

Temporal Oscillations in Neuronal Nets*

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Summary. A model for the interactions of cortical neurons is derived and analyzed. It is shown that small amplitude spatially inhomogeneous standing oscillations can bifurcate from the rest state. In a periodic domain, traveling wave trains exist. Stability of these patterns is discussed in terms of biological parameters. Homoclinic and heteroclinic orbits are demonstrated for the space-clamped system.

Key words: Neurobiology — Nonlinear integro-differential equations — Bifurcation theory.

1. Introduction

In a previous paper [4] spatially inhomogeneous equilibria were demonstrated in equations modeling idealized neuronal nets. These equilibria arose through an instability of the spatially homogeneous zero state to perturbations of some characteristic wave number. Bifurcation theory was used to show the existence and stability of the new equilibria, which occur when an eigenvalue of the linearized problem becomes positive by crossing the imaginary axis through zero. Another type of bifurcation may occur when a pair of complex conjugate eigenvalues cross the imaginary axis. In many instances this gives rise to temporal oscillations, through a Hopf bifurcation [6, 13, 3]. Such results have been used with great success in the analysis of systems of chemical reaction and diffusion [1, 10, 7].

Oscillation occurs throughout the brain and is an outstanding feature of the nervous system. Examples of such periodic behavior range from the repetitive firing of a single nerve cell [18] to the grand-mal epileptic seizures involving whole regions of the cortex [17]. It is shown that the equations for thalamo-cortical nets proposed by Wilson and Cowan [19] can exhibit small amplitude spatially inhomogeneous temporal oscillations. The importance of short-range lateral inhibition and strong disinhibition for the creation of inhomogeneous oscillations is demonstrated.

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Finally, large amplitude oscillations are shown to exist in local spatially decoupled net equations, using phase plane techniques.

Neuronal net equations may be derived in numerous ways and we briefly summarize one such derivation here (for details see the above papers). Consider a population of N cells with the following simple properties:

- i) the l th cell is connected to the j th cell with 'weight' k_{lj} ;
- ii) each cell sums its input currents linearly, and its membrane impedance generates a net change in membrane potential, at the axon hillock;
- iii) this change generates, in a nonlinear fashion, a propagated current pulse;
- iv) such current pulses then stimulate other cells and the process begins again.

In Ermentrout and Cowan [4] we showed that the following continuum equations embodied the above assumptions:

$$\frac{\partial \mathbf{Y}}{\partial t} = -\mathbf{Y} + \mathbf{S}(\mathbf{K} * \mathbf{Y} + \mathbf{P}); \quad \mathbf{Y}(0, r) = \phi(r); \quad \mathbf{Y}: R^+ \times R \rightarrow R^n \quad (1.1)$$

where \mathbf{Y} is the vector of firing frequencies of the cells, ϕ the initial data, $\mathbf{K} * \mathbf{Y}$ a matrix spatial convolution, \mathbf{P} the input current, and \mathbf{S} is a nonlinear threshold function. Generally, S_i is monotone increasing, bounded, with a Lipschitz constant, M_i . Furthermore $S_i'(\theta_i) = 0$, where θ_i is the 'threshold.' When \mathbf{K} is a compact integral operator (as it is in this paper) and the initial data are continuous, then both existence and uniqueness can be shown for (1.1) (Theorem 5.1 [14]). In the first paper, the stationary states of (1.1) were analyzed; here we study the steady state temporal behavior of such nets.

In the case when \mathbf{K} is a constant spatially independent matrix, rather than an integral operator, (1.1) becomes a system of nonlinear ordinary differential equations and the Hopf bifurcation theorem may be applied. One can then use any number of available formulas for the stability of these new limit cycles [13, 8]. In the case when $n = 2$, i.e., two populations of cells, one excitatory and one inhibitory, one can use phase-plane techniques to show the existence of large amplitude asymptotically stable limit cycles. In particular the origin is an unstable node; there are no other singular points, and all solutions starting in the neighborhood of the origin remain bounded, so there exists at least one asymptotically stable limit cycle. (We discuss this in Section 3.)

2. Linearization

In this section we consider spatially extensive interactions between two populations of excitatory and inhibitory cells. For a large class of kernels (connectivity functions), the stable local network becomes unstable through a pair of pure imaginary eigenvalues, giving rise to small amplitude periodic solutions. As in [4] and [19] we assume that all cells are interconnected, with the strength of interconnection depen-

dent only on the distance between pairs, and finally that $P = 0$. This leads to the coupled nonlinear integrodifferential equations:

$$\begin{aligned}\frac{\partial X}{\partial t}(r, t) &= -X(r, t) + S_e(\lambda \alpha_{ee} w_{ee} * X(r, t) - \alpha_{ie} w_{ie} * Y(r, t)) \\ \frac{\partial Y}{\partial t}(r, t) &= -Y(r, t) + S_i(\lambda \alpha_{ei} w_{ei} * X(r, t) - \alpha_{ii} w_{ii} * Y(r, t))\end{aligned}\quad (2.1)$$

with $w_{ij} * u \equiv \int_{-\infty}^{\infty} w_{ij}(r - r')u(r') dr'$, α_{ij} represents the synaptic weight of connections between population i and population j . S_j is a smooth function as described in Section 1 (an explicit form for S_j will be given in Section 3) and λ is a small parameter which may be interpreted as modifying the synaptic weight of the excitatory cells. Some simple assumptions must now be made so that the model, while remaining physically realistic, is mathematically tractable. Since by assumption the number of connections made between any two cells decreases isotropically with increasing distance between them, w_{ij} must be symmetric and decreasing for $r > 0$. In addition, as the range of spatial interactions decreases, we require (2.1) to become ordinary differential equations. Finally, in order that the eigenfunctions of the linearized operator be easily computable, the Fourier transform of w_{ij} must exist. These conditions may be represented as:

$$\begin{aligned}(1) \quad & \int_{-\infty}^{\infty} w_{ij}(r) dr = 1 \\ (2) \quad & w_{ij}(-r) = w_{ij}(r) \\ (3) \quad & \int_{-\infty}^{\infty} w_{ij}(r) e^{-ipr} dr \triangleq \hat{w}_{ij}(p),\end{aligned}\quad (2.2)$$

with $p \equiv \xi^2$ exists, and

a) $\lim_{p \rightarrow \infty} \hat{w}_{ij}(p) = 0$,

b) $\hat{w}_{ij}(p)$ is monotonically decreasing for $p > 0$.

