IEICE Proceeding Series

Inhibitory Feedback Loop Induces Anticipated Synchronization in Neuronal Networks

Fernanda S. Matias, Pedro V. Carelli, Claudio R. Mirasso, Mauro Copelli

Vol. 1 pp. 636-639
Publication Date: 2014/03/17
Online ISSN: 2188-5079

2012 International Symposium on Nonlinear Theory and its Applications
NOLTA2012, Palma, Majorca, Spain, October 22-26, 2012

Inhibitory Feedback Loop Induces Anticipated Synchronization in Neuronal Networks

Fernanda S. Matias† ‡, Pedro V. Carelli†, Claudio R. Mirasso‡ and Mauro Copelli†

†Departamento de Física, Universidade Federal de Pernambuco, Recife, Pernambuco 50670-901 Brazil
‡Instituto de Fisica Interdisciplinar y Sistemas Complejos, CSIC-UIB, Campus Universitat de les Illes Balears
E-07122 Palma de Mallorca, Spain
Email: fernanda@ifisc.uib-csic.es

Abstract—Anticipated synchronization (AS) was shown to occur in systems of two coupled neurons in a master-slave configuration, if the slave is subject to a delayed self-feedback. We show that AS can also occur in a canonical neuronal microcircuit with standard chemical synapses, in which the formal delayed negative self-feedback is replaced by an inhibitory feedback loop. This means that the delayed feedback that leads to AS is given by biologically plausible elements (an interneuron and chemical synapses). So the anticipation time is not hard-wired in the dynamical equations, but rather emerges from the circuit dynamics. In this scenario, the inhibitory synaptic conductance has an important role in the transition from delayed synchronization (DS) to AS.

1. Introduction

Synchronization of nonlinear systems has been extensively studied on a large variety of physical and biological systems. About a decade ago, Voss [1] discovered a new scheme of synchronization that he called "anticipated synchronization". He found that two identical dynamical systems coupled in a master-slave configuration can exhibit this anticipated synchronization if the slave is subjected to a delayed self-feedback. One of the prototypical examples proposed by Voss [1] is described by the equations

$$\begin{aligned} \dot{x} &= f(x(t)), \\ \dot{y} &= f(y(t)) + K[x(t) - y(t - t_d)]. \end{aligned} \tag{1}$$

$f(x)$ is a function which defines the autonomous dynamical system. The solution $y(t) = x(t + t_d)$, which characterizes the anticipated synchronization (AS), has been shown to be stable in a variety of scenarios, including theoretical studies of autonomous chaotic systems [1] and delayed-coupled maps [2], as well as experimental observations in lasers [3] and electronic circuits [4] .

More recently, AS was also shown to occur in a non-autonomous dynamical system, with FitzHugh-Nagumo models driven by white noise [5]. In these works, even when the model neurons were tuned to the excitable regime, the slave neuron was able to anticipate the spikes of the master neuron, working as a predictor [4]. The main difficulty in these models lies in requiring that the membrane potentials of the involved neurons be diffusively coupled. While a master-slave coupling of the membrane potentials could in principle be conceived by means of electrical synapses (via gap junctions) [6] or ephaptic interactions [7], no biophysical mechanism has been proposed to account for the delayed inhibitory self-coupling of the slave membrane potential.

In the brain, the vast majority of neurons are coupled via chemical synapses, which can be excitatory or inhibitory. In both cases, the coupling is directional and highly nonlinear, typically requiring a suprathreshold activation (e.g. a spike) of the pre-synaptic neuron to trigger the release of neurotransmitters. These neurotransmitters then need to diffuse through the synaptic cleft and bind to receptors in the membrane of the post-synaptic neuron. Binding leads to the opening of specific channels, allowing ionic currents to change the post-synaptic membrane potential [6]. This means that not only the membrane potentials are not directly coupled, but the synapses themselves are dynamical systems. We propose to bridge this gap, investigating whether AS can occur in biophysically plausible model neurons coupled via chemical synapses [8].

