

# A class of reaction–diffusion mechanisms which preferentially select striped patterns

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Reaction–diffusion systems which have reaction term satisfying  $f(-q) = -f(q)$  tend strongly to form striped patterns. Haken's slaving principle is used to derive differential equations for unstable mode amplitudes close to the Turing instability. This connects a dynamical symmetry to pattern selection, with possible relevance to biological and chemical pattern-forming phenomena.

## 1. Introduction

Biological pattern is commonly formed in two-dimensional domains: single layers of cells, surfaces of large single cells, single layers of nuclei in a multinucleate cell. In some instances, such as mammalian coat markings [1], what is presumably a single mechanism produces both striped and spotted patterns on various parts of the skin. One must then seek a mechanism which can be controlled by such influences as the shape of the region to behave in either of these ways.

By contrast, when a pattern forms very early in development and hierarchically governs the essential body plan of the organism, one needs a mechanism with extreme reliability both as to the geometry of the pattern units (stripes or spots) and their precise total number. We discuss here models which are capable of producing striped patterns in a very robust fashion, independent of the particular boundary conditions or size of the system. Two biological examples of stripe formation where such robustness is needed are discussed in section 5.

Reaction–diffusion theory, first proposed by Turing [2], remains one of the most promising kinds of mechanism for biological pattern formation [3–5]. Linear Turing theory is exactly soluble, but non-linear theory is still largely unexplored by analysis. The particular combination of linear modes which superpose to form a pattern is a function of the nonlinearities a given model includes. The usual method for studying the non-linear behaviour of a model has been numerical experimentation. In this Letter we report a study, both by computation and by analysis, of a class of non-linear reaction–diffusion models which have earlier been shown (by the former method) to have a strong tendency to form striped patterns [6].

## 2. A class of reaction–diffusion models which selects stripes

We consider two-component reaction–diffusion systems. The state of the system  $q(x, y, t)$  for  $(x, y)$  in a two-dimensional domain has time evolution given by

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$$\dot{q}_\alpha = f_\alpha(q) + D_\alpha \Delta q_\alpha, \quad \alpha = 1, 2, \quad (1)$$

where  $q=0$  is the spatially homogeneous steady state. Efforts to model the self-organization of *Drosophila* pair-rule gene expression products into striped patterns have led to the investigation of models anti-symmetric about  $q=0$

$$f(-q) = -f(q). \quad (2)$$

We are aware of three such reaction-diffusion models [7-9]. These three models have been found to have a strong tendency to produce stripes regardless of the boundary conditions [6-8] empirically by computation. Fig. 1 shows stages in the time evolution of

one of these models, the hyperchirality model [9], to its final state.

The ability of a local property of the reaction kinetics (2) to influence the pattern globally is at first sight surprising. Fig. 2, which compares the behaviour of two systems which have the same linearization, illustrates that this is a non-linear phenomenon. By analysis of (1) in the weakly non-linear regime close to the Turing instability, it will be shown in sections 3 and 4 that the only stable solutions of systems (2) are stripes.

