

## Desynchronization, Mode Locking, and Bursting in Strongly Coupled Integrate-and-Fire Oscillators

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We show how a synchronized pair of integrate-and-fire neural oscillators with noninstantaneous synaptic interactions can destabilize in the strong coupling regime resulting in non-phase-locked behavior. In the case of symmetric inhibitory coupling, desynchronization produces an inhomogeneous state in which one of the oscillators becomes inactive (oscillator death). On the other hand, for asymmetric excitatory/inhibitory coupling, mode locking can occur leading to periodic bursting patterns. The consequences for large globally coupled networks is discussed. [S0031-9007(98)07030-6]

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Recent studies of networks of neural oscillators have identified a number of important factors contributing to the synchronizing properties of synaptic interactions [1–7]. These include the time course of excitatory and inhibitory synapses and the type of neural response to small depolarizations. For example, it is found that slow excitatory synapses tend to be desynchronizing but can be synchronizing if the synapses are sufficiently fast [7]. On the other hand, noninstantaneous inhibitory synapses tend to be synchronizing [4–6]. Most work on the synchronization of coupled neural oscillators has been carried out in the weak coupling regime where phase-reduction methods can be applied [1,8]. However, in the case of *integrate-and-fire* (IF) and related spiking models it is possible to extend the analysis to the strong coupling regime [3,6,9–11]. So far most of the results obtained from the latter models have been consistent with the basic principles extracted from the weak coupling theory.

In this Letter we show that synaptic interactions found to be synchronizing in the weak coupling regime can actually become desynchronizing when the strength of interactions becomes large. We proceed by studying a pair of IF (type I) neural oscillators with noninstantaneous synaptic interactions. These are chosen such that the pair is synchronized for sufficiently small coupling. Linear stability analysis is carried out by considering perturbations of the oscillator firing times. We show that a discrete Hopf bifurcation in the firing times can occur at a critical value of the coupling leading to the formation of a non-phase-locked state. In the case of symmetric inhibitory coupling this results in one of the oscillators becoming quiescent (oscillator death). On the other hand, in the presence of a mixture of excitation and inhibition, mode locking is found to occur with the two oscillators exhibiting periodic bursting patterns. We interpret these results in terms of an analog version of the IF model.

We begin by considering two coupled IF oscillators whose state variables  $U_i(t)$ ,  $i = 1, 2$ , evolve according to the pair of equations

$$\frac{dU_i(t)}{dt} = I_i - U_i(t) + \epsilon \sum_{j=1,2} W_{ij} \int_0^\infty E_j(t - \tau) \times J(\tau) d\tau \quad (1)$$

with  $U_i(t^+) = 0$  whenever  $U_i(t) = 1$ . We allow for both mutual and self interactions as specified by the weight matrix  $\mathbf{W}$ ; the overall strength of the interactions is determined by the parameter  $\epsilon$ ,  $\epsilon > 0$ . The  $i$ th oscillator has an external input  $I_i$  with  $I_i > 1$  so that in the absence of any coupling,  $\epsilon = 0$ , each oscillator fires at a rate  $1/T_i$  with  $T_i = \ln[I_i/(I_i - 1)]$ . Neglecting the shape of an individual pulse, the output spike train of each oscillator is represented as a sequence of Dirac delta functions,  $E_i(t) = \sum_{n \in \mathbb{Z}} \delta(t - T_i^n)$ , where  $T_i^n$  is the  $n$ th firing time of the oscillator; that is,  $U_i(T_i^n) = 1$  for all integers  $n$ . We assume that each spike is converted to a postsynaptic potential whose shape is given by the  $\alpha$  function  $J(\tau) = \alpha^2 \tau e^{-\alpha \tau} \Theta(\tau)$  with large (small)  $\alpha$  corresponding to fast (slow) synapses, and  $\Theta(\tau) = 1$  if  $\tau > 0$  and zero otherwise. For simplicity, we neglect the effects of discrete axonal transmission delays.