Some typical connectivity functions are

i) $\frac{1}{2\sqrt{\pi}} \exp(-r^2)$ (Gaussian),

ii) $\frac{1}{2} \exp(-|r|)$ ('exponential'),

iii) $\frac{1}{\pi(1+r^2)}$ ('arctangent').

If the monotonicity assumption on the Fourier transform is relaxed, two additional kernels of biological interest are permitted:

iv) $w(r) = \begin{cases} 0 & |r| > 1 \\ \frac{1}{2} & |r| < 1 \end{cases}$ 'square',

v) $w(r) = \begin{cases} 1 - |r| & |r| < 1 \\ 0 & |r| > 1 \end{cases}$ 'triangle'.

Given such $w(r)$, the w_{lj} may be constructed as $w_{lj} = (w(r/\sigma_{lj})/\sigma_{lj})$, where σ_{lj} is a space constant determining the spread of connections between cells of type l to type j .

To determine stability, the eigenvalues of the linearized problem must be obtained. The linearized system is:

$$\frac{\partial}{\partial t} \begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} -u + S'_e(0)[\alpha_{ee}\lambda w_{ee} * u - \alpha_{ie}w_{ie} * v] \\ -v + S'_i(0)[\alpha_{ei}\lambda w_{ei} * u - \alpha_{ii}w_{ii} * v] \end{pmatrix} \equiv L(\lambda) \begin{pmatrix} u \\ v \end{pmatrix}. \quad (2.3)$$

With the above assumptions on the kernels, w_{lj} , (2.3) has a continuous spectrum of double eigenvalues of the form:

$$\begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} \exp(\sigma^+ t + i\xi r) + \begin{pmatrix} \phi_3 \\ \phi_4 \end{pmatrix} \exp(\sigma^- t - i\xi r).$$

As in [4], we fix a length 2δ , and require solutions to be spatially periodic, of period 2δ . (Thus we are actually studying a 'ring' of cells.) The operator, $L(\lambda)$, is now compact and the spectrum is discrete. To further facilitate the nonlinear analysis, we impose additional constraints:

$$\begin{aligned} X(r) &= X(-r), \\ Y(r) &= Y(-r), \end{aligned}$$

and consequently seek spatially even 2δ -periodic solutions to (2.1). Finally, due to the compactness, the right hand sides of (2.1) and (2.3) are Fredholm of index zero. With these assumptions bifurcation to temporally periodic solutions can be demonstrated [3] as long as some simple conditions hold analogous to those of the ordinary Hopf theorem. In particular it is required that $L(\lambda)$ have a pair of complex conjugate eigenvalues, $\beta(\lambda) \pm i\omega(\lambda)$ such that at λ_0 , $\beta(\lambda_0) = 0$, $\omega_0 \neq 0$, and $(\partial\beta(\lambda)/\partial\lambda)|_{\lambda=\lambda_0} \neq 0$. Finally the remaining eigenvalues must remain in the left half-plane for λ near λ_0 . Let $\hat{w}_{lj}(n^2) = \int_{-\infty}^{\infty} \exp(in\pi r/\delta) w_{lj}(r) dr$, $n \in Z$. Then the eigenfunctions of $L(\lambda)$ are of the form:

$$\begin{pmatrix} \phi_1^\pm(r) \\ \phi_2^\pm(r) \end{pmatrix} = \begin{pmatrix} \Phi_1^\pm(\lambda, n^2) \\ \Phi_2^\pm(\lambda, n^2) \end{pmatrix} \cos \frac{n\pi r}{\delta} \equiv \Phi^\pm \cos \xi nr; \quad \xi = \frac{\pi}{\delta} \quad (2.4)$$

and the Φ^\pm are complex vectors satisfying:

$$H(\lambda, n^2)\Phi^\pm = \sigma_n^\pm(\lambda)\Phi^\pm$$

with

$$H(\lambda, n^2) \equiv \begin{pmatrix} -1 + S'_e(0)\alpha_{ee}\hat{w}_{ee}(n^2) & -S'_e(0)\alpha_{ie}\hat{w}_{ie}(n^2) \\ \lambda S'_i(0)\alpha_{ei}\hat{w}_{ei}(n^2) & -1 - S'_i(0)\alpha_{ii}\hat{w}_{ii}(n^2) \end{pmatrix}$$

and σ_n^\pm are the corresponding complex conjugate eigenvalues of $H(\lambda, n^2)$, $\sigma_n^- = \bar{\sigma}_n^+$. Since H is a 2×2 matrix, the condition for the existence of a pair of pure imaginary eigenvalues is that the trace vanish and the determinant remain positive. Assuming that the reciprocal connections, α_{ei} and α_{ie} , are strong, the determinant:

$$\begin{aligned} \Delta(n, \lambda) &= (1 + S'_i(0)\alpha_{ii}\hat{w}_{ii}(n^2))(-1 + S'_e(0)\lambda\alpha_{ee}\hat{w}_{ee}(n^2)) \\ &\quad + S'_e(0)S'_i(0)\lambda\alpha_{ei}\alpha_{ie}\hat{w}_{ei}(n^2)\hat{w}_{ie}(n^2) \end{aligned} \quad (2.5)$$

is positive for all λ in $(\lambda_0 - \epsilon, \lambda_0 + \epsilon)$ where ϵ is a small positive number. The condition that the trace vanish gives a relationship between λ and n . Since

$$\text{Tr}(\lambda, n^2) = -2 + S'_i(0)\alpha_{ii}\hat{w}_{ii}(n^2) + S'_e(0)\alpha_{ee}\hat{w}_{ee}(n^2), \quad (2.6)$$

$\text{Tr}(\lambda, n) = 0$ implies:

$$\lambda_n = [2 + S'_i(0)\alpha_{ii}\hat{w}_{ii}(n^2)][S'_e(0)\alpha_{ee}\hat{w}_{ee}(n^2)]^{-1}. \quad (2.7)$$

(See Fig. 2.)

