

Stability of periodic oscillations in a network of neurons with time delay

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Abstract

Oscillatory behavior is investigated in the case of a network of oscillatory pairs of neurons with time-delayed connections. The uniform periodic solution is obtained from the numerical integration of a system reduced to a single pair of neurons. The stability of this periodic orbit in the network is estimated from a discretization of the time axis. It is shown that the periodic solution becomes unstable as the size of the system is increased. This loss of stability results in the appearance of spatiotemporally structured behavior, such as travelling waves.

Oscillatory activity is a common feature of natural [1,2] and artificial [3] networks of neurons. Oscillations can arise as an intrinsic property of individual neurons [4], or alternatively, from the synaptic interactions between neurons that would not oscillate otherwise [2,5]. In this paper, we investigate oscillatory phenomena of the latter kind.

The role of synchronized oscillations in the cerebral cortex was subject to much attention these last years (reviewed in Ref. [6]). Models of neural networks with time-delayed interactions were proposed to account for this oscillatory activity [7–10] and typically displayed robust oscillations for some conditions of input. Solvable models without time delay were also investigated in the same context [11–13]. Such models consider densely connected networks for which synchronized oscillations are usually seen. The present model addresses oscillatory behavior in the case of networks with local connectivity, which is closer to the connectivity of cerebral cortical neurons [14].

The type of model described here is derived from passive membrane equations with sigmoid-type of synaptic coupling. This is a simplified model of synaptic interaction which relies on the hypothesis that the output activity of the synapse can be expressed as a sigmoid function of the presynaptic membrane potential, with a time delay characteristic of propagation and release of transmitter. Similar types of models have been introduced previously [15–17] and were shown to display oscillatory behavior.

Limit cycle oscillations and bursting behavior were shown to occur in a single pair of neurons interconnected with excitatory and inhibitory synapses [17]. This system was described by a two-variable delay differential equation (DDE) in which limit cycle oscillations arose through a Hopf bifurcation and turn into bursting oscillations via a homoclinic bifurcation [17]. We investigate here the oscillatory behavior of a locally-connected network

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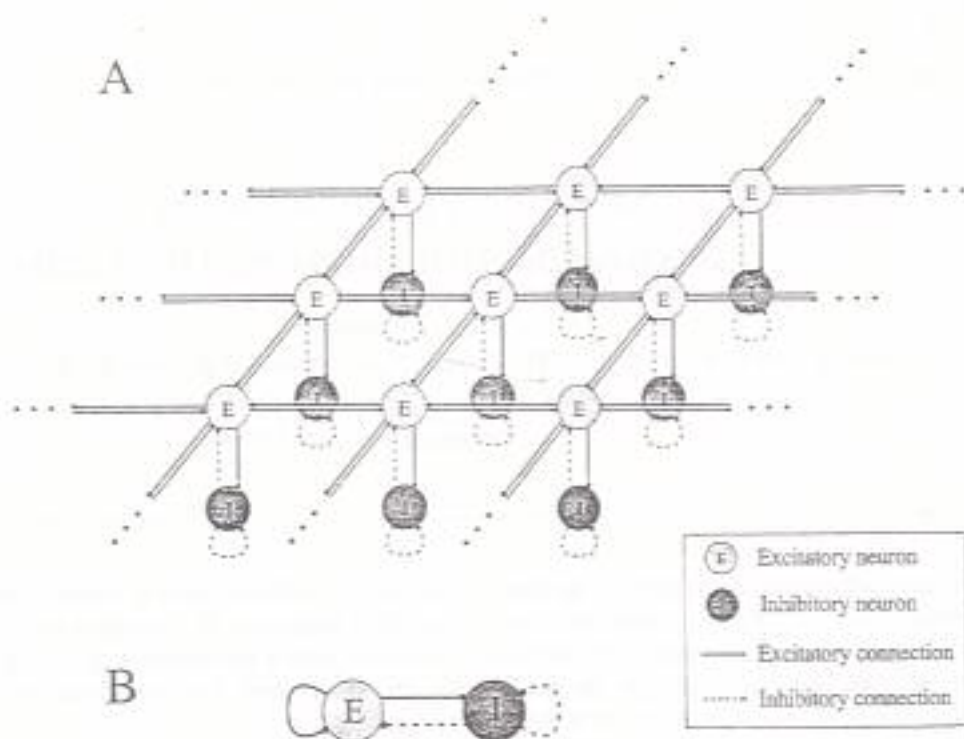