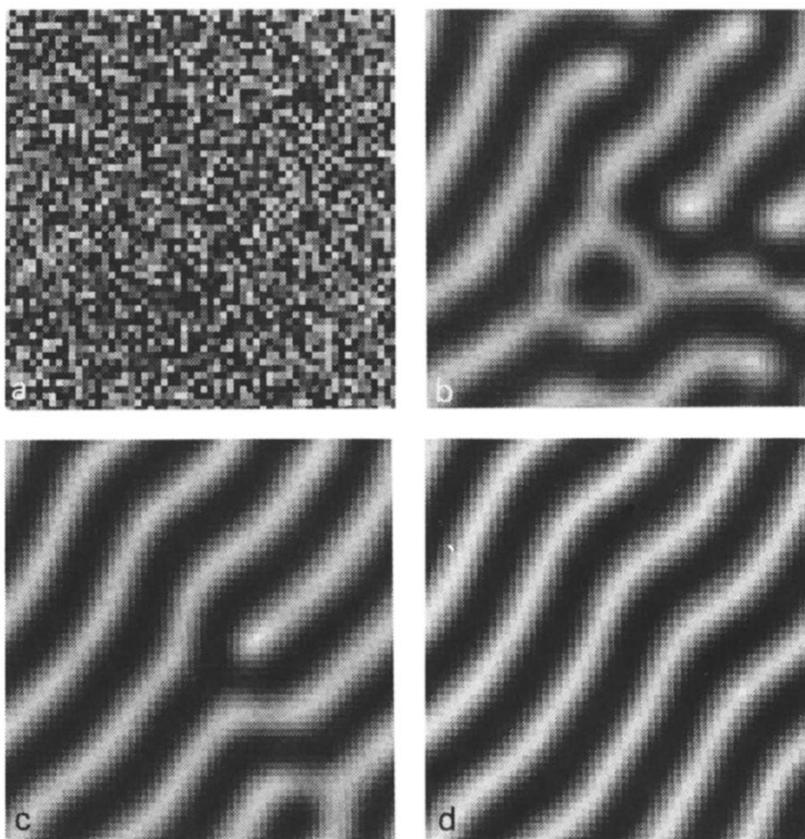


Fig. 1. Time evolution of  $q_1$  of eq. (1) from a random initial state to a stable set of stripes (black denotes concentration minima and white the concentration maxima). Computation with hyperchirality model [9] using a finite difference method on a  $60 \times 60$  grid of squares with periodic boundary conditions. All calculations were performed on an IBM 3090 with vector processing capabilities. (a) 0, (b) 10000, (c) 40000, (d) 100000 iterations. Parameters were chosen so that many modes are linearly unstable. These images are part of an animated sequence available, as a VHS video recording, upon request to the authors.