We define a phase-locked solution of Eq. (1) to be one for which the firing times satisfy  $T_j^n = (n - \theta_j)T$ ,  $\theta_j \in \mathbb{R} \setminus \mathbb{Z}$ , with the collective period  $T$  and phase difference  $\phi = \theta_2 - \theta_1$  determined from the pair of equations [6,11]

$$1 = (1 - e^{-T})I_i + \epsilon \sum_{j=1,2} W_{ij} K_T(\theta_j - \theta_i), \quad (2)$$

where  $K_T(\phi) = e^{-T} \int_0^T e^{t\hat{J}_T(t + \phi T)} dt$  and  $\hat{J}_T(t) = \sum_{n \in \mathbb{Z}} J(t + nT)$ . Equation (2) can be derived by integrating Eq. (1) between  $T_i^n$  and  $T_i^{n+1}$ . Suppose that  $I_i$  and  $W_{ij}$  are related according to

$$I_i = \bar{I} - \frac{\hat{\epsilon}_i K_{\bar{T}}(0)}{1 - e^{-\bar{T}}}, \quad \hat{\epsilon}_i = \epsilon \sum_{j=1,2} W_{ij} \quad (3)$$

for some  $\bar{I} > 1$  and  $\bar{T} = \ln[\bar{I}/(\bar{I} - 1)]$ . Then the synchronous state  $\phi = 0$  with collective period  $\bar{T}$  exists as a solution to Eq. (2). (If  $\hat{\epsilon}_i$  and  $I_i$  are both  $i$  independent

then such a solution is ensured by the underlying symmetry of the system). In order to investigate the linear stability of the synchronous state, we consider perturbations of the firing times of the form  $T_j^n = n\bar{T} + \delta_j^n$  [6,9,12]. Integrate Eq. (1) between two successive firing events and expand the resulting map for the firing times to first order in the perturbations  $\delta_j^n$ . This generates a linear delay-difference equation which has solutions of the form  $\delta_j^n = e^{n\lambda} \delta_j$ ,  $\lambda \in \mathbb{C}$ ,  $0 \leq \text{Im } \lambda < 2\pi$ . The eigenvalues  $\lambda$  satisfy the characteristic equation [12]

$$\text{Det} \begin{pmatrix} W_{11} \epsilon \tilde{G}_{\bar{T}}(\lambda) - A_1 & W_{12} \epsilon \tilde{G}_{\bar{T}}(\lambda) \\ W_{21} \epsilon \tilde{G}_{\bar{T}}(\lambda) & W_{22} \epsilon \tilde{G}_{\bar{T}}(\lambda) - A_2 \end{pmatrix} = 0 \quad (4)$$

with

$$A_i = (e^\lambda - 1)(\bar{T} - 1 + \hat{\epsilon}_i A) + \hat{\epsilon}_i B, \quad i = 1, 2, \quad (5)$$

$$A = \hat{J}_{\bar{T}}(0) - \frac{K_{\bar{T}}(0)}{1 - e^{-\bar{T}}}, \quad B = \tilde{G}_{\bar{T}}(0) = \frac{K'_{\bar{T}}(0)}{\bar{T}}, \quad (6)$$

$$\tilde{G}_T(\lambda) = e^{-T} \int_0^T e^t \sum_{n \in \mathbb{Z}} J'(t + nT) e^{-n\lambda} dt, \quad (7)$$

where  $'$  denotes differentiation. For  $J(\tau)$  given by an  $\alpha$  function, the functions  $K_T(\phi)$ ,  $\hat{J}_T(\phi)$ , and  $\tilde{G}_T(\lambda)$  can be evaluated explicitly by performing a summation over geometric series [12]. In particular, one finds that  $\tilde{G}_T(\lambda)$  has a pole at  $\lambda = -\alpha T$ .

One solution to Eq. (4) is  $\lambda = 0$ , which reflects invariance under constant phase shifts. Thus the condition for linear stability of the synchronous state is  $\text{Re } \lambda < 0$  for all other eigenvalues. For sufficiently small coupling, all solutions to Eq. (4) in the complex  $\lambda$  plane will be in an  $\epsilon$  neighborhood of either  $\lambda = 0$  or the pole at  $\lambda = -\alpha T$ . Therefore, taking  $\lambda = \mathcal{O}(\epsilon)$  and expanding Eq. (4) to second order in  $\epsilon$ , we obtain the following stability condition for the synchronous state:

$$\epsilon K'_{\bar{T}}(0) \text{Re } \hat{\nu} < 0, \quad (8)$$

where  $\hat{\nu}$  is the nonzero eigenvalue of the modified weight matrix  $\hat{W}_{ij} = W_{ij} - \delta_{i,j} \sum_{k=1,2} W_{ik}$ . It turns out that  $K'_{\bar{T}}(0) < 0$  for  $0 < \alpha < \infty$  and finite  $T$  so that Eq. (8) reduces to the condition  $\text{Re } \hat{\nu} > 0$ .