Fig. 1. Pattern of connectivity used in the model. (A) Connectivity pattern of the two-dimensional network. Nine pairs of excitatory (E) and inhibitory (I) neurons are illustrated. Each pair is connected to adjacent pairs via excitatory-to-excitatory connections only. (B) Reduced system consisting of a single pair of interconnected neurons with self-connections. This reduced system is used for calculating uniform solutions of the network.

constituted of pairs of neurons described by the same equations. We show that such a network displays spatially uniform oscillations which become unstable as the size of the system is increased.

We consider the case of a two-dimensional network of N pairs of neurons, where N is an integer squared. Connections between adjacent pairs of neurons are made between excitatory neurons (Fig. 1A). Labelling the membrane potential of excitatory and inhibitory neurons by X_i and Y_i respectively ($i = 1, \dots, N$), one obtains

$$\begin{aligned} \frac{dX_i}{dt} &= -\gamma(X_i - V_L) - (X_i - V_E) \frac{\Omega_1}{4} \sum_j F(X_j(t - \tau)) - (X_i - V_I) \Omega_2 F(Y_i(t - \tau)), \\ \frac{dY_i}{dt} &= -\gamma(Y_i - V_L) - (Y_i - V_E) \Omega_3 F(X_i(t - \tau)) - (Y_i - V_I) \Omega_4 F(Y_i(t - \tau)), \quad i = 1, \dots, N, \end{aligned} \quad (1)$$

where $\gamma^{-1} = 4$ ms is the time constant of the membrane, $V_L = -60$ mV is the leakage potential, $V_E = 50$ mV and $V_I = -80$ mV are the equilibrium potentials for synaptic excitation and inhibition respectively. $\Omega_1, \Omega_2, \Omega_3, \Omega_4$ are the synaptic weights for excitatory-to-excitatory, inhibitory-to-excitatory, excitatory-to-inhibitory and inhibitory-to-inhibitory connections respectively. $\tau = 2$ ms is the time delay due to signal propagation and synaptic transmission.

F is a sigmoid function used for synaptic interaction. $F(V)$ gives the output activity of the neuron in function of its membrane potential V :

$$F(V) = \frac{1}{1 + \exp[-\alpha(V + 25)]},$$

where $\alpha = 0.2$ mV $^{-1}$.

The connectivity pattern is homogeneous, in the sense that each excitatory neuron receives the same number of connections from adjacent excitatory neurons (Fig. 1A), with identical values for synaptic weights (Ω_1). The boundary conditions are taken as the discretized version of null-flux conditions^{#1}.

For such a spatially uniform connectivity, there exist spatially uniform solutions in the network. If we assume that there is a periodic solution $\{X_i(t) = X(t), Y_i(t) = Y(t)\}$ with $X(t+T) = X(t)$ and $Y(t+T) = Y(t)$ where T is the oscillation period, then Eqs. (1) reduce to a single pair of neurons with self-connections (illustrated in Fig. 1B):

$$\begin{aligned}\frac{dX}{dt} &= -\gamma(X - V_L) - (X - V_E)\Omega_1 F(X(t-\tau)) - (X - V_I)\Omega_2 F(Y(t-\tau)), \\ \frac{dY}{dt} &= -\gamma(Y - V_L) - (Y - V_E)\Omega_3 F(X(t-\tau)) - (Y - V_I)\Omega_4 F(Y(t-\tau)).\end{aligned}\quad (2)$$

This system is identical to that studied before [17] and was shown to possess a limit cycle, which corresponds in Eqs. (1) to a uniform periodic solution.