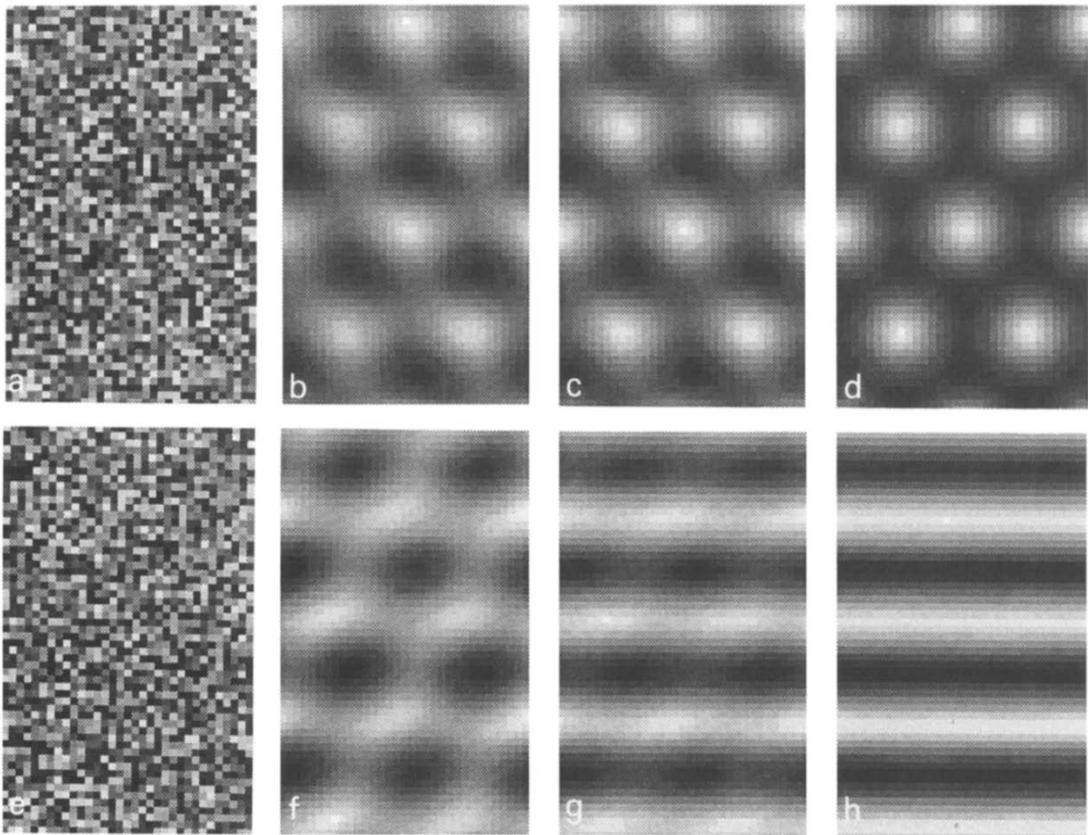


Fig. 2. Time evolution of  $q_1$  for (a)–(d) brusselator [10] and (e)–(f) hyperchirality model [9] to stable Turing structures. Parameters were chosen so that the two systems have the same linearization  $T$  and differ only in the non-linearities  $N$ . Computations performed on a  $57 \times 33$  grid with periodic boundaries as in fig. 1. With these parameters, conditions (9) are satisfied. Ratio of sides set to be approximately  $\sqrt{3}$  so that the arrangement of wavevectors depicted in fig. 3a satisfy the boundary conditions.

### 3. Non-linear interactions between modes in reaction–diffusion

In linear Turing theory ( $f(q)$  linear in  $q$ ) the solution  $q(t)$  is a superposition of non-interacting modes whose amplitudes have exponential time dependence. The mode with the largest positive growth rate dominates the pattern after a short time. With non-linear  $f(q)$  the linear modes interact, and the pattern selection properties of a model are a function of these interactions. In this section Haken's slaving principle [11,12] is used to derive a set of equations describing the time evolution of the amplitudes of the unstable modes when non-linearities are present.

(1) may be written as a sum of linear and non-linear parts

$$\dot{q}_\alpha = T_{\alpha\beta} q_\beta + N_\alpha(q), \quad (3)$$

where the Turing operator  $T_{\alpha\beta} = k_{\alpha\beta} - D_\alpha \delta_{\alpha\beta} \Delta$  is linear,  $k_{\alpha\beta} = (\partial f_\alpha / \partial q_\beta)_{q=0}$ , and  $\delta_{\alpha\beta}$  is the Kronecker delta.

$$N_\alpha = \sum_{\beta\gamma} g_{\alpha\beta\gamma}^{(1)} q_\beta q_\gamma + \sum_{\beta\gamma\delta} g_{\alpha\beta\gamma\delta}^{(2)} q_\beta q_\gamma q_\delta + \dots \quad (4)$$

contains the non-linearities. The models discussed in this Letter (hyperchirality model, brusselator) terminate at third order. However, the analysis extends to systems which contain additional terms.

The solution  $q(t)$  is expanded in terms of the right eigenvectors of  $T$

$$q(t) = \sum_{j,k} \xi_k^j u^j(k) \exp(ik \cdot r), \quad (5)$$

$$T u^j(k) \exp(ik \cdot r) = \sigma^j(k) u^j(k) \exp(ik \cdot r), \quad (6)$$

and  $j = +/ -$  distinguishes between the two eigenvalues  $\sigma$  of  $T$  for a given  $k$ . We have replaced  $k$  with  $k = |k|$  when a quantity does not depend on the direction of the wavevector. We treat plane waves, but otherwise leave the boundary conditions unspecified.