As usual, we define $\lambda_0 = \min \lambda_n$, and let \bar{n} denote that value of n corresponding to λ_0 . We also assume that for $n \neq \bar{n}$, $\lambda_n > \lambda_0$, i.e., there are never two pairs of complex conjugate eigenvalues crossing the imaginary axis simultaneously. (We conjecture that if there are two values of n such that $\lambda_0 = \lambda_{n_1} = \lambda_{n_2}$, then there may be quasiperiodic solutions bifurcating from λ_0 .)

There are two cases to consider, $\bar{n} = 0$ and $\bar{n} > 0$. In the former case, one can easily show that the bifurcating solutions are spatially homogeneous and bulk oscillation of net activity occurs. These bulk oscillations also correspond to small bifurcating solutions of the local net discussed in Section 1. The case $\bar{n} > 0$ corresponds to bifurcation at a nonzero wave number and generates spatially inhomogeneous oscillations. A necessary condition for $\bar{n} > 0$ is given by the following lemma.

Lemma 2.8. Under the assumptions (2.2) a necessary condition for $\bar{n} > 0$ is that

$$\sigma_{ii} > \sigma_{ee} \quad \text{and} \quad S'_i(0)\alpha_{ii} > 2\sigma_{ee}^2/(\sigma_{ii}^2 - \sigma_{ee}^2) \quad (2.9)$$

Proof. From Fig. 1, we see that $\lambda_{\min} \neq 0$ occurs only if $[\partial\lambda(n^2)/\partial n^2]|_{n^2=0} < 0$ where n^2 is viewed as a continuous variable (this is why we obtain only a necessary condition). Noting that $[\partial\hat{w}_{ij}/\partial n^2]|_{n^2=0} = \sigma_{ij}^2[\partial\hat{w}/\partial n^2]|_{n^2=0}$, $\hat{w}_{ij}(0) = 1$ and using (2.6) we find:

$$\frac{\partial\lambda}{\partial n^2} \Big|_{n^2=0} = -\frac{[2 + S'_i(0)\alpha_{ii}]\sigma_{ee}^2\hat{w}'(0)}{S'_e(0)\alpha_{ee}} + \frac{S'_i(0)\alpha_{ii}\sigma_{ii}^2\hat{w}'(0)}{S'_e(0)\alpha_{ee}}.$$

This must be negative, but since $\hat{w}'(0) < 0$ (due to the monotone decreasing condition):

$$-\sigma_{ee}^2[2 + S'_i(0)\alpha_{ii}] + S'_i(0)\alpha_{ii}\sigma_{ii}^2 > 0$$

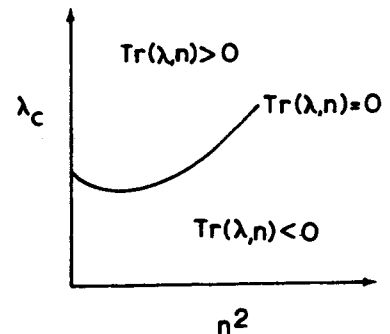


Fig. 1. Stability of the linearized system as a function of wave number, n^2 , and λ

or $S'_i(0)\alpha_{ii}(\sigma_{ii}^2 - \sigma_{ee}^2) > 2\sigma_{ee}^2$. Since α_{ij} , σ_{ij} , and $S'_i(0)$ are nonnegative this implies $\sigma_{ii} > \sigma_{ee}$ and $S'_i(0)\alpha_{ii} > 2\sigma_{ee}^2/(\sigma_{ii}^2 - \sigma_{ee}^2)$.

We assume that (2.9) holds and $\bar{n} > 0$. Let $\omega_0 = \omega(\lambda_0)$, where $\omega(\lambda_0)$ is given by

$$\omega(\lambda_0) = [S'_e(0)S'_i(0)\alpha_{ei}\alpha_{ie}\hat{w}_{ei}(\bar{n}^2)\hat{w}_{ie}(\bar{n}^2)\lambda_0 - (-1 + S'_e(0)\lambda_0\alpha_{ee}\hat{w}_{ee}(\bar{n}^2))^2]^{1/2}. \quad (2.10)$$

Near λ_0 the term $\text{Tr}(\lambda, n^2) - 4\Delta(\lambda, n^2)$ will remain negative so that $\beta(\lambda) = -\text{Tr}(\lambda, n^2)/2$ and $(\partial\beta/\partial\lambda)|_{\lambda_0} = S'_e(0)\alpha_{ee}\hat{w}_{ee}(\bar{n}^2) \neq 0$. Thus the transversality condition holds and the Hopf bifurcation theorem may be applied.

Remarks. The analysis described in the next few sections could easily be applied to the case of odd functions, but by considering odd solutions, we exclude the possibility of bulk oscillations. Such bulk activity is known to exist in a number of chemical and biological systems. The main reason we consider even solutions is that obtaining spatially inhomogeneous oscillatory solutions is trivial with the boundaries fixed at zero, since the zero wave number corresponds to the zero solution, which is by assumption unstable. Thus even if $\lambda(\bar{n})$, $\bar{n} = 0$ is the minimum λ , the first solution which is possibly stable must correspond to $\bar{n} = 1$. In two species reaction-diffusion equations it is easily shown that the trace is maximal for $\bar{n} = 0$, and thus the first wave number in which the trace vanishes is always 0. In (2.1), it is not the boundary conditions which give rise to the inhomogeneous solutions, but the structure of the equations.

The physical interpretation of lemma (2.8) is that disinhibition of sufficient strength (α_{ii} large) and range ($\sigma_{ii} > \sigma_{ee}$) are required to obtain spatially inhomogeneous oscillations. Furthermore, we require $\alpha_{ei}\alpha_{ie}\hat{w}_{ei}(n^2)\hat{w}_{ie}(n^2)$ to remain large in order that the determinant remain positive. Since $\hat{w}_{ei}(n^2) = \hat{w}(n^2\sigma_{ei}^2)$, $\hat{w}_{ie}(n^2) = \hat{w}(n^2\sigma_{ie}^2)$ and $\hat{w}(z^2)$ decreases as z^2 increases, we need σ_{ei} , σ_{ie} small so that $\hat{w}_{ei}(n^2)$ and $\hat{w}_{ie}(n^2)$ remain near 1. Since σ_{ei} and σ_{ie} determine the spread of lateral inhibition, we thus require short-range lateral inhibition as well.