Methods already employed for calculating the stability of periodic orbits in DDEs include estimation of the Floquet multipliers [18,19] or estimation of the stability of the fixed point associated to the periodic orbit after a Poincaré section [20]. These methods were applied to one-variable DDEs and cannot be used with the present equations. We use here another method, based on a discretization of the time axis, for estimating the stability of the uniform periodic orbit.

By linearizing the system around the periodic solution, one obtains

$$\begin{aligned}\frac{dx_i}{dt} &= -a_1 x_i - \frac{b_1}{4} \sum_j x_j(t-\tau) - b_2 y_i(t-\tau), \\ \frac{dy_i}{dt} &= -a_2 y_i - b_3 x_i(t-\tau) - b_4 y_i(t-\tau), \quad i = 1, \dots, N,\end{aligned}\quad (3)$$

where $a_1, a_2, b_1, \dots, b_4$ are time periodic coefficients of period T , defined as

$$\begin{aligned}a_1(t) &= -\gamma - \Omega_1 F_1(t) - \Omega_2 F_2(t), & a_2(t) &= -\gamma - \Omega_3 F_1(t) - \Omega_4 F_2(t), \\ b_1(t) &= -[X(t) - V_E]\Omega_1 \alpha F_1(t)[1 - F_1(t)], & b_2(t) &= -[X(t) - V_I]\Omega_2 \alpha F_2(t)[1 - F_2(t)], \\ b_3(t) &= -[Y(t) - V_E]\Omega_3 \alpha F_1(t)[1 - F_1(t)], & b_4(t) &= -[Y(t) - V_I]\Omega_4 \alpha F_2(t)[1 - F_2(t)],\end{aligned}\quad (4)$$

with $F_1(t) = F(X(t))$ and $F_2(t) = F(Y(t))$, and the following property has been used,

$$\left(\frac{\partial F(X)}{\partial X}\right)_{X=a} = \alpha F(a) [1 - F(a)].$$

The linearized system (3) can also be written in vectorial form:

$$\frac{d\mathbf{z}(t)}{dt} = A(t)\mathbf{z}(t) + B(t)\mathbf{z}(t-\tau),\quad (5)$$

where $\mathbf{z}(t) = (x_1, x_2, \dots, x_N, y_1, y_2, \dots, y_N)$ and $A(t)$ and $B(t)$ are matrices of size $4N^2$ with time periodic elements of period T .

The stability of the periodic solution is found by solving this equation. We choose here to use a discretization of the time axis which reduces the linearized system (5) to a discrete map. The eigenvalues of this map characterize the stability of the periodic orbit in the network.

^{#1} Periodic boundary conditions were also used and were found to give rise to a very similar behavior.

Keeping only the first-order terms in the expansion:

$$z(t+h) = z(t) + h \frac{dz(t)}{dt} + \dots, \quad (6)$$

where h is the discretization time step, one obtains

$$z(t+h) = z(t) + hA(t)z(t) + hB(t)z(t-\tau+h). \quad (7)$$

Here, $z(t-\tau)$ was replaced by $z(t-\tau+h)$, which reduces Eqs. (5) to an equivalent discretized form that allows estimation of the stability of the periodic orbit. In the limit as $h \rightarrow 0$, this system tends to (5).

By choosing the discretization step h as a sub-multiple of the time delay τ , such that $k h = \tau$ where k is a positive integer, one obtains

$$z(t+h) = z(t) + hA(t)z(t) + hB(t)z(t-(k-1)h). \quad (8)$$

If τ is a sub-multiple of the period T of the oscillation, such that $m\tau = T$, where m is a positive integer, then the same discretization can be repeated for the times $t, t-h, \dots, t-(k-2)h$:

$$\begin{aligned} z(t) &= z(t-h) + hA(t-h)z(t-h) + hB(t-h)z(t-kh), \\ z(t-h) &= z(t-2h) + hA(t-2h)z(t-2h) + hB(t-2h)z(t-(k+1)h), \quad \dots \\ z(t-(k-2)h) &= z(t-(k-1)h) + hA(t-(k-1)h)z(t-(k-1)h) \\ &\quad + hB(t-(k-1)h)z(t-(2k-2)h). \end{aligned} \quad (9)$$

