PHASE LOCKING STATES BETWEEN FAST-SPIKING INTERNEURONS COUPLED BY ELECTRICAL AND CHEMICAL SYNAPSES

Angelo Di Garbo, Alessandro Panarese, Santi Chillemi,

Istituto di Biofisica CNR, Area della Ricerca di Pisa, via G. Moruzzi 1, 56124 Pisa (Italy)
digarbo@ib.pi.cnr.it, a.panarese@ib.pi.cnr.it, chillemi@ib.pi.cnr.it

Abstract

The phase locking states in a pair of Fast Spiking interneurons coupled by electrical and inhibitory synapses are investigated by using the theory of weakly coupled oscillators. It is shown that increasing either the decay time constant of the inhibitory current or the firing frequency of the cells favours the emergence of synchronous discharges. We also found that adding the electrical coupling promotes synchronous regimes.

Keywords: Interneuron; FS; Inhibitory synapse; Electrical synapse, Synchronization

1. Introduction

The local circuits of GABAergig interneurons traditionally have been considered the modulators and regulators of principal cells. However, recent experimental findings suggest that they have also an important role in detecting and promoting synchronous activity [6, 7, 9]. The relevance of these results comes from the experimental evidences suggesting that the synchronous firing of cortical neurons in the gamma frequency range (30 – 80 Hz) is relevant for the coding of sensory information [4]. Moreover, both experimental and theoretical results relate the synchronous discharge of a population of inhibitory interneurons to some

features of their coupling, like the duration and intensity of the synaptic current [2, 12,13,14, 15, 16].

Recently it was found that the Fast Spiking (FS) neocortical inhibitory interneurons are interconnected by electrical synapses too [6, 9]. The relevance of electrical synapses for the emergence of synchronous neural activity is shown by the recent experimental finding that impairing of electrical synapses between cortical interneurons disrupts the synchronous oscillations in the gamma frequency band [1, 10]. However, at present it is not very clear how the simultaneously presence of electrical and inhibitory synapses determines the dynamical behaviour of a neural population.

From a theoretical point of view the dynamics of a pair of neurons connected by inhibitory and electrical synapses, each ones being modelled as a Leaky Integrate & Fire, was studied recently [11]. The main results found in this paper can be synthesized as follows: a) the increase of the stimulation current promotes synchrony; b) for fast (slow) inhibitory synapses increasing the intensity of the electrical coupling promotes synchrony (antisynchrony). In our contribution we study the same problem by using a biophysical model of each neuron and our results will be compared with those reported in [11].

2. Model description and analysis method

In [3] a four variables H-H like model for each FS cell was proposed; here, in order to simplify the computations, a reduction of that model will be employed. Let us begin by reporting the original model of FS cell:

$$\begin{aligned} &C\frac{dV}{dt} = I_E - g_{Na}m^3h(V-V_{Na}) - g_K n^4(V-V_K) - g_L(V-V_L);\\ &\frac{dx}{dt} = (x_\infty - x)/\tau_x; \qquad x_\infty = \alpha_x/(\alpha_x+\beta_x),\ \tau_x = 1/(\alpha_x+\beta_x),\ \ (x \equiv m,h,n), \end{aligned} \tag{1}$$

where $C = 1\mu F/cm^2$ and I_E is the external stimulation current, and $\alpha_m = 4.2\ exp[(V+34.5)/11.57]$, $\beta_m = 4.2\ exp[-(V+34.5)/27]$, $\alpha_h = 0.09\ exp[-(V+45)/33]$, $\beta_h = 0.09\ exp[(V+45)/12.2]$, $\alpha_n = 0.3\ exp[(V+35)/10.67]$, $\beta_n = 0.3\ exp[-(V+35)/42.68]$. The maximal specific conductances and the reversal potentials are, respectively: $g_{Na} = 100\ mS/cm^2$, $g_K = 40\ mS/cm^2$, $g_L = 0.1\ mS/cm^2$ and $V_{Na} = 55\ mV$, $V_K = -90\ mV$ and $V_L = -68\ mV$.

By setting in equation (1) $m = m_\infty$ and $h = 0.927-n$, this model reduces to a two dimensional one still retaining the main dynamical properties of the complete one. The transition from rest to periodic firing occurs by a saddle-node bifurcation as for the complete model (see the left panel of figure 1). Consequently, the excitability type is that of class I neural model (i.e. the periodic solution originates with arbitrarily low frequency values). There is a critical value of the stimulation current, $I^* \cong 0.254\ \mu A/cm^2$, above which the model generates periodic firing of arbitrarily low frequency (see right panel of figure 1).

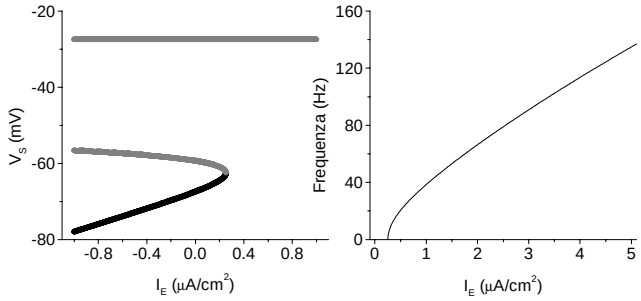

Figure 1. Characterization of the reduced model. Left panel: stationary value of membrane voltage against stimulation current; stable (black line), unstable (grey line). Right panel: discharge frequency.