2. The Model

We start with the original master-slave circuit of eqs. 1 and an unidirectional excitatory chemical synapse (M $\longrightarrow$ S in Fig. 1). The inhibitory feedback we propose is given by an interneuron (I) driven by the slave neuron, which projects back an inhibitory chemical synapse to the slave neuron (see Fig. 1). So the time-delayed negative feedback is accounted for by chemical inhibition which impinges on the slave neuron some time after it has spiked, simply because synapses have characteristic time scales. Such inhibitory feedback loop is one of the most canonical neuronal microcircuits found to play several important roles, for instance, in the spinal cord [9], thalamus [10], cortex, etc.

In the above network, each node is described by a Hodgkin-Huxley model neuron [11], consisting of four coupled ordinary differential equations associated to the membrane potential V and the ionic currents flowing across

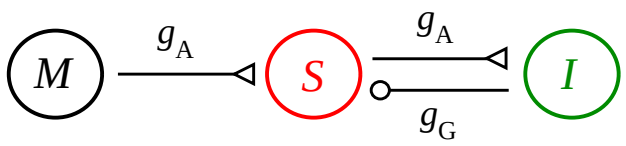


Figure 1: Three neurons coupled by chemical synapses in the master-slave-interneuron (MSI) configuration : excitatory AMPA synapses (with maximal conductance g_A) couple master (M) to slave (S) and slave to interneuron (I), whereas an inhibitory GABA$_A$ synapse (with maximal conductance g_G) couples interneuron to slave.

the axonal membrane corresponding to the Na, K and leakage currents. The gating variables for sodium are h and m and for the potassium is n. The equations read [12]:

$$C_m \frac{dV}{dt} = \overline{G}_{Na} m^3 h (E_{Na} - V) + \overline{G}_K n^4 (E_K - V) + G_m (V_{rest} - V) + I + \sum I_{syn} \quad (2)$$

$$\frac{dx}{dt} = \alpha_x(V)(1-x) - \beta_x(V)x\,, \quad (3)$$

where $x \in \{h, m, n\}$, and all parameters are in agreement with Ref. [12].

According to Rinzel and Miller [14], in the absence of synaptic currents the only attractor of the system of equations 2 and 3 for $I \lesssim 177.13$ pA is a stable fixed point, which loses stability via a subcritical Hopf bifurcation at $I \simeq 276.51$ pA. For 177.13 pA $\lesssim I \lesssim$ 276.51 pA, the stable fix point coexists with a stable limit cycle.

In our model the link between each node is a fast synapse AMPA (A) or GABA$_A$ (G) (excitatory or inhibitory respectively) [see Fig. 1]. Each synaptic current is given by

$$I^{(i)} = g_i r^{(i)} (V - E_i), \quad (4)$$

where V is the postsynaptic potential, g_i the maximal conductance and all parameters are following Destexhe et al [13].

The fraction $r^{(i)}$ ($i = A, G$) of bound (i.e. open) synaptic receptors is modelled by a first-order kinetic dynamics:

$$\frac{dr^{(i)}}{dt} = \alpha_i [T](1 - r^{(i)}) - \beta_i r^{(i)}, \quad (5)$$

where α_i and β_i are rate constants that depend on a number of different factors and vary significantly [15]. To exemplify some of our results, we initially fix some parameters. Then we allow these parameters to vary within the physiological range when exploring different synchronization regimes.

3. The Results

We describe results for the scenario where all neurons receive a constant current $I \geqslant 280$ pA and the rate constants are fixed ($\alpha_A = 1.1$ mM^{-1}ms^{-1}, $\beta_A = 0.19$ ms^{-1}, $\alpha_G = 5.0$ mM^{-1}ms^{-1} and $\beta_G = 0.30$ ms^{-1}). This corresponds to a situation in which the fixed points are unstable and, when isolated, they spike periodically. For different sets of inhibitory conductance values g_G our system can exhibit three different behaviors. To characterize them, we define t_i^M as the time the membrane potential of the master neuron is at its maximal value in the i-th cycle (i.e. its i-th spike time), and t_i^S as the spike time of the slave neuron which is nearest to t_i^M.

The delay τ_i is defined as the difference (see Fig. 2):

$$\tau_i \equiv t_i^M - t_i^S\,. \quad (6)$$

Initial conditions were randomly chosen for each computed time series. When τ_i converges to a constant value τ, a phase-locked regime is reached [16]. If $\tau < 0$ ("master neuron spikes first") we say that the system exhibits delayed synchronization (DS) [Fig. 2(a)]. If $\tau > 0$ ("slave neuron spikes first"), we say that anticipated synchronization (AS) occurs [Fig. 2(b)]. If τ does not converge to a fixed value, the system is in a phase drift (PD) regime [16].