By choosing

$$\begin{aligned} u_1(t+\tau) &= z(t+h), & u_1(t) &= z(t-(k-1)h), & u_2(t+\tau) &= z(t), & u_2(t) &= z(t-kh), \\ u_3(t+\tau) &= z(t-h), & u_3(t) &= z(t-(k+1)h), & \dots & & \\ u_k(t+\tau) &= z(t-(k-2)h), & u_k(t) &= z(t-(2k-2)h), \end{aligned}$$

one obtains the following map,

$$M(t)U(t+\tau) = N(t)U(t), \quad (10)$$

where U is a vector of components $\{u_1, \dots, u_k\}$, of dimension $2Nk$. The matrix $M(t)$ equals

$$\begin{pmatrix} I - I - hA(t) & 0 & \dots & 0 \\ 0 & I & -I - hA(t-h) & \vdots \\ \vdots & & \ddots & \\ 0 & \dots & I & -I - hA(t-(k-2)h) \\ 0 & \dots & 0 & I \end{pmatrix},$$

and the matrix $N(t)$ equals

$$\begin{pmatrix} hB(t) & 0 & \dots & 0 \\ 0 & hB(t-h) & & \vdots \\ \vdots & & \ddots & \\ 0 & 0 & hB(t-(k-2)h) & 0 \\ I + hA(t-(k-1)h) & 0 & \dots & 0 & hB(t-(k-1)h) \end{pmatrix}.$$

These two matrices are of dimension $4N^2k^2$.

If M is invertible, the discretized equation can be written as

$$U(t + \tau) = M^{-1}(t)N(t)U(t).$$

By choosing $J(t) = M^{-1}(t)N(t)$ and by reiterating m times, one obtains

$$U(t + \tau) = J(t)U(t), \quad (11)$$

$$U(t + 2\tau) = J(t + \tau)U(t + \tau) = J(t + \tau)J(t)U(t), \quad \dots, \quad (12)$$

$$\begin{aligned} U(t + m\tau) &= J(t + (m-1)\tau)U(t + (m-1)\tau) \\ &= [J(t + (m-1)\tau) \dots J(t + 2\tau)J(t + \tau)J(t)]U(t). \end{aligned} \quad (13)$$

The last of these equations can be written as

$$U(t + T) = J^{(m)}(T)U(t), \quad (14)$$

where the matrix $J^{(m)}(T)$ represents the linear mapping of the system, after discretization, over the period T of the oscillation. The eigenvalues of $J^{(m)}(T)$ determine the stability of the limit cycle: if one of these eigenvalues exceeds 1 in modulus, then the limit cycle is unstable.

The stability analysis is only possible for the values of the parameters for which the period T of the oscillation is a multiple of the time delay: $T = m\tau$. For the values considered here ($\Omega_2 = \Omega_3 = 12.5$ and $\Omega_4 = 0$), three values of Ω_1 give a period which fulfills this requirement. They were estimated numerically from Eq. (2). They are $\Omega_1 = 12.565$ (period of 34 ms; $m = 17$), $\Omega_1 = 13.910$ (period of 36 ms; $m = 18$) and $\Omega_1 = 15.270$ (period of 38 ms; $m = 19$).

The matrix $J^{(m)}$ was constructed for the three values of the parameters described above and for different values of the discretization step h . The eigenvalues were estimated numerically^{#2} and all of them were found to be real positive. In this case, the stability criterion for the periodic orbit becomes simply

$$\lambda_{\max} < 1, \quad (15)$$

where λ_{\max} is the largest positive eigenvalue.

