

## Confined Turing patterns in growing systems

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In this paper we address the problem of pattern formation in confined Turing systems in two dimensions, when one assumes the enhancement of the concentration of one of the chemicals at some of the confining surfaces. This model is suitable to study biological systems, such as the skin patterns shown by some marine fish. We also study numerically the dynamical growth of the system by changing the size of the confined region while dynamical diffusion and reaction phenomena take place. This idea is tested in two different models. This allows one to estimate the robustness of stripe formation. [S1063-651X(97)06807-4]

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In 1952, Turing established the basis to explain biological patterns using two interacting chemicals [1]. The experimental observation of a ‘‘Turing pattern’’ occurred in a chemical system nearly 40 years after their prediction by Turing [2,3], but it was not until very recently that the example of a Turing pattern in a biological system was confirmed in skin patterns of the angelfish (*Pomacanthus*) by Kondo and Asai [4]. In this work the authors propose and solve a system of two reaction-diffusion equations in a growing one-dimensional domain to explain the insertion of new stripes between the older ones during the growth of *Pomacanthus semicirculatus* and the rearrangement of the stripe pattern of *Pomacanthus imperator*.

Kondo and Asai’s interpretation was subject to criticism by Höfer and Maini [5], who did not find enough evidence to say that reaction-diffusion systems could provide a mechanistic basis for the strip-doubling phenomenon. In particular, they claim that a two-dimensional simulation would be a more realistic representation of the fish skin than a one-dimensional domain. Höfer and Maini argue that a mechanism that sets the distance between adjacent stripes and some kind of ‘‘memory’’ that conserves the location of old stripes is needed in order to explain the patterning dynamics of the *Pomacanthus*. Accordingly, in this work we shall show that a reaction-diffusion system is capable of describing the main features of the phenomena observed in the *Pomacanthus* skin. For that goal, we consider two sets of Turing equations known to form different kinds of patterns; these are solved in a two-dimensional spatial domain that simulates the fish shape, with zero flux boundary conditions. The key feature of our simulation is the enforcement of an enhanced source of the activator along some of the boundaries of the domain. This idea has close parallels with the mechanism of stripe formation in the *Drosophila* embryo where the pattern of the anteroposterior (head-tail) segmentation is caused by a high concentration of the *Bicoid* protein along the anterior (head) side [6].

To see how the boundary conditions and domain shape affect the stationary patterns from an initially homogeneous state, we study a simplified version of a model for glycolysis as the specific reaction mechanism, which has been extensively studied numerically by Dillon *et al.* [7] in one dimension. The Turing system of equations is

$$\begin{aligned}\frac{\partial u}{\partial t} &= \beta - \kappa u - uv^2 + D\nabla^2 u, \\ \frac{\partial v}{\partial t} &= \kappa u + uv^2 - v + D\delta\nabla^2 v.\end{aligned}\quad (1)$$

This represents a cross activator-inhibitor system with a uniform stationary-state solution at  $u_u = \beta(\kappa + \beta^2)^{-1}$  and  $v_u = \beta$ . A linear stability analysis of the solutions around this fixed point shows that the uniform stationary solution may be unstable to periodic fluctuations for small  $\delta < \delta_c$ , where  $\delta_c$  is some critical value that depends on the constants  $\kappa$  and  $\beta$ . Following Dillon *et al.*, we set the parameters  $\kappa = 1.0$  and  $\beta = 0.001$  and for these values  $\delta_c = 0.172$ . Therefore, we choose  $\delta = 0.10$ .

We choose different domain shapes bounded by curves  $C_1$ ,  $C_2$ ,  $C_3$ , and  $C_4$  on a plane where the diffusion of the reactants is set equal to zero. At some of these boundaries we assume that the source term  $\kappa$  for reactant  $u$  is enhanced by 1%.

The numerical solution of the coupled partial differential equations is accomplished by discretizing the Laplacian, which we write on a square lattice with lattice parameter  $b$  and with sites denoted by  $(i, j)$ . The stationary solutions were obtained numerically in a square lattice of 2500 points by a simple Euler method. When the initial state is the uniform solution  $u = u_u$  and  $v = v_u$ , the system remains stable in this state. However, when in some of the boundaries the source term  $\kappa$  is enhanced, a pattern of stripes is obtained whose formation does not need an initial perturbation.

