Stability criterion for a two-neuron reciprocally coupled network based on the phase and burst resetting curves

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Abstract

Previously we have used open loop phase resetting curves (PRCs) that were tabulated for postsynaptic neurons using a perturbation equal to a burst in the presynaptic neuron to predict the patterns exhibited by a closed loop circuit containing these bursting neurons. This requires the assumption that the phase resetting observed in the circuit is the same with or without the feedback that occurs in a closed circuit, yet both the duration and waveform of the bursts can change under these conditions. Experimental and theoretical studies have shown that the amount of phase resetting produced in a neural oscillator by a synaptic input depends not only on the stimulus timing (phase), but also on its intensity and duration. The effects of variations in the synaptic coupling due to the waveform of the burst envelope or changes in frequency were ignored here, but the effects of burst duration were incorporated into the stability analysis by tabulating the burst resetting curve (BRC) as a function of the phase of the presynaptic input in the open loop condition.

Keywords: Phase resetting curve, Bursting, Phase-locking, Stability

1 Introduction

We have previously developed methods to analyze ring networks using the PRC [1,2,3,7]. In open loop experiments (no feedback), a single stimulus is applied at a given time (*t*), or phase $\varphi = t/P_0$, during the ongoing rhythm of an endogenous oscillator and the relative change in the current cycle period is tabulated as a phase resetting curve (PRC). The stimulus is a free-running burst of the presynaptic neuron, and the beginning of each cycle is measured from the burst onset (phase zero). The intrinsic period (P_0), and the intrinsic burst duration (b_0) can be transiently lengthened or shortened by a hyperpolarizing perturbation to the values P_1 and b_1, and the duration of the second cycle may be perturbed as well, often due to changes in the burst duration of the presynaptic neuron (Fig. 1A). We define the *k*th (k = 1,2) order effects of the perturbation on the oscillator's phase by $F_k(\varphi) = P_k/P_0 - 1$ [5,10], and on its burst by $G_k(\varphi) = b_k/b_0 - 1$ (Fig. 1 B, C).

Figure 1 shows the protocol (1A), the PRC (1B) and the BRC (1C) for a Type II Morris Lecar (ML) model neuron [4]. Since the ML model does not burst, we divided the waveform into burst and interburst using an arbitrary threshold of 0 mV. The synaptic current was $I_{syn} = g_{syn}m(V)\cdot(V\text{-}E_{syn})$, where g_{syn} is the conductance of the synapse, m is the synaptic activation, V is the membrane potential of the postsynaptic neuron, and E_{syn} is the synaptic reversal potential, which was set to -90 mV for inhibitory synapses. The synaptic activation function, $m = \left(1 + e^{(V_{1/2} - V)/s}\right)^{-1}$, was a steep function of potential so that the synapse is fully activated during the burst and deactivated between bursts ($V_{1/2}$ = 0 mV, s = 0.1 mV).