Fig. 2a shows the maximal eigenvalue as a function of the discretization step h for $N = 1$. This is equivalent to evaluating the stability of the periodic orbit in the two-variable system (2). It can be seen that as $h \rightarrow 0$, the value of λ_{\max} tends to a value λ_0 . In the limit for very small h , λ_{\max} can be expanded as

$$\lambda_{\max} = \lambda_0 + \lambda_1 h + \lambda_2 h^2 + \dots \quad (16)$$

The value of λ_0 was approached by reducing h as much as possible^{#3}, and the value of λ_0 was extrapolated using expression (16).

^{#2} Numerical estimation was performed using a NAG (Numerical Algorithm Group) algorithm (see also Ref. [21]) on IBM 3090 computers with large virtual memory.

^{#3} Diagonalization of large matrices $J^{(m)}(T)$ by computer means typically requires very large memory space but reasonable computer time.

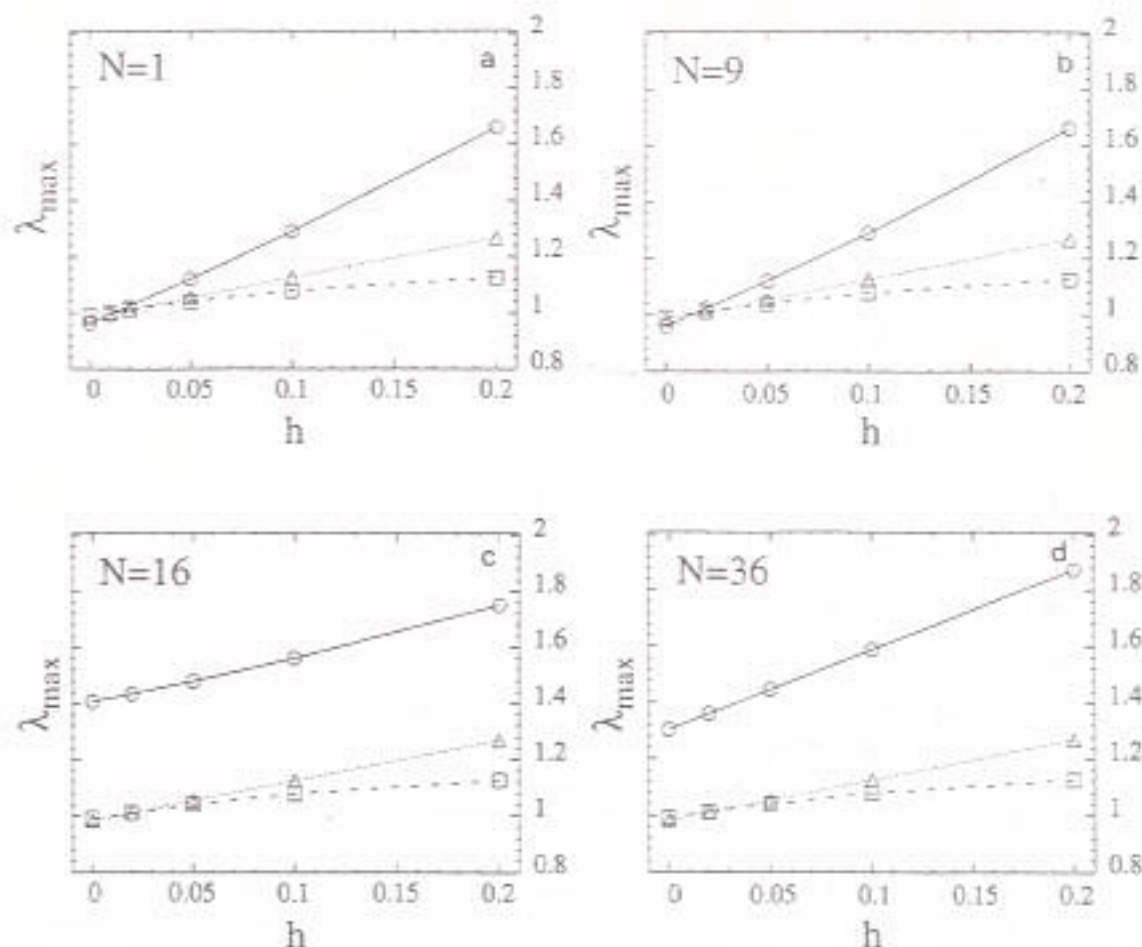


Fig. 2. Maximal eigenvalue λ_{\max} as a function of the discretization step h (in ms). Four different network sizes are illustrated ($N = 1$, $N = 9$, $N = 16$ and $N = 36$). The extrapolated value of λ_{\max} in $h = 0$ gives an estimation of the stability of the periodic orbit in the network. The three curves correspond to three values of m : $m = 17$ (dashed-squares, $\Omega_1 = 12.565$), $m = 19$ (dotted-triangles, $\Omega_1 = 13.91$) and $m = 18$ (solid-circles, $\Omega_1 = 15.27$). For $N = 16$ and $N = 36$ the $m = 19$ eigenvalues indicate that the periodic orbit is unstable, as shown by their convergence to a value greater than unity at $h = 0$.

For $N = 1$, $\lambda_0 < 1$, and the periodic orbit is stable, as expected. For $N > 1$, the extrapolated value λ_0 provides an estimation of the stability of the uniform periodic oscillation in a network of size N . Figs. 2b–2d show the values of λ_{\max} for networks of size $N = 9$, $N = 16$ and $N = 36$. Fig. 3 reports the values extrapolated for λ_0 as a function of the size of the network. Both figures show that the uniform oscillation can become unstable for $N > 9$.

The numerical simulation of the network confirmed the stability analysis. For $N = 9$ (Fig. 4A), the whole system oscillates in phase; whereas for $N \geq 16$ (Figs. 4B, 4C), this uniform oscillation is unstable and the network shows spatiotemporal patterns, such as travelling waves. This type of spatiotemporal activity is commonly seen in excitable media (reviewed in Ref. [22]) and was also analyzed in neural networks [23]. Numerical simulations also showed that the transition between uniform oscillations and spatiotemporal behavior do not depend on the particular values chosen for the parameters²⁴. For larger sizes of the network, more irregular spatiotemporal

²⁴ Numerical simulations with longer range of random connectivity were performed and qualitatively similar results were observed [24]. The behavior was the same and independent of small variations in other parameters of the model.

