transition $A \rightarrow B$, then travels slowly approximately along the right stable branch of the $x_1$ nullcline $B \rightarrow C$ (firing), then jumps back rapidly to $D$, and returns slowly to the rest state $A$ approximately along the left stable branch of the $x_1$ nullcline (refractory phase). If $a$ is close to unity, these four points are approximately given by $A = (-a, -a + a^3/3)$, $B = (2, -2/3)$, $C = (1, 2/3)$ and $D = (-2, 2/3)$. A rough estimate for $A'$ is $(a - 2, -a + a^3/3)$. The two slow phases $B \rightarrow C$ and $D \rightarrow A$ can be approximated by $y_i \approx x_1 - x_1^3/3$, and

(b) Delay-induced antiphase oscillations

Figure 8. Delay-induced oscillations. (a,b) Time series of both subsystems (red curves, activator $x_i$; green curves, inhibitor $y_i$; black dashed lines, fixed point values of the activator and the inhibitor). (c,d) Phase portraits of (c) activators and (d) inhibitors. The parameters are $a = 1.05$, $\varepsilon = 0.01$, $C = 0.5$ and $\tau = 3$. 

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hence $\dot{y}_1 \approx \dot{x}_1(1-x_1^2) = x_1 + a$, which gives

$$\dot{x}_1 = \frac{x_1 + a}{1-x_1^2}. \quad (4.6)$$

This can be solved analytically, describing the firing phase (+) and the refractory phase (−):

$$\int_{x_2}^{x} \, dx_1 \frac{1-x_1^2}{x_1 + a} = (a^2 - 1) \ln \frac{a+2}{a+x} - a(\pm 2-x) + 2 - \frac{x^2}{2} = t. \quad (4.7)$$

Integrating from B to C gives the firing time

$$T_f = \int_{1/2}^{1} \, dx_1 \frac{1-x_1^2}{x_1 + a} = (a^2 - 1) \ln \frac{a+2}{a+1} - a + \frac{3}{2}. \quad (4.8)$$

For $\epsilon=0.01$ and $a=1.05$, the analytical solution is in good agreement with the numerical solution in figure 2b, including the firing time $T_f=0.482$ (analytical approximation: 0.491).

For a rough estimate, in the following, we shall approximate the spike by a rectangular pulse:

$$x_1(t) \approx \begin{cases} 
2, & \text{if } t < T_f, \\
-a, & \text{if } t \geq T_f. 
\end{cases} \quad (4.9)$$

If the first subsystem is in the rest state, and a spike of the second subsystem arrives at $t=0$ (after the propagation delay $\tau$), we can approximate the initial dynamic response by linearizing $x_1, y_1$ around the fixed point $(x_1^*, y_1^*)$ and approximating the feedback by a constant impulse during the firing time $T_f$. The fast dynamic response along the $x_1$ direction is then given by

$$\varepsilon \delta \dot{x}_1 = \xi \delta x_1 + 2C, \quad (4.10)$$

with $\xi < 0$. This inhomogeneous linear differential equation can be solved with the initial condition $x_1(0) = -a$,

$$x_1(t) = -a + \frac{2C}{|\xi|} \left( 1 - \exp \left( -\frac{|\xi|}{\varepsilon} t \right) \right). \quad (4.11)$$
Figure 10. Regime of oscillations in the \((\tau, C)\) parameter plane for initial conditions corresponding to single-pulse excitation in one system. The oscillation period \(T\) is colour coded. The transition between black and colour marks the bifurcation line. Inset (a): the oscillation period versus \(\tau\) in a cut at \(C=0.8\). Inset (b): schematic of the saddle-node bifurcation of a stable (red solid line) and unstable (blue dashed line) limit cycle. The maximal oscillation amplitude is plotted versus the delay time \(\tau\) and the stable fixed point is plotted as a solid black line. The grey background marks the bistable region. The parameters are \(a=1.05\) and \(\epsilon=0.01\).

Figure 11. Influence of delayed self-feedback upon coupled oscillations. The mean ISI is colour coded in the control parameter plane of the self-feedback gain \(K\) and delay \(\tau_K\). White areas mark regimes of irregular oscillations where the ISI variance becomes large (greater than 0.01). Time series corresponding to the points (a)–(f) are shown in figure 12. The other parameters are \(a=1.3\), \(\epsilon=0.01\), \(C=0.5\) and \(\tau=3\).