Eq. (1) can then be transformed into an infinite set of ordinary differential equations for the (complex) mode amplitudes  $\xi_k^j$ . For details of the procedure we refer the reader to Haken's work [11,12] and simply quote the result

$$\begin{aligned} \dot{\xi}_k^j &= \sigma^j(k) \xi_k^j + \sum_{\substack{k'k'' \\ j'j''}} a_{kk'k''}^{jj'j''} \xi_{k'}^{j'} \xi_{k''}^{j''} \delta_{k,k'+k''} \\ &+ \sum_{\substack{k'k''k''' \\ j'j''j'''}} b_{kk'k''k'''}^{jj'j''j'''} \xi_{k'}^{j'} \xi_{k''}^{j''} \xi_{k'''}^{j'''} \delta_{k,k'+k''+k'''}, \end{aligned} \quad (7)$$

where

$$\begin{aligned} a_{kk'k''}^{jj'j''} &= \sum_{\alpha\beta\gamma} v_{\alpha}^j(k) u_{\beta}^{j'}(k') u_{\gamma}^{j''}(k'') g_{\alpha\beta\gamma}^{(1)}, \\ b_{kk'k''k'''}^{jj'j''j'''} &= \sum_{\alpha\beta\gamma\delta} v_{\alpha}^j(k) u_{\beta}^{j'}(k') u_{\gamma}^{j''}(k'') u_{\delta}^{j'''}(k''') g_{\alpha\beta\gamma\delta}^{(2)}. \end{aligned} \quad (8)$$

The  $v$  appearing in these equations are the left eigenvectors of  $T$ .

The analysis so far is exact. To apply the slaving principle, the terms  $\xi_k^j$  are neglected for the stable modes. The validity of this approximation depends on the conditions

$$\begin{aligned} \sigma^+(k) &> 0 \quad \text{for } |k| = k_c, \\ \sigma^j(k) &< 0 \quad \text{otherwise,} \\ |\sigma^j(k)| &\gg |\sigma^+(k_c)|, \end{aligned} \quad (9)$$

which hold near the onset of the Turing instability. Then the fast relaxing modes may be eliminated from (7). The calculation is considerably simplified for the systems we are immediately interested in (2) as  $g^{(1)} = 0$ . The stable mode amplitudes are then third order in the unstable modes, and do not contribute to the  $\xi_{k_c}^+$  until the fifth-order term, which we do not need here. Eq. (7) becomes

$$\begin{aligned} \dot{\xi}_{k_c}^+ &= \sigma^+(k_c) \xi_{k_c}^+ \\ &+ \sum_{\text{unstable modes}} b_{k_c k_c k_c k_c}^{++++} \xi_{k_c}^+ \xi_{k_c}^+ \xi_{k_c}^+ \delta_{k,k'+k''+k'''} \end{aligned} \quad (10)$$

Presence of the Kronecker delta implies a geometrical relationship (depicted in fig. 3b) between modes contributing to the sum. With