The spatial oscillations grow from the enhanced surface in 20 000 iterations with a time step of 0.002. The solutions converge to a stationary state within an error of  $\sim 10^{-5}$ . The number of stripes in the pattern depends on the parameter  $D/b^2$ , which in our case was set to 4. This might seem trivial since Dirichlet boundary conditions should favor stripes parallel to the boundary. However, the stripes are not formed well if the enhancement field is set equal in all four boundaries. In this case a lattice of spots appears. This is important because it shows that the formation of stripes is very sensitive to the size of the system in units of the wavelength, the

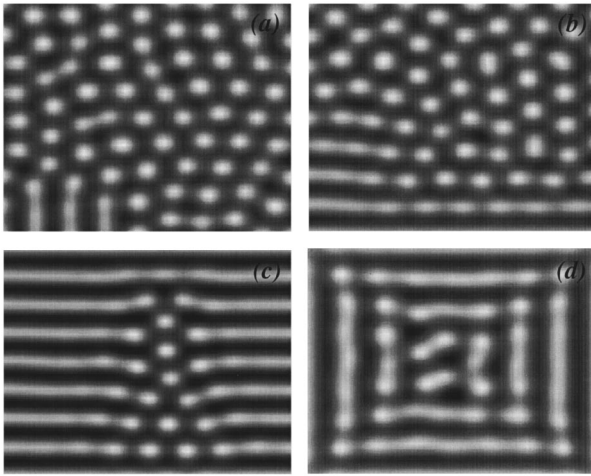


FIG. 1. Patterns obtained in a square lattice starting with a randomized state obtained with random deviations of 10% from the uniform state: (a) without an enhancement of the source parameter  $\kappa$  in the boundaries and with an enhancement of 10% in (b) only the lower boundary, (c) the upper and lower boundaries, and (d) all four boundaries. Observe the formation of an imperfect lattice of dots near the center.

shape of the boundaries, and possibly the point in phase space where one starts the calculation or the initial conditions.

In order to separate the influence of the latter factors, namely, the presence of a fixed source in the boundary, and the initial conditions we performed the calculations shown in Fig. 1, where different enhancement conditions are considered, starting with a randomized initial state with variations of 10%. As observed, the absence of a field in the boundary produces mainly a pattern of spots. Imperfect stripes are formed when there is an enhancement in one, two, or four of the boundaries. However, the spotted pattern is never defeated.

This means that in this model a pattern of stripes is obtained only if there is a source field and the system starts very near the uniform state. However, the model of Eq. (1) is perfectly able to produce patterns morphologically very similar to the ones observed in the marine angelfish *Pomacanthus*. One starts with uniform initial conditions and mimics the shape of the fish with parabolas. At some boundaries one assumes that there are suitable sources. In Fig. 2(a) a calculation with uniform initial conditions and with a field in the lower and upper boundaries is shown. Observe the conservation on the “wavelength” that forces the appearance of new stripes in the wider zones, as observed in the angelfish *Pomacanthus imperator*.

If the source is imposed on the vertical straight boundaries, a vertical pattern of slightly bent stripes is obtained, as shown in Fig. 2(b). This could mimic the pattern observed in the species *Pomacanthus semicirculatus*. The model could also reproduce the pattern observed in other fish, such as the zebra fish, that presents horizontal stripes without caring about its shape. This could be done by setting the enhancement field in the lower straight boundary, as shown in Fig. 2(c). However, the present model seems to be more appropriate to obtain combined patterns of patches and stripes, as the one found in the *Danio malabaricus*.