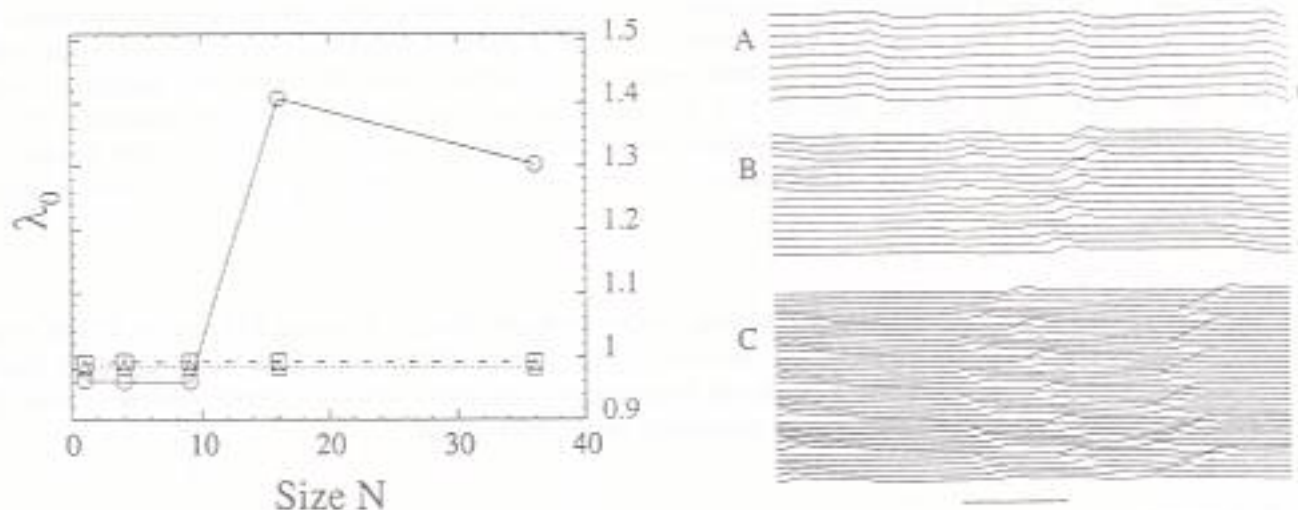


Fig. 3. Maximal eigenvalue λ_0 as a function of the size of the network. The eigenvalue is represented as a function of the size expressed as N , the number of pairs of neurons. For $m = 17$ (dashed-squares) and $m = 18$ (dotted-triangles), λ_0 remains lower than unity and the uniform periodic solution is stable for all sizes considered. For $m = 19$ (solid-circles), the uniform periodic solution is stable for small networks ($\lambda_0 < 1$ for $N \leq 9$) and loses stability for larger networks ($\lambda_0 > 1$ for $N > 9$).

Fig. 4. Activity of the network obtained from numerical integration. The simultaneous superimposed traces show the activity of each excitatory neuron in the network after a transient time of 500 ms. (A) $N = 9$, the network shows a uniform periodic oscillation. (B) $N = 16$, (C) $N = 36$, travelling waves of activity are seen. Vertical calibration bars are 100 mV and the horizontal calibration bar is 20 ms. $\Omega_1 = 15.27$, $\Omega_2 = \Omega_3 = 12.5$, $\Omega_4 = 0$. The system was integrated using a Runge-Kutta algorithm modified for DDE, with a constant integration step of 0.008 ms.

activity appears^{#5}.

A stability analysis of the uniform fixed points was also performed [24] using a method developed by Marcus and Westervelt [26]. The fixed points of the network were shown to possess the same stability as in a single pair of neurons, independently of the size of the network. Therefore the typical dynamical behavior of the network as a function of Ω_1 is as follows. For small values of the excitatory synaptic weights the system remains in a resting stationary state whose value and stability do not depend on the size of the system. For higher values of Ω_1 , uniform periodic solutions appear. Contrary to fixed points, the stability of these uniform oscillations critically depends on the size of the network. For still higher values of Ω_1 , or for larger sizes, these oscillations become unstable and other spatiotemporal patterns of oscillatory activity appear.

Generally, the size of the system and the extent of the connectivity have a determinant role for the stability of the uniform oscillation. It can be shown that for "all-to-all" coupling, the periodic orbit in the present model is always stable, in accordance with some models [13,27] but in contradiction with others [8]. One of the most striking features of the present model is that the uniform periodic oscillation can destabilize as only the size of the system is increased (continuous curve in Fig. 3).

By analogy with similar equations introduced by Wilson and Cowan [28], the variables X and Y can also be interpreted as the fraction of excitatory and inhibitory cells active per unit of time. Anatomical data [14,29] show that inhibitory cells tend to send their connections vertically, in contrast with the long range horizontal connectivity of some excitatory cells. In this case, each pair of X_i - Y_i neurons could be thought to represent the activity of a population of excitatory and inhibitory cells, connected to adjacent populations via lateral excitatory

^{#5} Such type of activity is very similar to spatiotemporal chaos or chemical turbulence. A more detailed account of the characterization of spatiotemporal chaos in the network is in preparation [25].

connections.

Contrary to many models of the cerebral cortex which predict robust oscillations under some conditions of input, the present model predicts that synchronized oscillations are not a stable phenomenon in networks with local connectivity. Other studies [27] have shown that coupled oscillators with local connectivity are also subject to an instability of uniform oscillations. These results taken together naturally lead to the suggestion that the localized connectivity of cortical neurons is a structural feature which prevents the synchronization of large cortical territories. However, this question needs to be addressed by biologically more plausible models, that must take into account the details of the anatomy of the cortex [14] as well as the complex intrinsic properties of cortical cells [30].

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