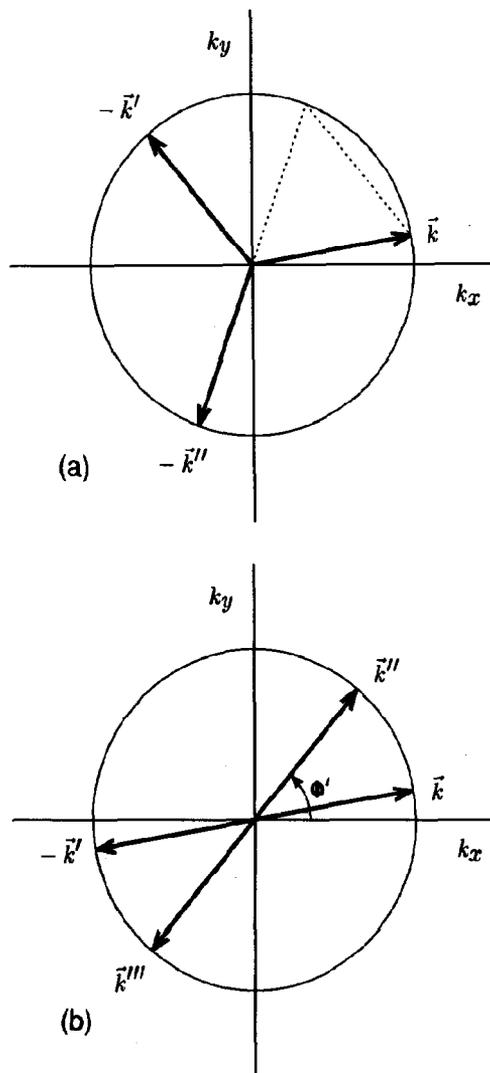


Fig. 3. Arrangement in  $k$ -space of wavevectors for modes having  $|k| = k_c$  and satisfying (a)  $\delta_{k,k'+k''} = 1$  in the quadratic term of (7), and (b)  $\delta_{k,k'+k''+k'''} = 1$  in the cubic term. For the form of (7) to remain unchanged under symmetry operations of spatial translation and rotation the wavevectors must sum to zero.

$$\sigma = \sigma^+(k_c), \quad \xi_\phi = \xi_{k_c}^+ \quad (11)$$

and

$$b_{k_c k_c k_c k_c} = b < 0 \quad (12)$$

for global stability, where  $\phi$  is the angle  $k_c$  makes with a fixed direction (see fig. 3), and noting that

$$\xi_{-\phi} = \xi_\phi^* \quad (13)$$

must hold for  $q(t)$  to be real, we find

$$\begin{aligned} \dot{\xi}_\phi &= \sigma \xi_\phi + 3b \xi_\phi \xi_\phi^* \xi_\phi + 6b \sum_{\phi'} \xi_\phi \xi_\phi^* \xi_{\phi'} \\ 0 < \phi, \phi' < \pi, \quad \phi' \neq \phi. \end{aligned} \quad (14)$$

#### 4. Solutions to the mode amplitude equations

Our approach in analyzing the behaviour of (14) is to first find the fixed points  $\dot{\xi}_\phi = 0$  and then examine the stability of each solution. An alternate approach [11] employs the generalized Landau-Ginzburg free energy associated with (14). The absence of quadratic terms in (14) and the lack of any angle dependence in the cubic term simplify the problem greatly, and it is possible to write down all of the steady states of (14), and describe completely their linear stability. The number of unstable modes available to the system, and their wavevector directions depend on the exact boundary conditions of the system. However, the procedure is the same in all cases, as shown in (b).

(a) *Simple example - four modes unstable.* For concreteness we start with the simple example of the unit square with periodic boundary conditions. Suppose that there are only four unstable modes corresponding to striped patterns in mutually perpendicular directions. The unstable modes have  $\phi = 0, \pi/2, \pi, 3\pi/2$  and  $k_c = 2\pi l_c, l_c \in \mathbb{Z}^+$ . This constrains  $l_c^2$  to integers which cannot be written as the sum of two squares. Then eqs. (14) are

$$\begin{aligned} \dot{\xi}_0 &= \sigma \xi_0 + 3b \xi_0 \xi_0^* \xi_0 + 6b \xi_0 \xi_{\pi/2}^* \xi_{\pi/2} \\ \dot{\xi}_{\pi/2} &= \sigma \xi_{\pi/2} + 3b \xi_{\pi/2} \xi_{\pi/2}^* \xi_{\pi/2} + 6b \xi_{\pi/2} \xi_0^* \xi_0. \end{aligned} \quad (15)$$

Eq. (15) has fixed points

$$(I) \quad \xi_0^* \xi_0 = -\sigma/3b, \quad \xi_{\pi/2} = 0, \quad \text{or}$$

$$\xi_{\pi/2} \xi_{\pi/2}^* = -\sigma/3b, \quad \xi_0 = 0, \quad (16)$$

$$(II) \quad \xi_0^* \xi_0 = \xi_{\pi/2} \xi_{\pi/2}^* = -\sigma/9b. \quad (17)$$