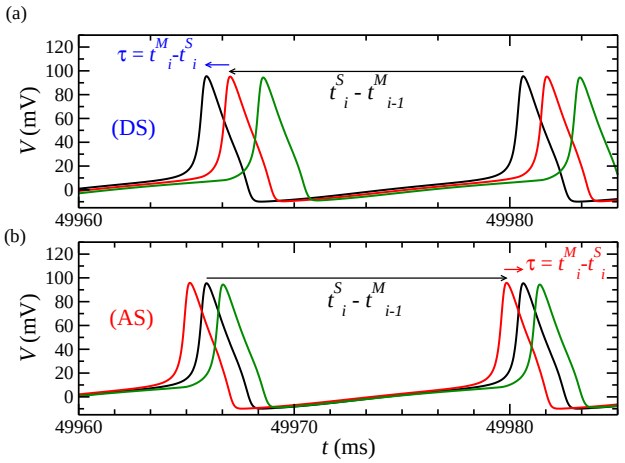


Figure 2: Membrane potential V as a function of time for an external current $I = 280$ pA in the master (M), slave (S), and interneuron (I) neurons. The plot illustrates two regimes: (a) $g_G = 20$ nS leads to delayed synchronization (DS), where $\tau < 0$ (blue), and (b) $g_G = 40$ nS leads to anticipated synchronization (AS), where $\tau > 0$ (red).

In Fig. 3 we display a three-dimensional projection of the phase diagram of our model. We varied g_A (g_G) along the horizontal (vertical) axis and compute the correspondent time delay τ which is coded by the colors. We observe that the three different regimes: DS (blue), AS (red) and PD (white) are distributed in large continuous regions, having a clear transition between them. Several features in these results are worth emphasizing. First note that g_G and g_A (the parameters varied in Fig. 3) do not change the time scales of the synaptic dynamical variables (r), only the synaptic strength.

Secondly, τ varies smoothly with g_G and g_A. This continuity somehow allows us to interpret $\tau > 0$ as a legitimately anticipated regime. The reasoning is as follows. For $g_G = 0$, we simply have a master-slave configuration in which the two neurons spike periodically. Due to the excitatory coupling, the slave's spike is always closer to the master's spike which preceded it than to the master's spike which succeeded it [as in e.g. Fig. 2(a)]. Moreover, the time difference is approximately 1.5 ms, which is comparable to the characteristic times of the synapse. In that case, despite the formal ambiguity implicit in the periodicity of the time series, the dynamical regime is usually understood as "delayed synchronization". We interpret it in the following sense: the system is phase-locked at a phase difference with a well defined sign [16]. Increasing g_G, the time difference between the master's and the slave's spikes eventually changes sign [as in e.g. Fig. 2(b)]. Even though the ambiguity in principle remains, there is no reason why we should not call this regime "anticipated synchronization" (again a phase-locked regime, but with a phase difference of opposite sign). In fact, we have not found any parameter change which would take the model from the situation in Fig. 2(a) to that of Fig. 2(b) by gradually *increasing* the lag of the slave spike until it approached the next master spike. If that ever happened, τ would change discontinuously (by its definition). Therefore, the term "anticipated synchronization" by no means implies violation of causality and should just be interpreted with caution.

Third, it is interesting to note that the largest anticipation time can be longer (up to 3 ms, i.e. about 20% of the interspike interval) than the largest time for the delayed synchronization ($\approx$ 1.5 ms). If one increases g_G further in an attempt to obtain even larger values of τ, however, the system undergoes a bifurcation to a regime with phase drift [which marks the begin of the white region in Fig. 3]. In the DS and AS regimes the master and slave neurons spike at the same frequency. However, when the system reaches the PD regime the mean firing rate of the slave neuron becomes higher than that of the master.