3. Stability and Form of Periodic Solutions

In the appendix, formulas for the oscillatory solutions and their stability are derived. If the amplitude is normalized to be $\varepsilon = \left\| \begin{pmatrix} X \\ Y \end{pmatrix} \right\|$ then we can expand the frequency, ω , the small parameter, λ , and the activities x , y in terms of ε :

$$\begin{aligned} \omega &= \omega_0 + \varepsilon\omega_1 + \varepsilon^2\omega_2 & \begin{pmatrix} X(r, t) \\ Y(r, t) \end{pmatrix} &= \varepsilon \begin{pmatrix} X_1(r, t) \\ Y_1(r, t) \end{pmatrix} + \varepsilon^2 \begin{pmatrix} X_2(r, t) \\ Y_2(r, t) \end{pmatrix} + \dots \\ \lambda &= \lambda_0 + \varepsilon\lambda_1 + \varepsilon^2\lambda_2 \end{aligned}$$

Let \bar{n} be the critical wave number and ω_0 the corresponding critical frequency. Assume without loss of generality that $\lambda_0 = 1$. Then from A10 we find to lowest order in ε :

$$\begin{aligned} \begin{pmatrix} X(r, t) \\ Y(r, t) \end{pmatrix} &= \varepsilon \cos \frac{\bar{n}\pi^2}{\delta} \begin{pmatrix} \cos(\omega_0 + \varepsilon^2\omega_2)t \\ \zeta \cos((\omega_0 + \varepsilon^2\omega_2)t - \theta) \end{pmatrix} + O(\varepsilon^2) & \tan \theta &= \frac{-1 + \beta_{ee}}{0} \\ & & \zeta &= \frac{\beta_{ei}}{\beta_{ie}} \end{aligned} \quad (3.1)$$

Table 1. Parameter values leading to stable small amplitude oscillations

Recurrent excitation β_{ee}	$\left(\frac{\beta_{ei}}{\beta_{ie}}\right)$	Frequency, ω_0
+	+	-
+	-	+
+/-	-	+
+/-	+	-
-	+	-

+ means large, - means small, +/- means intermediate

The lowest order term in the expansion for λ is

$$\lambda = 1 + \varepsilon^2 \gamma_2; \quad \gamma_2 = \frac{\omega_0 C}{\beta_{ee} \tan \theta} \left\{ \frac{1 + \zeta^2}{\beta_{ee} - 1} (1 - 3\omega_0^2) + (3 - \omega_0^2)(\zeta^2 - 1) \right\} \tag{3.2}$$

where $C > 0$ is a constant depending only on the derivatives of the nonlinearity.

The sign of γ_2 determines the direction of bifurcation; $\gamma_2 < 0$ yields subcritical bifurcation, $\gamma_2 > 0$ supercritical (see Fig. 2). From various theorems on stability of the bifurcating solutions we know that subcritical solutions are unstable and supercritical ones stable. Thus the calculations for direction of bifurcation also give stability, i.e., $\gamma_2 > 0$ stable and $\gamma_2 < 0$ unstable.

If we let $\beta = 1/(\beta_{ee} - 1)$ then β may take on values between 0 and 1, corresponding, respectively, to infinite recurrent excitation (or infinite disinhibition) and minimal excitation (zero disinhibition). In Fig. 3 the ratio of the cross terms, β_{ei}/β_{ie} , is plotted against the zero-order term of the frequency, ω_0 , for various values of β to show regions of stable small amplitude solutions. Table 1 summarizes the results in terms

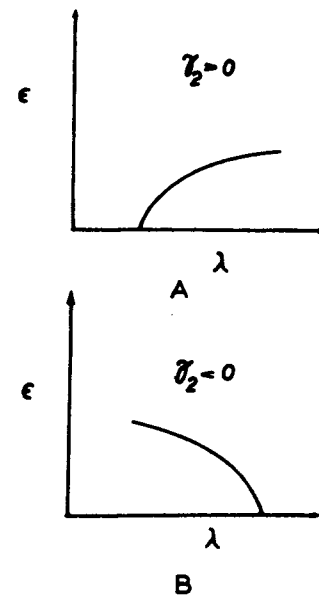


Fig. 2. Bifurcation diagram for model equations

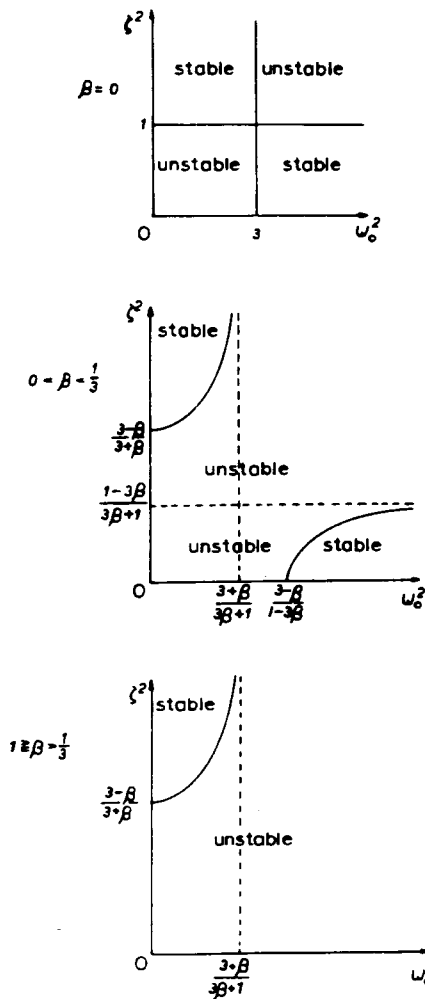


Fig. 3. Stability of bifurcating solutions. $\zeta = \beta_{ei}/\beta_{ie}$, $\beta = 1/(\beta_{ee} - 1)$

of frequency, recurrent excitation, and the crossterm ratio. The only circuits that give rise to low amplitude solutions via bifurcation are shown in Fig. 4. The two separate cases, $\bar{n} = 0$ and $\bar{n} \neq 0$, will be discussed separately.