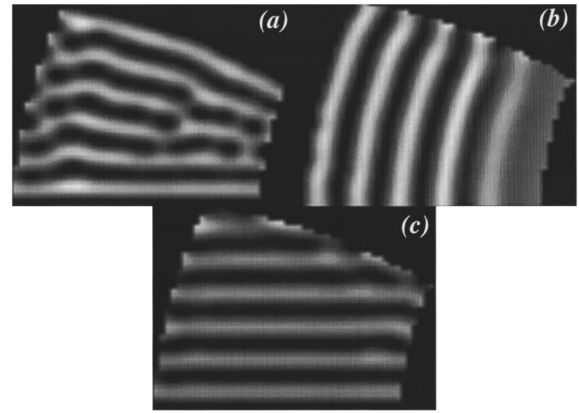


FIG. 2. Calculation starting with the uniform state and modeling the shape of the fish with fields on the (a) horizontal and (b) vertical boundaries. Observe the deformations and bendings of the stripes due to the form of the boundaries. (c) Pattern obtained when only the lower straight boundary contains a field. Observe that the influence of the curved boundaries is now negligible.

These calculations demonstrate that a Turing system is able to mimic the stripe patterns found in the angelfish, as stated by Kondo and Asai [4]. However, we have detected a natural tendency of model Eq. (1) to form patterns of spots when one departs from the uniform fixed point. Furthermore, the marine angel fish has stripe patterns that evolve as the fish grows, a central issue addressed by the time calculation of Ref. [4]. We shall address this now.

The patterns obtained so far are static and could be considered as valid only if the two characteristic times of the dynamical process of growth, namely, the diffusion time and the fish growing time, are extremely different. In order to study this issue we have performed calculations of Eq. (1) in a continuously growing lattice, assuming that the boundary grows as the reactants diffuse. This was done by changing the parameter  $D/b^2$  by a small amount in each iteration, that is, we set a slow uniform dilation of the lattice so that  $b = \alpha t$ , where the constant  $\alpha$  is fixed so that  $b$  doubles its size in 40 000 iterations.

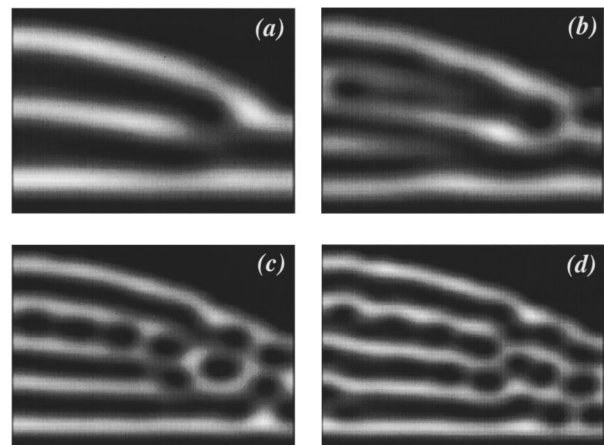


FIG. 3. Calculation modeling the growth of the fish *Pomacanthus imperator* with Eq. (1). The lattice represents systems of larger size because the parameter  $D/b^2$ , which gives the distance scale, is made smaller as time runs. The series (a)–(d) are equally spaced snaps of the growing process.

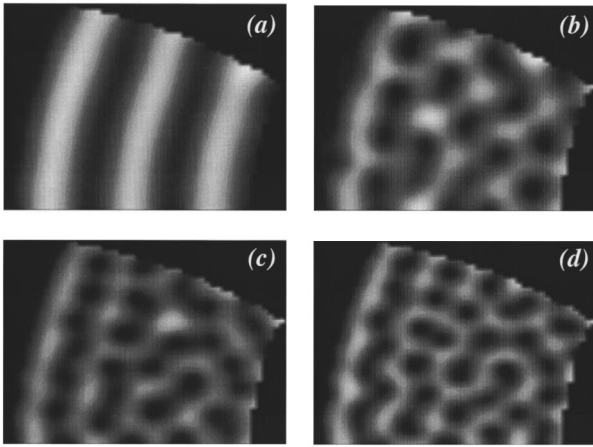


FIG. 4. Calculation modeling the growth of the fish *Pomacanthus semicirculatus* with Eq. (1). The series (a)-(d) was obtained as in Fig. 3.