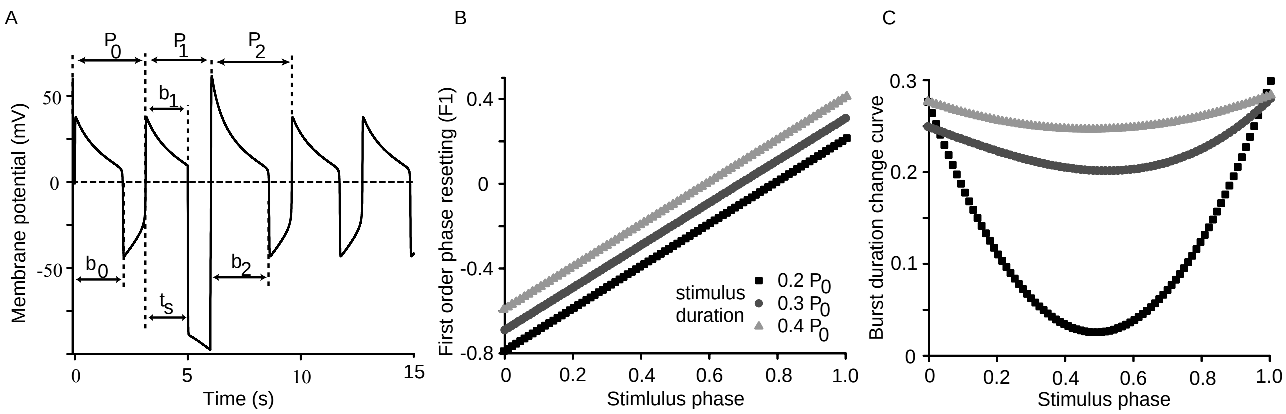

Figure 1 Example PRC and BRC from open loop simulations. A) Perturbed membrane potential trace for Type II Morris-Lecar (ML) model neuron. B) A strong inhibitory perturbation produces an almost linear first order PRC. C) The BRC in response to strong inhibitory inputs.

2 Method

Our goal was to derive a stability criterion for 1:1 phase-locked mode(s) in a reciprocally inhibitory two-neuron network by considering both the phase resetting and the change in burst duration effects. A 1:1 phase-locked mode can exist if it satisfies the periodicity constraint that the stimulus interval (t_s) of one neuron equals the recovery interval (t_r) of the other (Fig. 2). The stimulus interval, $t_s = P_0\cdot(\varphi + F_2(\varphi, \tau))$, is defined as the time elapsed between the initiation of a burst in the reference neuron and the receipt of the input stimulus. The resetting is treated as though it occurs at the onset of the stimulus. The recovery interval, $t_r = P_0\cdot(1\text{-}\varphi + F_1(\varphi, \tau))$, is the time elapsed between the receipt of the stimulus and the subsequent burst of the reference neuron. The phase φ is the open loop normal stimulus interval $\varphi = t_s/P_0$, and τ is the normalized presynaptic stimulus duration normalized by the presynaptic intrinsic burst duration. A mapping (Fig. 2) between the stimulus and the recovery intervals of the two neurons in the nth cycle is given by

$$t_{s,1}[n] + t_{r,1}[n] = P_1[n] \Leftrightarrow t_{r,1}[n] + t_{r,2}[n-1] = P_{10}\cdot(1 + F_{11}(\varphi_1[n], \tau_2[n]) + F_{21}(\varphi_1[n-1], \tau_2[n-1])),$$

$$t_{s,2}[n] + t_{r,2}[n] = P_2[n] \Leftrightarrow t_{r,1}[n] + t_{r,2}[n] = P_{20}\cdot(1 + F_{12}(\varphi_2[n], \tau_1[n+1]) + F_{22}(\varphi_2[n-1], \tau_1[n])), \quad (1)$$

where F_{ij} is the ith (i = 1,2) order PRC of neuron j, and the normalized burst duration is $\tau_i[n] = b_i[n]/b_{i0}$. We assume a steady 1:1 phase-locked mode $(\varphi_1^*, \varphi_2^*, \tau_1^*, \tau_2^*)$ in the limit as $n \to \infty$, and a perturbation $\Delta[n] = (\Delta\varphi_1[n], \Delta\varphi_2[n], \Delta\tau_1[n], \Delta\tau_2[n])^T$. The superscript T indicates the transpose.

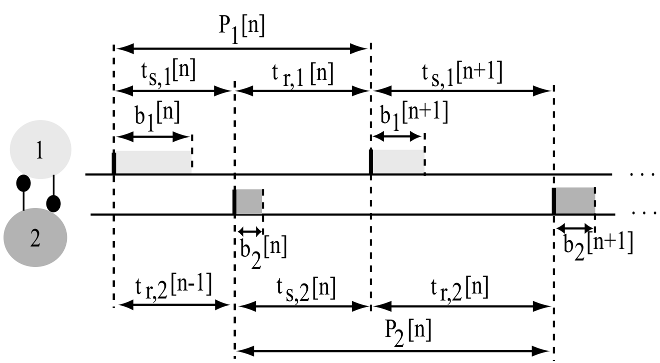

Fig. 2 Schematic representation of an alternating firing 1:1 pattern in a reciprocally inhibitory two-neuron ring network. The burst onset is marked with a vertical thick black line and the burst duration for each neuron is indicated by a filled rectangle.