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Note that this equation is not valid for large $t$ since (i) the linearization breaks down and (ii) the pulse duration $T_f$ is exceeded. For small $t$, equation (4.11) can be expanded as

$$x_1(t) = -a + \frac{2C}{\varepsilon} t,$$

which is equivalent to neglecting the upstream flow field $-|\xi|\delta x_1$ in equation (4.10) near the stable fixed point $A$ compared with the pulling force $2C$ of the remote spike, which tries to excite the system towards $B$. Once the system has crossed the middle branch of the $x_1$ nullcline at $A'$, the intrinsic flow field

Figure 12. Different modes of oscillation corresponding to different self-feedback parameters $K, \tau$ (red curves, activators $x_i(t)$; green curves, inhibitors $y_i(t)$). (a,b) Antiphase oscillations for (a) $K=0.05$, $\tau_K=3$ (period $T=6$) and (b) $K=0.5$, $\tau_K=2$ ($T=2$); (c,d) in-phase oscillations for (c) $K=0.05$, $\tau_K=3$ (period $T=3$) and (d) $K=0.5$, $\tau_K=1.5$ ($T=1.5$); (e) oscillator death for $K=0.9$, $\tau_K=0.9$; (f) bursting pattern for $K=0.5$, $\tau_K=3.2$. The other parameters are $a=1.3, \varepsilon=0.01, C=0.5$ and $\tau=3$.
accelerates the trajectory rapidly towards B, initiating the firing state. Therefore, there is a turn-on delay $\delta$, given by the time the trajectory takes from A to $A'$, i.e. $x_1(\delta) \approx a-2$, according to equation (4.12):

$$\delta = (a - 1) \frac{\varepsilon}{C}. \quad (4.13)$$

Since the finite rise time of the impulse has been neglected in our estimate, the exact solution $\delta$ is slightly larger and does not vanish at $a=1$.

With increasing $a$ the distance $A-A'$ increases, and so does $\delta$. The small additional phase shift $\delta$ between the spike $x_1(t)$ and the delayed pulse $x_2(t-\tau)$ results in a non-vanishing coupling term at the beginning and at the end of the spike $x_1(t)$. This is the reason that (i) the spike is initiated and (ii) it is terminated slightly before the turning point of the $x_1$ nullcline. The latter effect becomes more pronounced if $a$ is increased or $\tau$ is decreased (figure 9). Both lead to a shift of the initial starting point of the spike emission on the left branch of the nullcline towards D, and hence to a longer distance up to the middle branch of the nullcline, which has to be overcome by the impulse $x_2$, hence to a larger turn-on delay $\delta$, and therefore to an earlier termination of the spike $x_1$. This explains why the firing phase is shortened, and the limit cycle loop is narrowed from both sides with increasing $a$ or decreasing $\tau$ (figure 9). In the case of $a=1.05$ and $\tau=3$ (figure 9a), the delay time is large enough for the two subsystems to closely approach the fixed point A before being perturbed again by the remote signal. If the delay time becomes much smaller, e.g. for $\tau=0.8$ (figure 9b), the excitatory spike of the other subsystem arrives while the first system is still in the refractory phase, so that it cannot complete the return $D \rightarrow A$ to the fixed point. In this case, $a$ in equation (4.13) has to be substituted by a larger value $\tilde{a}$ with $a<\tilde{a}<1.7$ in order to get a better estimate of $\delta$. Note that, without the phase shift $\delta$, the coupling term $C[x_2(t-\tau)-x_1(t)]$ would always vanish in the $2\tau$-periodic state.

Next, we shall investigate the conditions on the coupling parameters $C$ and $\tau$ allowing for the limit cycle oscillations. On the one hand, if $\tau$ becomes smaller than some $\tau_{\text{min}}$, the impulse from the excitatory neuron arrives too early to trigger a spike, since the system is still early in its refractory phase. On the other hand, if $C$ becomes too small, the coupling force of the excitatory neuron is too weak to excite the system above its threshold and pull it far enough towards B.

In figure 10, the regime of oscillations is shown in the parameter plane of the coupling strength $C$ and the coupling delay $\tau$. The oscillation period is colour coded. The boundary of this coloured region is given by the minimum coupling delay $\tau_{\text{min}}$ as a function of $C$. For large coupling strength, $\tau_{\text{min}}$ is almost independent of $C$; with decreasing $C$ it sharply increases, and at some small minimum $C$ no oscillations exist at all. At the boundary, the oscillation sets in with finite frequency and amplitude, as can be seen in the insets of figure 10, which show a cut of the parameter plane at $C=0.8$. The oscillation period increases linearly with $\tau$. The mechanism that generates the oscillation is a saddle-node bifurcation of limit cycles (see inset of figure 10b), creating a pair of a stable and an unstable limit cycle. The unstable limit cycle separates the two attractor basins of the stable limit cycle and the stable fixed point.