The electrical and chemical synapses were modelled as follows. The inhibitory postsynaptic current is $I_{Sy}(t) = g_{Sy} S_{\mathrm{Pre}}(t)(V(t) - V_{\mathrm{Rev}})$, where g_{Sy} is the maximal specific conductance (in *mS/cm*^{2}) and V_{Rev}=-75 *mV* is the reversal potential.

The variable $S_{\mathrm{Pre}}(t)$ evolves according to equation $\dot{S}_{\mathrm{Pre}} = \alpha T(V_{\mathrm{Pre}})(1 - S_{\mathrm{Pre}}) - \tau^{-1} S_{\mathrm{Pre}}$, where α is the channel opening rate, $T(V_{\mathrm{Pre}}) = 1/(1 + e^{-V_{\mathrm{Pre}}})$ represents the dependence of transmitter concentration on presynaptic voltage and τ is the time constant of the synaptic current. Experimentally it was found that for FS cells the mean value of the decay time constant of their inhibitory current it is $<\tau>$ = 2.6 *ms* [8].

Similarly, the electrical synapse is described by $I_{El}(t) = g_{El}(V(t) - V_{\mathrm{Pre}})$, where g_{El} is the maximal specific conductance (in *mS/cm*^{2}). Values of g_{Sy} and g_{El} within the physiological range were derived from the experimental estimates of the maximal conductances: G_{Sy} = 0.8 *nS* and G_{El} = 0.2 *nS* [8]. Assuming a soma radius R_{Soma} = 7.5 μm of a FS cell gives: g_{Sy} = $G_{Sy} / 4\pi R_{\mathrm{Soma}}^2 \cong 0.1122$ *mS/cm*^{2} and $g_{El} = G_{El} / 4\pi R_{\mathrm{Soma}}^2 \cong 0.028$ *mS/cm*^{2}.

To study the phase locking states between two coupled FS cells we will use the theory of weakly coupled oscillators [5]. In the weak coupling regime the state of each oscillator is defined by its phase θ_i. In the case of two identical oscillators the time evolution of their phase difference $\phi = \theta_2 - \theta_1$ is determined by the equation $\dot{\phi} = \varepsilon(H_1(-\phi) - H_1(\phi)) = \varepsilon D(\phi)$. Let ϕ_S be a fixed point of it, then it will be stable or unstable according as $\dot{D}(\phi_S) < 0$ ($\dot{D}(\phi_S) > 0$), respectively. For inhibitory coupling it is $H_1(\phi) = T^{-1} \int_0^T Y_1(t)\, s_0(t + \phi)(V_{\mathrm{Re}\,v} - V_0(t))dt$, where V_0(t) represents the *T*-periodic voltage component of the solution of the unperturbed neuron

model and $s_0(t)$ is the solution of $\dot{S}_{\mathrm{Pre}} = \alpha T(V_{\mathrm{Pre}})(1 - S_{\mathrm{Pre}}) - \tau^{-1} S_{\mathrm{Pre}}$ with $V_{Pre}(t) = V_0(t)$. Similarly, for the electrical synapse it is $H_1(\phi) = T^{-1}\int_0^T Y_1(t)\,(V_0(t+\phi) - V_0(t))dt$. In both cases $Y_1(t)$ is the first component of the solution of the adjoint equation (see reference [5] for details). When inhibitory and electrical synapses are present, $H_1(\phi)$ is the sum of the corresponding terms and the existence and stability of the corresponding phase locked states depends on the ratio g_{El} / g_{Sy}. All integrals involved in the definition of the function $H_1(\phi)$ were evaluated numerically by using the Trapezoidal algorithm. The integration of the reduced model of FS cell was performed by using the forward Euler method with time step equal to 0.001 ms.

3. Results

The left panel of figure 2 shows the stationary values of the phase difference between two coupled identical FS cells. There is a critical value of τ, denoted by $\tau^*(I_E)$, such that for $\tau < \tau^*(I_E)$ the system gets a bistable regime (synchrony and antisynchrony), while for $\tau > \tau^*(I_E)$ only the synchronous states are stable. For $\tau = \tau^*(I_E)$ a subcritical pitchfork bifurcation occurs and the unstable phase locking states having ϕ different from 0 and 0.5, behave as separatrices between inphase and antiphase states. This is equivalent to say that they are the states in phase space separating the basins of attraction of the synchronous and antisynchronous states. Moreover $\tau^*(I_E)$ is a monotonically increasing function of I_E and this suggests that increasing the firing frequency does not promote synchronization. We have further investigated this last points and found that this behavior depends on the value of the reversal potential for the inhibitory synapse: for instance for V_{Rev} = -80 *mV* this behaviour disappears and $\tau^*(I_E)$ becomes a monotonically decreasing function of I_E (data not shown).