The linear stability matrix  $A_{ij} = \partial \dot{\xi}_i / \partial \xi_j$  is

$$A = \begin{pmatrix} \sigma + 6b(\xi_0^* \xi_0 + \xi_{\pi/2}^* \xi_{\pi/2}) & 6b \xi_0 \xi_{\pi/2}^* \\ 6b \xi_{\pi/2} \xi_0^* & \sigma + 6b(\xi_0^* \xi_0 + \xi_{\pi/2}^* \xi_{\pi/2}) \end{pmatrix} \quad (18)$$

evaluated at the fixed points. For solution (II), **A** has a negative and a positive eigenvalue indicating a saddle point. With solution (I) we find two negative eigenvalues, so the only stable pattern is a set of stripes, in either the  $x$  or the  $y$  direction.

(b) *General case - N unstable modes.* Suppose now there is an arbitrary number,  $N$ , of directions  $\phi$  for which plane waves with wavevector  $|k_\phi| = k_c$  satisfy the boundary conditions. Then there are  $N$  coupled ordinary differential equations to be solved. The mode amplitudes at a fixed point are labelled so that

$$\begin{aligned} \xi_{\phi_i} &\neq 0, \quad i = 1 \dots M, \\ \xi_{\phi_i} &= 0, \quad i = M+1 \dots N. \end{aligned} \quad (19)$$

Then (14) yields  $M$  coupled linear equations for the  $M$  unknowns  $\xi_{\phi_i}^* \xi_{\phi_i}$

$$\sigma + 3b \xi_{\phi_i}^* \xi_{\phi_i} + 6b \sum_{\substack{j=1 \dots M \\ j \neq i}} \xi_{\phi_j}^* \xi_{\phi_j} = 0, \quad (20)$$

which has the unique solution

$$\xi_{\phi_i}^* \xi_{\phi_i} = \frac{-\sigma}{3b(2M-1)}, \quad i = 1 \dots M. \quad (21)$$

Linear stability analysis may be employed to show that the only stable fixed points have  $M=1$ , corresponding to a striped pattern. The instability of the solutions consisting of a superposition of modes follows from [13]

$$A_{ij} A_{ji} > 0, \quad i \neq j, \quad (22)$$

where

$$A_{ij} < 0. \quad (23)$$

We see that striped patterns are selected as there is

a mutual inhibition of amplitude for each pair of modes, so that the modes "compete".

### 5. Relevance to biological and chemical pattern formation

In this section we list three cases of striped pattern formation where there is an anti-symmetric departure from the unpatterned state, and for contrast a fourth example in which a spotted array of concentration maxima is found.

(a) *Ocular dominance stripes*. The ocular dominance stripes found in some mammalian brains is a biological example of a striped pattern where symmetry (2) is likely to hold for the developmental mechanism. In layer IVc of the primary visual cortex information from the two eyes is found to be received in a set of alternating parallel "ocular dominance stripes" [14]. Bands of cells are connected to either the right or left eye, but are otherwise equivalent. This arrangement arises from an initially unpatterned state in the first few weeks following birth, and is thought to involve competitive interactions between left and right eye synapses. It is significant that asymmetrizing the virtual input during development (for example, by covering one eye with a patch) appears to disrupt stripe formation. Two existing models [15,16] of ocular dominance stripe formation possess the symmetry (2).

(b) *Segmentation in Drosophila* [17]. Despite a vast and rapidly increasing body of experimental data on developmental genetics, it remains unsettled whether the earliest segmentation events in *Drosophila* are controlled by reaction-diffusion or quite differently. The pattern is of 14 parallel stripes of equal width and alternating in character. Certain genes are activated only in odd-numbered stripes, others only in the even-numbered ones. This pattern inspired our interest in models with form (2). But of the three examples listed here, it is the one in which it is least clear that (2) is anywhere present in the chemistry.