Suppose that Eq. (8) does hold for a given weight matrix  $\mathbf{W}$  and that the pair of IF oscillators are synchronized for sufficiently small  $\epsilon$ . The question we wish to address is whether or not increasing the coupling  $\epsilon$  can destabilize the synchronous state. First note that destabilization cannot occur due to a real eigenvalue crossing the origin. [Simply set  $\lambda = 0$  in Eq. (4).] Therefore, we need to investigate the possibility of a pair of pure imaginary eigenvalues  $\lambda = \pm i\omega_c$  occurring at some critical coupling  $\epsilon_c$  thus signaling the onset of a discrete Hopf bifurcation in the firing times. Having established the ex-

istence of such an instability, we can then look for new solutions beyond the bifurcation point by direct numerical solution of the dynamical system. Beyond the bifurcation point we expect the sequence of interspike intervals  $\Delta_k^n = T_k^{n+1} - T_k^n$ ,  $n \in \mathbb{Z}$  to lie on some closed invariant circle exhibiting periodic or quasiperiodic behavior.

We shall illustrate the above ideas by considering two particular choices of  $\mathbf{W}$ .

(i) *Symmetric inhibitory coupling* ( $W_{11} = W_{22} = 0$ ,  $W_{12} = W_{21} = -1$ ).—For this example,  $\hat{\nu} = 2$  so that the inhibitory pair of oscillators has a stable synchronous state for sufficiently small  $\epsilon$ . In Ref. [6], a return map argument was used to derive the stability condition (8) for arbitrary coupling. As we shall now show, such a condition is necessary but not sufficient, since the oscillators can desynchronize via a Hopf bifurcation in the strong coupling regime. Setting  $\lambda = i\omega_c$  in Eq. (4) for the given weight matrix and equating real and imaginary parts leads to a pair of equations whose solutions determine  $\omega_c$  and the corresponding critical coupling  $\epsilon_c$ . The solution branches for  $\epsilon_c$  are plotted as a function of  $\alpha$  in Fig. 1a. Crossing the solid transition curve in Fig. 1a from below signals the destabilization of the synchronous state due to excitation of the linear eigenmode  $(\delta_1, \delta_2) = (1, -1)$ . The direct numerical solution of Eq. (1) shows that there emerges an inhomogeneous state consisting of one active

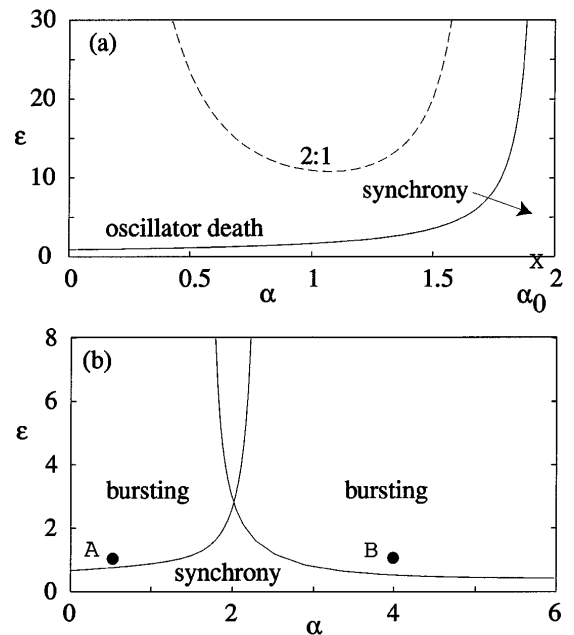


FIG. 1. Critical coupling  $\epsilon_c$  for the desynchronization of a pair of IF oscillators is plotted as a function of the inverse rise time  $\alpha$ . External bias  $\bar{T} = 1.5$ . (a) Symmetric inhibitory coupling. The 1:1 synchronous state becomes unstable as the solid transition curve is crossed from below leading to oscillator death. The dashed curve signals excitation of a 2:1 mode-locked state. (b) Asymmetric excitatory-inhibitory coupling. The 1:1 synchronous state becomes unstable when either transition curve is crossed from below leading to bursting.

oscillator and one passive oscillator. This is an example of so-called oscillator death. It is also possible to excite a 2:1 mode-locked state by crossing the dashed transition curve in Fig. 1a; the two oscillators are synchronized [due to the excitation of the linear eigenmode  $(\delta_1, \delta_2) = (1, 1)$ ] but fire doublets. Note that there exists a critical inverse-rise time  $\alpha_0$  such that for sufficiently fast synapses ( $\alpha > \alpha_0$ ) the synchronous state remains stable for all  $\epsilon$ .