Case 1, $\bar{n} = 0$: This solution solves both the coupled and the local network equations. As previously remarked, one effect of spatial coupling is to synchronize the elemental circuits so that they all oscillate at the same phase. For the remainder of this case the discussion will be restricted to the local network. Some very strong conclusions can be made about both the stable and unstable solutions using phase-plane techniques. The small amplitude stable solutions are often called soft bifur-

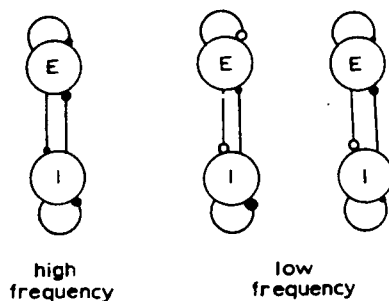


Fig. 4. Local circuits giving rise to stable small amplitude oscillations. Small circles give relative strengths of connections. Open circles are excitatory and filled circles are inhibitory

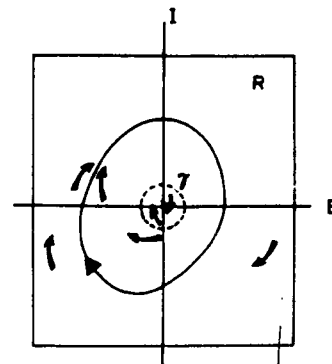


Fig. 5. Phase portrait of limit cycle for local equations. $E =$ excitatory, $I =$ inhibitory

cations and exhibit smooth transition to the new solutions. The unstable small amplitude oscillations are sufficient to prove the existence of large-amplitude hard limit cycles. To show this, assume the bifurcation diagram is as in Fig. 2b. Then the existence part of the Hopf theorem states there is a small amplitude unstable limit cycle around the origin for $\lambda < \lambda_0$. The origin is asymptotically stable for $\lambda < \lambda_0$ and is the only singular point. All trajectories are bounded by the box in Fig. 5; any point in the annulus R with γ , the unstable limit cycle as its inner boundary,

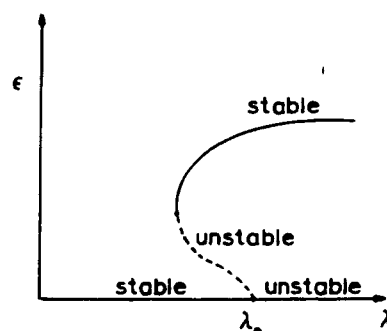


Fig. 6. Bifurcation diagram for local equations showing hysteresis

must remain in γ so there is at least one asymptotically limit cycle in R . This is the so-called hard limit cycle. Furthermore, for $\lambda < \lambda_0$, and sufficiently close, the network has two stable states: the rest state at zero and the hard limit cycle. Thus the system exhibits a threshold as well: if the initial conditions lie inside γ , the system returns to equilibrium, while if they lie outside of γ the system enters the oscillatory state. For $\lambda > \lambda_0$ there again are no other critical points and the origin is unstable so there must be a limit cycle. The above arguments lead to the conjectured bifurcation diagram of Fig. 6. Responses to sub- and superthreshold stimuli are illustrated in Fig. 7.

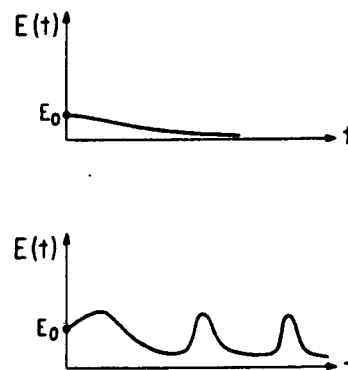


Fig. 7. (a) Subthreshold stimulus; (b) Superthreshold stimulus

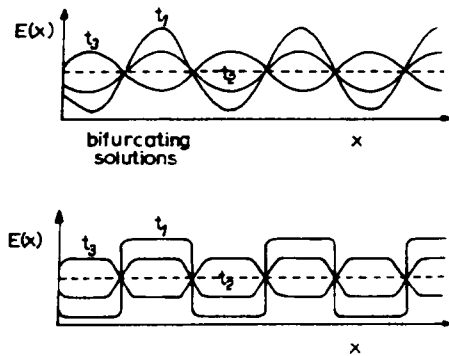


Fig. 8. Bifurcating solutions: small λ and large λ

Case 2, $n \neq 0$: In this case spatially periodic temporal oscillations are obtained in the form of standing waves. All the cells are synchronized at the same frequency and phase, with a spatial cosine amplitude modulation. As above, these results demonstrate the existence of small amplitude solutions which are stable supercritically and unstable subcritically. We utilized the planar character of the local equations to prove the existence of at least one large amplitude limit cycle when the bifurcation is subcritical and the resulting bifurcating solution unstable. Unfortunately, similar results about the fully coupled equations cannot be obtained. Careful numerical studies indicate that for parameters leading to subcritical bifurcation there are indeed large amplitude spatially periodic oscillations both sub- and supercritically. Fig. 8 illustrates the large amplitude solutions as well as the stable bifurcating solutions at various parameter values. The main difference is that there are many more high frequency components in the large amplitude solutions, as can be seen from the sharp transition regions between high and low amplitude.

4. Waves in Circular Networks

When the condition that the solutions be even in space is relaxed, traveling waves can be shown to exist. These waves depend only on the relative coordinate, $\xi = \omega t - \mathbf{k} \cdot \mathbf{r}$, where ω is the frequency and \mathbf{k} the wave vector. The waves have the property that at each point in space the network exhibits an oscillation of frequency and with t fixed, the network is spatially periodic of frequency $|\mathbf{k}|$, in the direction of \mathbf{k} .

Wave-like activity is ubiquitous in biological systems. Examples in neurobiology range from the periodic wavetrains of the Hodgkin–Huxley axon to evoked potentials, spreading depression, and EEG waves. These results show that even a simple two-component model is sufficient to generate such wavetrains. In a forthcoming paper, we show the existence of a large variety of other wavelike solutions when the extent of the medium is infinite. Here the periodicity assumption is somewhat artificial, but is mathematically convenient.

The type of waves discussed here are planar, i.e., their fronts have no curvature and travel along the vector \mathbf{k} . Since multiple recording of the activities of a large number of close-packed neurons is difficult, it is hard to differentiate between traveling

oscillatory waves and standing oscillations. The principal testable difference is in the phase relationship: standing waves are all in phase, while traveling waves exhibit distinct phase differences. (For recent experiments concerning traveling waves see [15, 16, 17].)