(c) *Microtubulin dissipative structures*. Microtubules are polymers of a protein, tubulin, which are active in developmental processes in living cells. Tabony and Job [18] polymerized tubulin in thin layers of solution with other chemicals present to

provide a thermodynamic driving force for polymerization. Using optical techniques, and small-angle neutron scattering, they showed that arrays of microtubules were formed as stripes of oriented nematic liquid crystals in which alternate stripes have orthogonal orientations of microtubules ( $45^\circ$  to the stripe direction in one,  $135^\circ$  in the next).

(d) *Spotted patterns in Castets' gel-strip reactor*. The presence of quadratic terms in the net production functions  $f(q)$  (i.e.  $g^{(1)} \neq 0$ ) introduces a second-order contribution to the mode amplitude equations having the form

$$c_{\phi+\pi/3}^* c_{\phi-\pi/3}^* \quad (24)$$

With  $c > 0$  three plane waves (with  $k$  at the vertices of an equilateral triangle) may cooperate to form a stable steady state which is a hexagonal array of spots. The calculation in this case is more complex, as some of the stable modes are second order in the unstable mode amplitudes, and may contribute to the cubic term. Figs. 2a-2d show the steady state pattern of a computation with the brusselator [10] in which the steady state pattern is a hexagonal array of spots. Under identical conditions, we have found that the hyperchirality model invariably produces stripes.

Recently the existence of steady state chemical patterns (Turing structures) has been confirmed experimentally by Castets et al. [19] in a chlorite-iodide-malonate reaction in a gel-strip reactor. The (three-dimensional) pattern observed appears to be a superposition of plane waves analogous to the arrangement shown in fig. 3a. This allows us to predict the existence of quadratic terms in the reaction kinetics of their system.

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**References**

- [1] J.D. Murray, *Sci. Am.* 258 (1988) 80.
- [2] A.M. Turing, *Phil. Trans. Roy. Soc. (London)* B 237 (1952) 37.
- [3] L.G. Harrison, *J. Theor. Biol.* 125 (1987) 369.
- [4] L.G. Harrison, *Kinetic theory of living pattern and form* (Cambridge Univ. Press, Cambridge), in press.
- [5] J.D. Murray, *Biomathematics*, Vol. 19, *Mathematical biology* (Springer, Berlin, 1989).
- [6] M.J. Lyons, L.G. Harrison, B.C. Lakowski and T.C. Lacalli, *Can. J. Phys.* 68 (1990) 772.
- [7] B.N. Nagorcka, *J. Theor. Biol.* 132 (1988) 277.
- [8] T.C. Lacalli, *J. Theor. Biol.* 144 (1990) 171.
- [9] L.G. Harrison and T.C. Lacalli, *Proc. Roy. Soc. B* 202 (1978) 361.
- [10] G. Nicolis and I. Prigogine, *Self-organization in nonequilibrium systems* (Wiley, New York, 1977).
- [11] H. Haken, *Synergetics*, 3rd Ed. (Springer, Berlin, 1983).
- [12] H. Haken and H. Olbrich, *J. Math. Biol.* 6 (1978) 317.
- [13] J.J. Tyson, *J. Chem. Phys.* 62 (1975) 1010.
- [14] D.H. Hubel and T.N. Wiesel, *Proc. Roy. Soc. B* 198 (1977) 1.
- [15] N.V. Swindale, *Proc. Roy. Soc. B* 208 (1980) 243.
- [16] J.R. Thomson, Z. Zhang, Wm. Cowan, M. Grant, J.A. Hertz and M.J. Zuckermann, *Physica Scripta* T33 (1990) 102.
- [17] P.W. Ingham, *Nature* 335 (1988) 25.
- [18] J. Tabony and D. Job, *Nature* 346 (1990) 448.
- [19] V. Castets, E. Dulos, J. Boissonade and P. De Kepper, *Phys. Rev. Letters* 64 (1990) 2953.