(ii) *Asymmetric excitatory/inhibitory coupling* ( $W_{11} = W_{22} = 1, W_{12} = -2, W_{21} = 1$ ).—For this example,  $\hat{\nu} = 3$ , so once again there exists a stable synchronous state for sufficiently small  $\epsilon$ . In contrast to the previous example, a critical coupling for a Hopf bifurcation in the firing times exists for all  $\alpha$  as displayed in Fig. 1b. The direct numerical solution of Eq. (1) shows that beyond the Hopf bifurcation point the two oscillators exhibit periodic bursting patterns (Fig. 2). This can be understood in terms of mode locking associated with periodic variations of the interspike intervals on attracting invariant circles (Fig. 3). Suppose that the  $k$ th oscillator has a periodic solution of length  $M_k$  so that  $\Delta_k^{n+pM_k} = \Delta_k^n$  for all integers  $p$ . If  $\Delta_k^1 \gg \Delta_k^n$  for all  $n = 2, \dots, M_k$ , say, then the resulting spike train exhibits bursting with the interburst interval equal to  $\Delta_k^1$  and the number of spikes per burst equal to  $M_k$ . Two important aspects of the spike trains displayed in Fig. 2 should be noted. First, although the data are taken for parameter values close to the bifurcation curves of Fig. 1b, the frequency  $\omega$  of the variations in the interspike intervals differs significantly from the critical frequency  $\omega_c$ . Moreover, the size of the fluctuations in the interspike intervals is large compared to  $\sqrt{\epsilon - \epsilon_c}$ . This suggests that the Hopf bifurcation is subcritical rather than supercritical. In other words, when the synchronous state destabilizes there is a jump to a coexisting attracting invariant circle (a hard excitation). This also implies that the observed behavior will be robust in the presence of small amounts

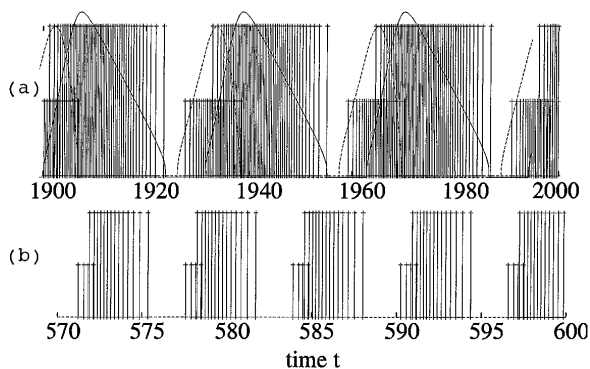


FIG. 2. Spike train dynamics for a pair of IF oscillators with both excitatory and inhibitory coupling as in Fig. 1b. The firing times of the two oscillators are represented with lines of different heights (marked with a +). Part (a) corresponds to point A in Fig. 1b, while (b) shows an example of spike train dynamics at point B. Smooth curves represent variation of firing rate in analog version of model (with  $T_{\text{ref}} = 0$ ).

of noise. Second, although both oscillators have different interburst intervals ( $\Delta_1^1 \neq \Delta_2^1$ ) and numbers of spikes per burst ( $M_1 \neq M_2$ ), their spike trains have the same total period, that is,  $\sum_{n=1}^{M_1} \Delta_1^n = \sum_{n=1}^{M_2} \Delta_2^n$ .

Further insight into the above results can be obtained by considering an analog version of the IF model in which the output activity of an oscillator is now represented as a short-term average firing rate rather than as a sequence of spikes. Such an analog model can be expressed in terms of an integral equation for an effective synaptic current  $X_i(t)$  [12]:

$$X_i(t) = \epsilon \sum_{j=1,2} W_{ij} \int_0^\infty J(\tau) f(X_j(t - \tau)) d\tau + I_i - \bar{I} \tag{9}$$

with the firing rate  $f(X)$  determined from the IF model,

$$f(X) = \left[ T_{\text{ref}} + \ln\left(\frac{\bar{I} + X}{\bar{I} + X - 1}\right) \right]^{-1} \Theta(\bar{I} + X - 1) \tag{10}$$

and  $T_{\text{ref}}$  is an absolute refractory period. (This is introduced to ensure that the firing rate has an upper bound.) Choosing  $I_i = \bar{I} - \hat{\epsilon}_i f(0)$  [cf. Eq. (3)], we ensure that  $X_j = 0, j = 1, 2$  is a fixed point of Eq. (9). Linearization about this homogeneous state, which plays an analogous role to the synchronous state of the IF model, leads to the stability condition (independent of  $\alpha$ )

$$\sqrt{\epsilon f'(0)} \text{Re } \nu_k < 1, \tag{11}$$

where  $\nu_k, k = 1, 2$  are the eigenvalues of  $\mathbf{W}$ . It follows that the fixed point is stable in the weak coupling regime.