The existence proof for these wavelike solutions is a simple application of the implicit function theorem on the appropriately defined subspaces. We shall not give the proof here; details may be found in [5]. (Note the theorem is proved on the infinite line for reaction diffusion equations, so that some changes must be made.) Unlike the waves discussed in part one of Kopell and Howard [10], these waves exist in a bounded medium and consequently stable solutions exist. Supercritical solutions can be shown to exist in a manner analogous to Section 3. Indeed, Kopell and Howard studied a system on the whole line, while here we consider the system in a compact domain. To examine stability, we only need to consider perturbations of the critical wave number since there is only a discrete family of periodic solutions (see Sattinger).

5. Other Nonperiodic Behavior

Computer simulations indicate that a variety of other wave-like solutions of (2.1) exist, such as traveling pulses and wave fronts, but little analytically is known about such solutions. On the other hand there are a number of bifurcation results we can use to show that the local (uncoupled) equations admit homoclinic and heteroclinic orbits as well as periodic solutions. An orbit $O(t)$ is homoclinic if $\lim_{t \rightarrow -\infty} O(t) = \lim_{t \rightarrow \infty} O(t) = p$, where p is a critical point of the system. A heteroclinic orbit is one in which $\lim_{t \rightarrow -\infty} O(t) = p_1$ and $\lim_{t \rightarrow +\infty} O(t) = p_2$ where $p_1 \neq p_2$. The importance of these phenomena is that each can give rise to propagating waves if of sufficient amplitude. In a later paper this wavelike activity will be discussed; here we shall consider only bifurcation to homo- and heteroclinic orbits in the local equations. The result is due to Kopell and Howard and involves bifurcation from a double zero eigenvalue, hence two parameters are necessary to destroy the double degeneracy. As in the previous bifurcation theorems used, a transversality condition is necessary for both parameters, and it turns out that a nonzero inhibitory threshold is required.

Theorem (11). *Let $\dot{X} = F(\mu, \lambda, X) \triangleq A(\mu, \lambda)X + Q(X, X) + R(X, \mu, \lambda)$ be a smooth two-parameter family of ordinary differential equations on R^2 such that $R(0, \mu, \lambda) = 0$, and $A(\mu, \lambda)$ is a 2×2 matrix, Q a quadratic form, and $R(X, \mu, \lambda) = o(x_i x_j, \mu x_i, \lambda x_i, \mu \lambda)$. Also assume:*

1. $A(0, 0)$ has a double zero eigenvalue, and a single eigenvalue e .
2. The mapping $(\mu, \lambda) \rightarrow (\det A(\mu, \lambda), \text{tr } A(\mu, \lambda))$ has a nonzero Jacobian at $(\mu, \lambda) = (0, 0)$.
3. The matrix $[A(0, 0), Q(e, e)]$ obtained by augmenting $A(0, 0)$ using the vector $Q(e, e)$ has rank two.

Then, it follows that there is a curve $f(\mu, \lambda) = 0$ such that if $f(\mu_0, \lambda_0) = 0$ then $\dot{X} = F(\mu_0, \lambda_0, X)$ has a homoclinic orbit. This one parameter family of homoclinic

orbits in (X, μ, λ) -space is on the boundary of a two-parameter family of periodic solutions. For all (μ, λ) sufficiently small, if $X = F(\mu, \lambda, X)$ has neither a homoclinic orbit nor a periodic solution, there is a unique trajectory joining critical points (e.g., a heteroclinic point).

In order to use the theorem, we need to pick two parameters in the local network equations:

$$\begin{pmatrix} \frac{dX_1}{dt} \\ \frac{dX_2}{dt} \end{pmatrix} = \begin{pmatrix} -X_1 + S(\alpha_{11}\lambda X_1 - \alpha_{12}X_2) \\ -X_2 + S_i(\alpha_{21}X_1, \mu) \end{pmatrix} \quad (6.1)$$

with $S(u) = 1/(1 + \exp(-u)) - \frac{1}{2}$; $S_i(u, \mu) = 1/(1 + \exp(-(u - (\theta + \mu)))) - 1/(1 + \exp(\theta + \mu))$. (6.1) may be recast in the following form:

$$\begin{aligned} \begin{pmatrix} \dot{X}_1 \\ \dot{X}_2 \end{pmatrix} &= \begin{pmatrix} -1 + S'(0)\alpha_{11}(\lambda_0 + \lambda) & -S'(0)\alpha_{12} \\ \alpha_{21}S'_i(0, \mu) & -1 \end{pmatrix} \begin{pmatrix} X_1 \\ X_2 \end{pmatrix} \\ &\quad + (S'_i(0)[\alpha_{21}X_1]^2) + R(X, \lambda, \mu) \\ &\equiv A(\mu, \lambda) \begin{pmatrix} X_1 \\ X_2 \end{pmatrix} + Q \begin{pmatrix} X_1 \\ X_2 \end{pmatrix} + R(X, \lambda, \mu). \end{aligned}$$

The trace and determinant must vanish at $\lambda = \mu = 0$, i.e.,

$$(-2 + S'(0)\alpha_{11}\lambda_0) = 0; \quad (1 - S'(0)\alpha_{11}\lambda_0) + S'(0)S'_i(0, 0)\alpha_{12}\alpha_{21} = 0.$$

This yields equations for λ_0 and θ . We require that $\alpha_{12}\alpha_{21}$ be sufficiently large, so that θ is nonzero. Next, the map $(\mu, \lambda) \rightarrow (\det A, \text{tr } A)$ must be nonsingular and hence the Jacobian must have a nonzero determinant at $(\mu, \lambda) = (0, 0)$. This map is given by

$$\begin{pmatrix} \lambda \\ \mu \end{pmatrix} \rightarrow \begin{pmatrix} -2 + S'(0)\alpha_{11}(\lambda_0 + \lambda) \\ -(-1 + S'(0)(\lambda_0 + \lambda)\alpha_{11} + S'_i(0, \mu)S'(0)\alpha_{21}\alpha_{12}) \end{pmatrix}$$

and the Jacobian at $(0, 0)$ is

$$\begin{pmatrix} S'(0) & 0 \\ -S'(0) & S'(0)\alpha_{21}\alpha_{12}S'_i(0, 0) \end{pmatrix}.$$