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5. Delayed self-feedback and delayed coupling

In this section, we consider the simultaneous action of delayed coupling and delayed self-feedback. Here, we choose to apply the self-feedback term symmetrically to both activator equations, but other feedback schemes are also possible:

\[
\begin{align*}
\dot{x}_1 &= x_1 - \frac{x_1^3}{3} - y_1 + C[x_2(t-\tau) - x_1(t)] + K[x_1(t-\tau_K) - x_1(t)], \\
\dot{y}_1 &= x_1 + a, \\
\dot{x}_2 &= x_2 - \frac{x_2^3}{3} - y_2 + C[x_1(t-\tau) - x_2(t)] + K[x_2(t-\tau_K) - x_2(t)], \\
\dot{y}_2 &= x_2 + a.
\end{align*}
\] (5.1)

By a linear stability analysis similar to §4a it can be shown that the fixed point remains stable for all values of \(K\) and \(\tau_K\) in the case of \(a>1\), as without self-feedback. Redefining \(\xi = 1 - a^2 - C - K\), one obtains the factorized characteristic equation

\[
1 - \xi \lambda + \varepsilon \lambda^2 = \lambda Ke^{-\lambda \tau_K} \pm \lambda Ce^{-\lambda \tau}.
\] (5.2)

Substituting the Hopf condition \(\lambda = i\omega\) and separating into real and imaginary parts yields for the imaginary part

\[
-\xi = K \cos(\omega \tau_K) \pm C \cos(\omega \tau). \tag{5.3}
\]

This equation has no solution for \(a>1\), since \(|\xi| = a^2 - 1 + C + K > C + K\).

The adopted form of control not only allows for the synchronization of the two cells for identical values of \(\tau\) and \(\tau_K\), but also generates an intricate pattern of synchronization islands or stripes in the control parameter plane (figure 11) corresponding to single-spike in-phase and antiphase oscillations with constant ISIs (see also figure 12a–d). Furthermore, for adequately chosen parameter sets of coupling and self-feedback control, we observe effects such as bursting patterns (figure 12f) and oscillator death (figure 12e). In addition to these effects, there exists a control parameter regime in which self-feedback has no effect on oscillation periods (shaded yellow in figure 11).

Figure 11 shows the control parameter plane for coupling parameters of the uncontrolled system in the oscillatory regime (\(C=0.5\) and \(\tau=3\)). We observe three principal regimes: (i) control has no effect on the oscillation period (yellow in figure 11), although the form of the stable limit cycle is slightly altered (figure 12a), (ii) islands of in-phase and antiphase synchronization (colour coded in figure 11; figure 12b–d), and (iii) oscillator death (black in figure 11; figure 12e).

Figure 13 shows the average phase synchronization time as a function of the coupling delay \(\tau\) and the self-feedback delay \(\tau_K\) for fixed \(K=0.5\). The bright straight rays at rational \(\tau_K/\tau\) indicate long intervals during which both subsystems remain synchronized. A particularly long average synchronization time is found if the two delay times are equal.

6. Conclusion

Our analysis has focused on a model of two coupled neurons, which may be viewed as a network motif for larger neural networks. We have shown that delayed feedback from other neurons or self-feedback from the same neuron can crucially affect the...
dynamics of coupled neurons. In the case of noise-induced oscillations in instantaneously coupled neural systems, time-delayed self-feedback can enhance or suppress stochastic synchronization, depending upon the delay time. This offers promising perspectives with respect to potential therapies of pathological neural synchrony as occurring, for example, in Parkinson’s disease. It suggests that, by carefully choosing the delay time, feedback control applied locally to a neural subpopulation can suppress the global synchronization of the neurons.

In the case of delay-coupled neurons without driving noise sources, the propagation delay of the spikes fed back from other neurons can induce periodic oscillations for sufficiently large coupling strength and delay times. Bistability of a fixed point and limit cycle oscillations occur even though the single excitable element displays only a stable fixed point. The two neurons oscillate with a phase lag of $\pi$. If self-feedback is applied additionally, e.g. by axonal reflections (figure 1a) in networks of electrically coupled pyramidal cells (Schmitz et al. 2001), synchronous zero-lag oscillations can be induced in some ranges of the control parameters, while in other regimes antiphase oscillations or oscillator death as well as more complex bursting patterns can be generated.

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References


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