To get insights into more physiological conditions we consider the three large-scale network shown in Fig. 4(a). Each one is composed by hundreds of Izhikevich neurons sparsely connected that receive an independent Poisson spike train (resulting from 100 excitatory neurons at rate $r = 24$ Hz). With no coupling between the populations the master and the slave populations oscillate. In the master-slave-interneuron configuration each neuron in the slave population receives excitatory (inhibitory) synapses from some neurons in the master (interneuron) population and sends excitatory synapses to some neurons in the interneuron population. Depending on the synaptic conductances of those synapses (specially g_{MS} and g_{IS} shown in Fig. 4(a)) the master and slave population synchronize. For all parameters shown in Fig. 4(b) the two population have same mean frequency and their mean membrane potential are highly correlated. We can define τ_i as in Eq 6, where t_i^M

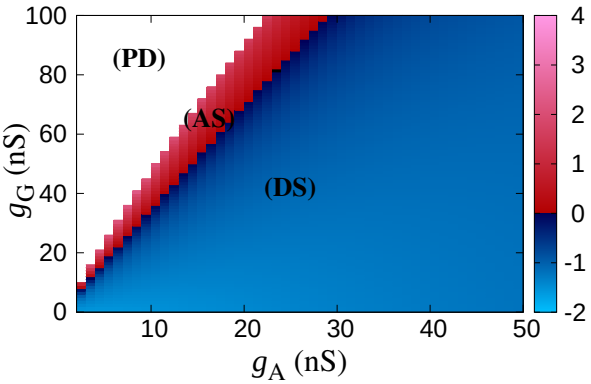
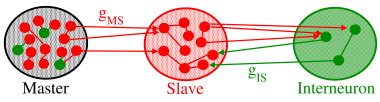


Figure 3: Color-coded delay τ (right bar) in the (g_A, g_G) projection of parameter space: DS (blue), AS (red) and PD (white, meaning that no stationary value of τ was found).

(t_i^S) is the time the mean membrane potential of the master (slave) population is at its maxim umvalue in the *i*-th cycle. Due to the Poisson input the period of oscillation varies in each cycle and also τ_i, so we define τ as the mean of the τ_i in many cycles. Similar to the 3-neuron motif, τ can be positive (AS) or negative (DS), respectively the red and the blue regions in Fig. 4(b).

(a)



(b)

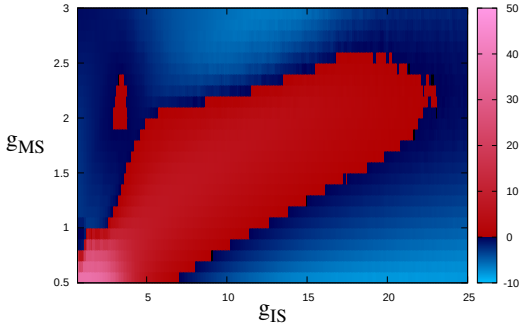


Figure 4: (a) Three large-scale networks coupled in a master-slave-interneuron configuration. The master population is composed of 80% excitatory neurons and 20% inhibitory ones. The slave (interneuron) population is composed only by excitatory (inhibitory) neurons. (b) Color-coded delay τ (right bar) in the (g_{IS}, g_{MS}) projection of parameter space: DS (blue), AS (red).

4. Concluding remarks

In summary, we have shown that a biologically plausible model of a 3-neuron (MSI) motif can exhibit an attractor in phase space where anticipated synchronization is stable. The transition from the DS to the AS regime is a smooth function of the synaptic conductances. Typically, a further increase in the inhibitory conductance g_G leads to a second transition from AS to PD, a quasiperiodic regime in which the slave firing frequency is larger than that of the master. Naturally, our system can also exhibit subharmonic responses if parameter space is sufficiently explored, most notably p/q-subharmonic locking structured in Arnold tongues.

We have also varied the synaptic decay rates (β and α), as well as input currents (I) within well accepted physiological ranges (data not shown). In all the scenarios there is always a continuous region in parameter space where AS is stable. Replacing the constant current by a global periodic driver (arguably a more realistic situation), we obtain a model of a 4-neuron motif [8] which exhibits the same three regions of the simpler model (data not shown). Moreover, when replacing each neuron by a randon network DS and AS regimes are also observed depending on the inhibitory synaptic conductace. Therefore the phenomenon seems to be robust at microcircuit scale and also in large-scale networks.