The determinant is nonzero only if $S'_i(0, 0)$ is nonzero which occurs as long as θ is nonzero, since all other terms are positive. The eigenfunction, e , is:

$$\begin{pmatrix} 1 \\ \frac{-1 + S'(0)\alpha_{11}\lambda_0}{S'(0)\alpha_{12}} \end{pmatrix}.$$

Thus the augmented matrix of condition 3 is:

$$\begin{pmatrix} -1 + S'(0)\alpha_{11}\lambda_0 & -S'(0)\alpha_{12} & 0 \\ \alpha_{21}S'_i(0, 0) & -1 & S'_i(0, 0)\alpha_{21}^2 \end{pmatrix}.$$

Because $S'_i(0, 0)$ is nonzero, this matrix has rank two and condition 3 holds. So, there is a one parameter family of homoclinic orbits of (6.1). Evidently, when the number of neuronal populations increases, more exotic temporal behavior is found. Recent results have been obtained when two pairs of eigenvalues cross the imaginary

axis simultaneously and quasiperiodic solutions obtain. For this to occur four or more populations are necessary. For three population nets many other states may occur.

Recalling a remark made in Section 2, we might ask what type of spatiotemporal behavior can be expected if there are two wave numbers, n and $n + 1$, which correspond to a minimal λ , i.e., two pairs of eigenvalues which cross the imaginary axis at the same location. This is bifurcation from a double eigenvalue, which in some cases can give rise to secondary bifurcations [2, 12, 9]. Little work has been done for the case when these double eigenvalues are pure imaginary, since most results on secondary bifurcation are on two-dimensional reaction-diffusion equations which cannot have such degeneracy. Suppose we consider a two-dimensional reaction-diffusion scheme which has been linearized. Then the matrix corresponding to $H(\lambda, n^2)$ is

$$H(\lambda, n^2) = \begin{pmatrix} a_{11}(\lambda) - D_1 n^2 & a_{12}(\lambda) \\ a_{21}(\lambda) & a_{22}(\lambda) - D_2 n^2 \end{pmatrix}.$$

In order for a pair of imaginary eigenvalues to occur for two different values of n , for some λ_c, n_1, n_2 we require:

$$\text{Tr } H(\lambda, n_1^2) = a_{11}(\lambda_c) + a_{22}(\lambda_c) - n_1^2(D_1 + D_2) = 0,$$

$$\text{Tr } H(\lambda, n_2^2) = a_{11}(\lambda_c) + a_{22}(\lambda_c) - n_2^2(D_1 + D_2) = 0.$$

This can never happen so that two pairs of pure imaginary eigenvalues cannot occur with a two-component reaction-diffusion system. We conjecture that secondary bifurcation will occur and some of the secondary solutions will be quasiperiodic in space and time. Actual construction of such solutions could be done via some type of two-timing perturbation [9]. In a forthcoming work, we hope to obtain some results on the secondary branches of these rich equations [submitted for publication].

If the primary states represent some sort of simple neural oscillation, such as occurring in sleep, etc., then perhaps these secondary states represent pathological states (epilepsy, etc.).

Appendix A

Calculation of Direction of Bifurcation

We seek solutions to (2.1) of frequency ω near ω_0 , with $\omega_0 = \sqrt{\Delta(\lambda, \bar{n})}$. Let $t = (\omega_0 + \varepsilon^2 \omega_1 + \varepsilon \omega_2 + \dots)^{-1} \tau$, and expand λ, X, Y in terms of $\varepsilon = \left\| \begin{pmatrix} X(r, \tau) \\ Y(r, \tau) \end{pmatrix} \right\|$

$$\begin{pmatrix} X(r, \tau) \\ Y(r, \tau) \end{pmatrix} = \varepsilon \begin{pmatrix} x_1(r, \tau) \\ y_1(r, \tau) \end{pmatrix} + \varepsilon^2 \begin{pmatrix} x_2(r, \tau) \\ y_2(r, \tau) \end{pmatrix} + \dots$$

$$\lambda = 1 + \varepsilon \gamma_1 + \varepsilon^2 \gamma_2 + \dots$$

To make the analysis simpler, we shall assume that the thresholds are zero and the nonlinearities are odd. We expand $S_f(u)$ in Taylor series:

$$S_f(u) = S_f'(0)u + \frac{S_f'''(0)u^3}{6} + \dots \quad (\text{A1})$$

We remark that $S'_j(0) > 0$ and $S'_j(0) < 0$, since the threshold is zero. Substituting the expansions for X , Y , t , and λ into (2.1) and ω collecting powers of ε leads to the following family of linear equations:

$$\left(\omega_0 \frac{\partial}{\partial \tau} - L_0 \right) \begin{pmatrix} x_n(r, \tau) \\ y_n(r, \tau) \end{pmatrix} = - \sum_{j=1}^{n-1} \omega_j \frac{\partial}{\partial \tau} \begin{pmatrix} x_{n-j}(r, \tau) \\ y_{n-j}(r, \tau) \end{pmatrix} + \begin{pmatrix} a_n(r, \tau) \\ b_n(r, \tau) \end{pmatrix} \quad (\text{A2})$$

where

$$L_0 \begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} -u + S'_e(0) \alpha_{ee} w_{ee} * u & -S'_e(0) \alpha_{ie} w_{ie} * v \\ -v + S'_i(0) \alpha_{ei} w_{ei} * u & -S'_i(0) \alpha_{ii} w_{ii} * v \end{pmatrix}.$$

The first few a_n , b_n are,

$$\begin{aligned} \text{i)} \quad & a_1(r, \tau) = b_1(r, \tau) = 0 \\ \text{ii)} \quad & a_2(r, \tau) = f_{11} \alpha_{ee} \gamma_1 w_{ee} * x_1(r, \tau) \\ & b_2(r, \tau) = f_{21} \alpha_{ei} \gamma_1 w_{ei} * x_1(r, \tau) \\ \text{iii)} \quad & a_3(r, \tau) = f_{11} \alpha_{ee} w_{ee} * [\gamma_2 x_1(r, \tau) + \gamma_2 x_2(r, \tau)] \\ & \quad + f_{13} [\alpha_{ee} w_{ee} * x_1(r, \tau) - \alpha_{ie} w_{ie} * y_1(r, \tau)]^3 \\ & b_3(r, \tau) = f_{21} \alpha_{ee} w_{ee} * [\gamma_2 x_1(r, \tau) + \gamma_1 x_2(r, \tau)] \\ & \quad + f_{23} [\alpha_{ei} w_{ei} * x_1(r, \tau) - \alpha_{ii} w_{ii} * y_1(r, \tau)]^3 \end{aligned} \quad (\text{A3})$$

with $f_{jk} = S_j^{(k)}(0)/k!$

Let $\beta_{ij} = S'_i(0) \alpha_{ij} \hat{w}_{ij}(\bar{n}^2)$.