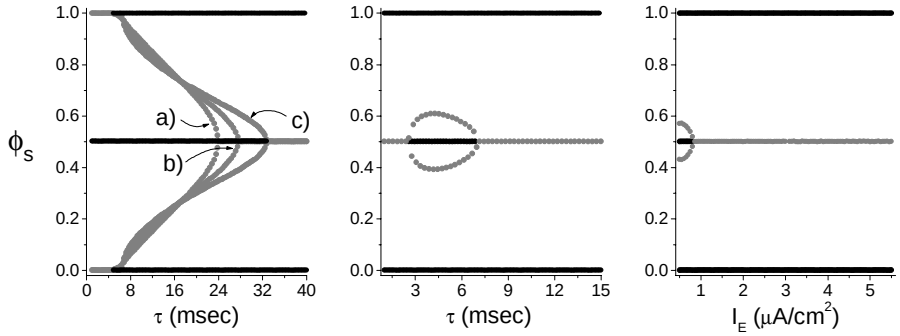

Figure 2. Phase locking states for two identical FS cells. Left panel: g_{EI} =0 and a) I_E =0.5 $\mu A/cm^2$, b) I_E =0.8 $\mu A/cm^2$, c) I_E =1.6 $\mu A/cm^2$. Middle panel: g_{EI} / g_{Sy} = 0.3 and I_E =0.8 $\mu A/cm^2$; Right panel: g_{EI} / g_{Sy} = 0.3 and τ = 2.6 *ms*. For all panels the grey (black lines) lines represent unstable (stable) phase locking states.

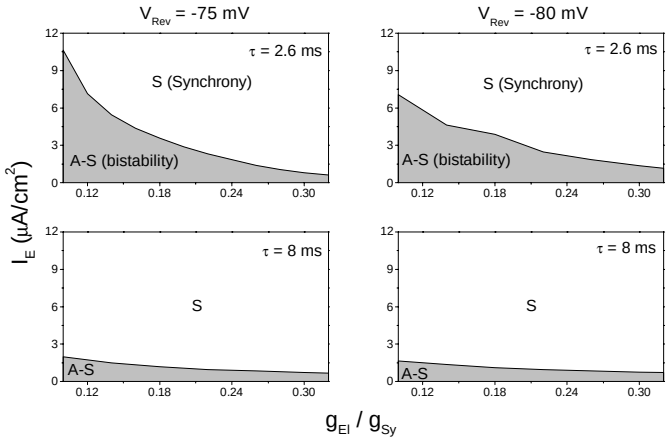

Figure 3. Bidimensional state diagrams for a pair of coupled FS cells. Left panels: V_{Rev} = -75 mV; Right panels: V_{Rev} = -80 mV. For all panels the white (light grey) region identifies the stable synchronous (synchronous and antysynchronous) phase locking regimes.

The middle panel of figure 2 shows that the presence of the electrical coupling affects dramatically the stability properties of the phase locked states (see for comparison the curve b in the left panel): now, stable synchronous states occur for values of τ close to the experimental ones.

In the right panel of figure 2 the stationary values of phase difference are reported against the stimulation current for τ = 2.6 *ms*. Then, the result is that increasing the stimulation current increases the probability to get synchronous states. For the value of I_E (~0.85 $\mu A/cm^2$) a subcritical pitchfork bifurcation occurs and for I_E > 0.85 only stable synchronous phase locking states exist. Simulations of a pair of reciprocally coupled cells are in good agreement with the previous results (data not shown).

In Figure 3 the bidimensional state diagrams characterizing the phase locking states for two values of V_{Rev} and two values of τ are reported. From the left panels it follows that increasing the electrical coupling intensity promotes the synchrony in the coupled cells. Moreover a parameter that plays a critical role is τ. Infact, for τ = 2.6 *ms* the probability to get synchronous states from random initial conditions is lower than that corresponding to τ = 8 *ms*. A similar conclusion holds even for the case V_{Rev} = -80 mV (right panels).

Comparing the top panels of figure 3 shows that lowering the values of the reversal potential for the inhibitory synapses increases the probability to get synchronous phase locking states. The same occurs when τ = 8 *ms* (bottom panels), but in this case the effect is less significant.

4. Conclusions

As shown by recent experimental and theoretical studies, networks of inhibitory interneurons can synchronize their firing discharges. The coupling parameters seem to be

critical for the emergence of synchronous activity. In this report we use a two variables biophysical model of the FS cells obtained by reduction of a four variable one proposed in [3]. The existence and stability of phase locking states for a pair of coupled FS cells were investigated in the weak coupling regime. In the case the cells interact only by inhibitory synapses regions of τ values where bistability occurs (antiphase and inphase) exist. Moreover, the increase of the decay time constant, τ, of the inhibitory synapses favours the emergence of synchrony. When the electrical coupling is introduced the τ - region where stable synchronous states occur, widens.

We found that increasing the stimulation currents or the intensity of the electrical coupling promotes the emergence of stable synchronous phase locking states. Our results are in good agreement with those reported in [11]. The only differences is that in our case synchronization is promoted for slow synapses too. Lastly, the reversal potential of the inhibitory current is shown to be a critical parameter affecting the probability of emergence of synchronous states.

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