Our results offer a number of possibilities for further investigation. We are also investigating whether the structure of the phase diagram can be qualitatively reproduced via a phase-response curve analysis [18, 13] of the neuronal motifs studied here. Since the DS-AS transition amounts to a smooth inversion in the timing of the pre- and post-synaptic spikes, our results could have a bearing on spike-time-dependent plasticity models.

References

[1] H. U. Voss, *Phys. Rev. E*, vol.61, pp.5115, 2000; H. U. Voss, *Phys. Rev. E*, vol.64, pp.039904, 2001; H. U. Voss, *Phys. Rev. Lett*, vol.87, pp.014102, 2001

[2] C. Masoller and D.H. Zanette, *Physica A*, vol.300, pp.359-366, 2001

[3] S. Sivaprakasam,E.M. Shahverdiev, P.S. Spencer and K.A. Shore, *Phys. Rev. Lett.*, vol.87, pp.154101, 2001; Y. Liu, Y. Takiguchi, P. Davis, T. Aida, S. Saito, and J.M. Liu, *Appl. Phys. Lett.*, vol.80, pp.4306, 2002.

[4] M. Ciszak, C.R. Mirasso, R. Toral and O. Calvo, *Phys. Rev. E*, vol.79, pp.046203, 2009.

[5] M. Ciszak, O. Calvo, C. Masoller, C.R. Mirasso and R. Toral, *Phys. Rev. Lett.*, vol.90, pp.204102, 2003; M. Ciszak, F. Marino,R. Toral and S. Balle, *Phys. Rev. Lett.*, vol.93, pp.114102, 2004; R. Toral, C. Masoller, C.R. Mirasso, M. Ciszak and O. Calvo, *Physica A*, vol.325, pp.192, 2003.

[6] *Essentials of Neural Science and Behavior*, edited by E.R. Kandel and T.M. Jessel (Appleton Lange, Norwalk, 1995).

[7] A. Arvanitaki, *J. Neurophysiol*, vol.5, pp.89-108, 1942.

[8] Matias, F. S. and Carelli, P. V. and Mirasso, C. R. and Copelli, M. *Phys. Rev. E*, vol.84, pp.021922, 2011.

[9] *The Synaptic Organization of the Brain*, edited by G.M. Shepherd (Oxford University Press, New York, 1998).

[10] U. Kim, M.V. Sanchez-Vives and D.A. McCormick, *Science*, vol.278, pp.130-134, 1997; D. Debay, J. Wolfart, Y. Le Franc, G. Le Masson and T. Bal, *J. Physiol.*, pp.540-558, 2004.

[11] A.L. Hodgkin and A.F. Huxley, *J. Physiol.*, vol.117, pp.500-544, 1952.

[12] C. Koch, *Biophysics of Computation* (Oxford University Press, New York, 1999).

[13] *Methods in Neuronal Modeling: From Ions to Networks*, 2nd ed., edited by C. Koch and I. Segev (MIT Press, Cambridge, MA, 1998).

[14] J. Rinzel and R.N. Miller, *Math. Biosci.*, vol.49, pp.27-59, 1980.

[15] J.R.P. Geiger, J. Lübke, A. Roth, M. Frotscher and P. Jonas, *Neuron*, vol.18, pp.1009-1023, 1997; M. Bartos, I. Vida, M. Frotscher, A. Meyer, H. Monyer, J.R.P. Geiger and P. Jonas, *Proc. Natl. Acad. Sci.*, vol.99, pp.13222-13227, 2002; M. Hausser, and A. Roth, *Proc. Natl. Acad. Sci.*, vol.99, pp.13222-13227, 2002; U. Kraushaar and P. Jonas, *J. Neurosci.*, vol.20, pp.5594-5607, 2000;

[16] S. H. Strogatz *Nonlinear Dynamics and Chaos: with Applications to Physics, Biology, Chemistry and Engineering* (Addison-Wesley, Reading,MA, 1997).

[17] R. Vicente and L.L. Gollo and C.R. Mirasso and I. Fischer and G. Pipa *PNAS*, vol.105, pp.17157-17162, 2008.

[18] G.B. Ermentrout, *Neural Comput.*, vol.8, pp.979-1001, 1996.