ε^0 terms. The solution for x_0 , y_0 is the real phase normalized eigenfunction of $((\partial/\partial\tau) - L_0)$:

$$\begin{pmatrix} x_1(r, \tau) \\ y_1(r, \tau) \end{pmatrix} = \begin{pmatrix} \cos \tau \\ \zeta \cos \tau - \theta \end{pmatrix} \cos \frac{\bar{n}\pi r}{\delta} \quad (\text{A4})$$

with

$$\zeta = \frac{\beta_{ei}}{\beta_{ie}} \quad \text{and} \quad \begin{aligned} \cos \theta &= \omega_0 / \sqrt{\beta_{ie} \beta_{ei}} \\ \sin \theta &= (-1 + \beta_{ee}) / \sqrt{\beta_{ie} \beta_{ei}} \end{aligned}$$

ε terms. This gives the inhomogeneous equation

$$\left(\frac{\partial}{\partial \tau} + L_0 \right) \begin{pmatrix} x_2(r, \tau) \\ y_2(r, \tau) \end{pmatrix} = \begin{pmatrix} a_2(r, \tau) \\ b_2(r, \tau) \end{pmatrix} - \omega_1 \frac{\partial}{\partial \tau} \begin{pmatrix} x_1(r, \tau) \\ y_1(r, \tau) \end{pmatrix} \equiv \begin{pmatrix} f_1 \\ g_1 \end{pmatrix}. \quad (\text{A5})$$

In order for a solution to exist, the right hand side must be orthogonal to the adjoint eigenfunctions of $((\partial/\partial\tau) - L_0)$. These eigenfunctions are readily computed:

$$\begin{pmatrix} \phi_1^*(r, \tau) \\ \phi_2^*(r, \tau) \end{pmatrix} = \begin{pmatrix} 1 \\ -1/\zeta e^{i\theta} \end{pmatrix} e^{i\theta} \cos \frac{\bar{n}\pi r}{\delta} \quad \text{and} \quad \begin{pmatrix} \bar{\phi}_1^*(r, \tau) \\ \bar{\phi}_2^*(r, \tau) \end{pmatrix}. \quad (\text{A6})$$

The inner product is

$$\int_0^{2\pi} d\tau \int_{-\delta}^{\delta} (f_1 \bar{\phi}_1^* + f_2 \bar{\phi}_2^*) dr \equiv \left\langle \begin{pmatrix} f_1 \\ f_2 \end{pmatrix}, \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} \right\rangle.$$

Applying orthogonality conditions leads to

$$\begin{pmatrix} \beta_{ee} - \frac{\beta_{et}}{\zeta} \cos \theta & \sin 2\theta \\ -\frac{\beta_{et}}{\zeta} \sin \theta & 1 - \cos 2\theta \end{pmatrix} \begin{pmatrix} \gamma_1 \\ \omega_1 \end{pmatrix} = 0. \quad (\text{A7})$$

This has a nontrivial solution if the determinant is zero, i.e., $\beta_{ee} \sin^2 \theta = 0$. Since $\theta \in (0, \pi/2)$ and $\beta_{ee} \geq 2$, this is impossible so $\gamma_1 = \omega_1 = 0$. By normalizing the amplitude of our solutions to be ε we have automatically required that

$$\left\langle \begin{pmatrix} x_n(r, \tau) \\ y_n(r, \tau) \end{pmatrix}, \begin{pmatrix} \phi_1^*(r, \tau) \\ \phi_2^*(r, \tau) \end{pmatrix} \right\rangle = 0 \quad \text{for } n \neq 1,$$

so the solution to (A5) is

$$\begin{pmatrix} x_2(r, \tau) \\ y_2(r, \tau) \end{pmatrix} = 0.$$

ε^2 terms. This leads to a pair of linear inhomogeneous equations as above. Applying the orthogonality conditions gives the following equations for (γ_2, ω_2) .

$$\begin{pmatrix} \beta_{ee} - \frac{\beta_{et} \cos \theta}{\zeta} & \sin 2\theta \\ -\frac{\beta_{et}}{\zeta} \sin \theta & 1 - \cos 2\theta \end{pmatrix} \begin{pmatrix} \gamma_2 \\ \omega_2 \end{pmatrix} = \begin{pmatrix} \kappa(1 + \zeta^2 \cos 2\theta) - \rho \zeta^2 \sin 2\theta \\ \kappa \zeta^2 \sin 2\theta + \rho[1 + \zeta^2 \cos 2\theta] \end{pmatrix};$$

$$\rho = 3\omega_0 - \omega_0^3, \quad \kappa = 1 - 3\omega_0^2. \quad (\text{A8})$$

We solve for γ_2 :

$$\gamma_2 = \frac{\omega_0 C}{\alpha_{ee}} \tan \left\{ \frac{1 + \zeta^2}{\beta_{ee} - 1} (1 - 3\omega_0^2) + (3 - \omega_0^2)(\zeta^2 - 1) \right\}, \quad (\text{A9})$$

with a similar complicated expression for ω_2 . Here we have assumed that $S_e(u) = S_i(u)$, so that $C > 0$ is a positive constant depending on the derivatives of S_e . To second order the solution to (2.1) is

$$\begin{pmatrix} X(r, \tau) \\ Y(r, \tau) \end{pmatrix} = \varepsilon \cos \frac{\bar{n}\pi r}{\delta} \begin{pmatrix} \cos((\omega_0 + \varepsilon^2 \omega_2)t) \\ \zeta \cos((\omega_0 + \varepsilon^2 \omega_2)t - \theta) \end{pmatrix} + O(\varepsilon^2). \quad (\text{A10})$$

Remarks. The analysis has been greatly simplified by letting the thresholds vanish. Even if we had not made this requirement, γ_1, ω_1 still would be zero, but the expressions for γ_2 and ω_2 would be extremely complicated.

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