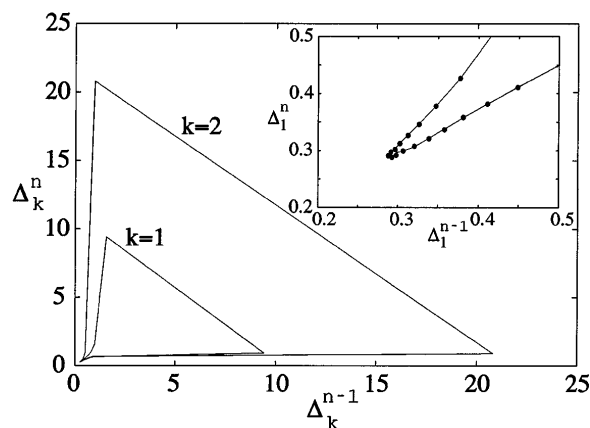


FIG. 3. A plot of the interspike intervals ( $\Delta_k^{n-1}, \Delta_k^n$ ) beyond the discrete Hopf bifurcation point (as for Fig. 2a) of the linearized firing map shows a projection of dynamics on an invariant circle. Points on the orbit of the full nonlinear firing map are connected by lines. Note that each triangular region is associated with only one of the oscillators, highlighting the difference in interburst intervals (see also Fig. 2a). The inset is a blowup of orbit points for one of the oscillators within a burst.

Moreover, it is simple to establish that for symmetric inhibitory coupling the fixed point undergoes a subcritical pitchfork bifurcation at some critical value  $\epsilon_c$ . Destabilization leads to the formation of a state in which one neuron is passive (zero firing rate), which is consistent with the behavior found for the IF model with slow synapses. Similarly, in the case of an excitatory/inhibitory pair of analog neurons, the fixed point destabilizes via a subcritical Hopf bifurcation leading to a hard excitation in which both oscillators have time-varying firing rates. The period of fluctuations is the same for both oscillators, which is in good agreement with the periodicity of the bursting patterns of the IF model particularly when  $\alpha$  is small [see smooth curves in Fig. 2a].

We briefly discuss some related work. First, van Vreeswijk [10] has shown that networks of IF oscillators with global excitatory coupling can destabilize from an asynchronous state via a Hopf bifurcation in the firing times. However, this leads to slow ( $\omega_c \approx 0$ ) and small amplitude variations in the average firing rates of the oscillators. This can be understood by looking at a corresponding network of excitatory analog neurons, which can only bifurcate to another homogeneous time-independent state. Second, Han *et al.* [13] have demonstrated how desynchronization can lead to bursting firing patterns in a simplified Hodgkin-Huxley system. The mechanism for dephasing in their study is weak diffusive coupling rather than strong synaptic coupling with delays as considered here. Interestingly, in both cases bursting arises without the need for additional slow ionic currents.

In conclusion, we have shown how a pair of IF oscillators can desynchronize in the strong coupling regime via a discrete Hopf bifurcation in the firing times. This generates a non-phase-locked state whose time-averaged behavior is consistent with that of a corresponding analog model for sufficiently slow synapses. One finds that this result generalizes to larger networks. For example, a network of  $N$  identical IF oscillators with all-to-all inhibitory coupling can be handled within this framework by setting  $W_{ii} = 0$  and  $W_{ij} = -1/(N - 1)$  for  $j \neq i$  in Eq. (2) and extending the sum over  $j$  from 2 to  $N$ . Once again, the

synchronous state is guaranteed to exist from the underlying symmetry of the system and its stability for weak coupling is given by Eq. (8). Moreover, the characteristic equation governing the bifurcation structure for arbitrary coupling is easily expressed when one considers perturbations of the firing times in the basis of eigenvectors of  $\mathbf{W}$ , possessing eigenvalues  $1/(N - 1)$  [ $(N - 1)$  fold degenerate] and  $-1$ . Beyond the bifurcation point one finds a state with active and passive clusters. Interestingly, a lattice of oscillators with long-range inhibition and short-range excitation desynchronizes to a state with spatially periodic variations in activity. Indeed, a Turing-Hopf instability in the firing times turns out to be a fundamental mechanism for pattern formation in IF networks as will be demonstrated elsewhere [12].

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