3 Results

In order to determine the stability of the 1:1 phase-locked mode, if it exists, we linearized the maps (1) around the steady state by substituting for phase, $\varphi_i[n] = \varphi_i^* + \Delta\varphi_i[n]$, and burst durations, $\tau_i[n] = \tau_i^* + \Delta\tau_i[n]$ in (1), and using the appropriate first order partial derivatives to obtain a system of two equations in four unknowns:

$$P_{10}(-\Delta\varphi_1[n] + m_{11}\Delta\varphi_1[n] + h_{11}\Delta\tau_2[n]) + P_{20}(-\Delta\varphi_2[n-1] + m_{12}\Delta\varphi_2[n-1] + h_{12}\Delta\tau_1[n-1])$$
$$\cong P_{10}(m_{11}\Delta\varphi_1[n] + h_{11}\Delta\tau_2[n] + m_{21}\Delta\varphi_1[n-1] + h_{21}\Delta\tau_2[n-1]),$$
$$P_{10}(-\Delta\varphi_1[n] + m_{11}\Delta\varphi_1[n] + h_{11}\Delta\tau_2[n]) + P_{20}(-\Delta\varphi_2[n] + m_{12}\Delta\varphi_2[n] + h_{12}\Delta\tau_1[n])$$
$$\cong P_{20}(m_{12}\Delta\varphi_2[n] + h_{12}\Delta\tau_1[n] + m_{22}\Delta\varphi_2[n-1] + h_{22}\Delta\tau_1[n-1]), \quad (2)$$

where $m_{ij} = (\partial F_{ij}/\partial\varphi)_\tau$ is the slope of the ith order PRC for neuron j with respect to phase at a constant burst duration, and $h_{ij} = (\partial F_{ij}/\partial\tau)_\varphi$ is the slope of the ith order PRC for neuron j with respect to burst duration at a constant phase. To determine the slopes h we generated PRCs at different burst durations at a constant phase. The above mapping does not apply in the case of burst truncation because of the calculation of the second order resetting based on the burst duration calculated for the nth cycle, which may be altered in the nth cycle by truncation, violating causality. The burst duration in the closed loop was assumed to result from the sum of transient effects on two previous bursts

$$b_1[n] = b_{10}(1 + G_{11}(\varphi_1[n], \tau_2[n]) + G_{21}(\varphi_1[n-1], \tau_2[n-1])),$$

$$b_2[n] = b_{20}(1+ G_{12}(\varphi_2[n], \tau_1[n]) + G_{22}(\varphi_2[n-1], \tau_1[n-1])), \tag{3}$$

where $G_{ik} = b_i /b_{k0} -1$ is the ith order (i = 1,2) relative change in the burst duration for the neuron labeled k. These two equations provide an additional constraint on the 1:1 modes considered because the burst duration was assumed to be constant for each neuron in the 1:1 locking. The effect must dissipate between inputs such that the trajectory returns near the limit cycle before the next input is received. By linearizing the additional set of equations (3) we get

$$\Delta\tau_1[n] \cong p_{11}\Delta\varphi_1[n] + q_{11}\,\Delta\tau_2[n] + p_{21}\Delta\varphi_1[n-1] + q_{21}\Delta\tau_2[n-1],$$

$$\Delta\tau_2[n] \cong p_{12}\Delta\varphi_2[n] + q_{12}\,\Delta\tau_1[n] + p_{22}\Delta\varphi_2[n-1] + q_{22}\Delta\tau_1[n-1], \tag{4}$$

where $p_{ij} = (\partial G_{ij}/\partial\varphi)_\tau$ is the slope of the ith order BRC for neuron j with respect to phase at a constant burst duration in the presynaptic neuron, and $q_{ij} = (\partial G_{ij}/\partial\tau)_\varphi$, is the slope of the ith order BRC for neuron j with respect to the input burst duration at constant phase. The fluctuation equations (2) and (4) could be combined in a compact matrix equation:

$$\begin{pmatrix} P_{10} & 0 & -P_{20}h_{12} & 0 \\ P_{10}(1-m_{11}) & P_{20} & P_{20}h_{22} & -P_{10}h_{11} \\ p_{11} & 0 & -1 & q_{11} \\ 0 & p_{12} & q_{12} & -1 \end{pmatrix}\Delta[n] + \begin{pmatrix} P_{10}m_{12} & P_{20}(1-m_{21}) & 0 & P_{10}h_{21} \\ 0 & P_{20}m_{22} & 0 & 0 \\ p_{21} & 0 & 0 & q_{21} \\ 0 & p_{22} & q_{22} & 0 \end{pmatrix}\Delta[n-1] = 0\,.$$

The characteristic polynomial of the above equation was obtained using the Z-transform method (not shown). Although the characteristic polynomial of the above first order recursion is of fourth degree it can be reduced to a second degree polynomial if all BRC contributions are neglected (p_{ij} = 0 and q_{ij} = 0, for all orders i = 1, 2 and neuron indices i = 1,2), and the PRC is insensitive to changes in burst duration (h_{ij} = 0, for all i and j). The characteristic equation becomes [7]:

$$\lambda^2 - \lambda((1-m_{11})(1- m_{12}) - m_{21} - m_{22}) + m_{21}m_{22} = 0. \tag{6}$$

The above solution is valid only if the closed loop stimulus to every neuron in the network produces the same resetting as the corresponding open loop stimulus, which may not be true if the burst duration is variable. To ensure the stability of the steady 1:1 phase-locked mode all the characteristic roots must be inside the unit circle ($|\lambda| < 1$). By neglecting the second order PRC contributions to the total phase resetting (m_{2j} = 0, for all neurons j = 1, 2) we recover a previously derived expression for the characteristic root $\lambda = (1-m_{11})\,(1-m_{12})$ [3], which is valid only if every neuron receives identical stimuli both in open and closed loop, and the neurons return to their unperturbed activity during one cycle (strongly attracting limit cycle). The stability condition is again $|\lambda| < 1$, which means that the fluctuations $\Delta[n]$ decay to zero as $n \to \infty$.

If the PRCs are insensitive to burst duration (all $h_{ij} = 0$) at the phase-locking point then the contribution of the dependence of the postsynaptic burst duration on the presynaptic stimulus phase (p_{ij}) also drops out and the characteristic polynomial is

$$[\lambda^2 - \lambda((1-m_{11})(1-m_{12})-m_{21}-m_{22}) + m_{21}m_{22}][\lambda^2(-1+q_{11}q_{12}) + \lambda(q_{11}q_{22}+q_{21}q_{12}) + q_{12}q_{22}] = 0. \quad (7)$$

However, because of the requirement that burst duration remain constant from cycle to cycle, the terms for the dependence of the postsynaptic burst duration on the presynaptic burst duration remain, and the stability criterion reduces to a product of two second degree characteristic polynomials (7), one reflecting the previously determined dependence on the slopes of the PRCs and the other on the dependence on the slopes of the BRCs.

4 Discussion and conclusions

Much theoretical work on the stability of synchrony and phase locked modes has focused on weakly coupled, simple integrate and fire neurons or Type I oscillators [4,6], which enables the use of phase models, but these models do not generalize to the relaxation oscillator models that characterize bursting neurons, at least not for strong inputs that saturate as a function of synaptic strength and exert their effects largely by virtue of terminating a burst due to their strength, or by delaying a postsynaptic burst due to their long duration. The major result of this study is the generalization of a stability criterion for a two-neuron network reciprocally firing in an alternating pattern to the case in which the duration of the closed loop stimuli is different from the open loop stimulus. We neglected the possibility that the stimulus intensity might vary as a result of feedback by using a definition of the synaptic coupling in which it was essentially on during a burst and off otherwise. In the case of strong inhibitory couplings, the first order PRC at least is nearly independent of the stimuli intensity [9], because a sufficiently strong perturbation is assumed to consistently cause a switch from one branch of the limit cycle to another, with no other effects.

5 Acknowledgments

This research was supported by NSF IBN-0118117 (Carmen C. Canavier) grant.

6 References

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