A series of patterns simulating the growth of *Pomacanthus imperator* is shown in Fig. 3. The size of the fish in 3(d) is a factor of 1.6 larger than in 3(a) and there are 5000 iterations between the figures. Observe that as the fish grows, the stripe pattern evolves to a patchy pattern, not observed in grown-up fish. The problem is even worse in the simulation of the growth of *Pomacanthus semicirculatus*, shown in Fig. 4, where a spotty pattern is definitely established in big fish.

This competition between spots and stripes in Turing patterns has been addressed many times [7,8] and various models for biological [9] and chemical [10] pattern formation have been put forth. It is difficult to select a particular one as the model that is more appropriate for a given case. Our intention is to study the effect of our particular boundary conditions and shape on a different model. We choose an activator-substrate system thoroughly studied in the past [11], which is able to produce spots, periodic, and striped labyrinth patterns according to the values of the parameters used. The equations read

$$\frac{\partial u}{\partial t} = \beta_u - \rho_u \frac{v^2 u}{1 + \phi v^2} + D \nabla^2 u,$$

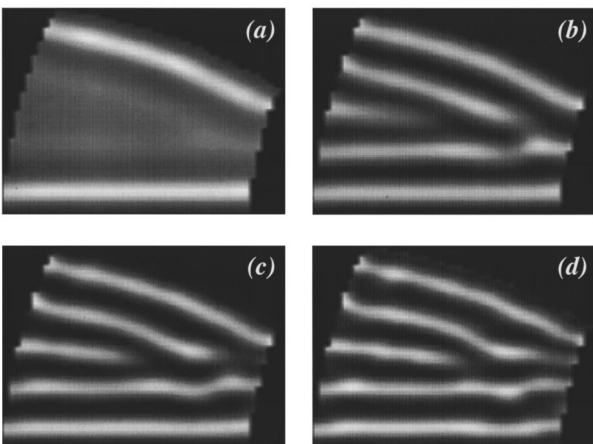


FIG. 5. Calculation modeling the growth of the fish *Pomacanthus imperator* with Eq. (2). The series (a)-(d) was obtained as with the former model.

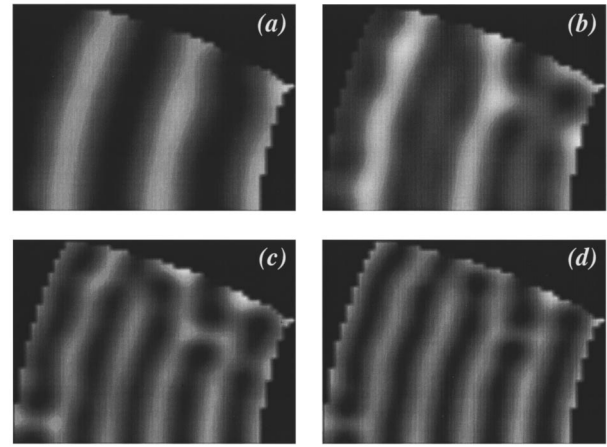


FIG. 6. Calculation modeling the growth of the fish *Pomacanthus semicirculatus* with Eq. (2).

$$\frac{\partial v}{\partial t} = \beta_v - \kappa_v v + \rho_v \frac{v^2 u}{1 + \phi v^2} + D \delta \nabla^2 v, \quad (2)$$

where the notation of Eq. (1) in Ref. [11] has been changed in order to compare with our Eq. (1), taken from Ref. [7]. Using our numerical methods, we have reproduced the labyrinth pattern shown in Fig. 2(c) of Ref. [11] using the parameters given there when one imposes periodic boundary conditions and a random initial state. The parameters in our calculations using this model are  $\delta=0.025$ ,  $\rho_u=0.02$ ,  $\rho_v=0.01$ ,  $\kappa_v=0.01$ ,  $\beta_u=0.02$ ,  $\beta_v=0.0$ , and  $\phi=0.1$ .

Growing patterns were obtained with this model and they are shown in Fig. 5 for the *Pomacanthus imperator* and in Fig. 6 for the *Pomacanthus semicirculatus*. The way of growing was exactly as in Figs. 3 and 4. Observe that the stripes are more stable, although the tendency to form spots is also present.

This tendency could be avoided if the enhancement fields are set only in the upper curved boundary. The series of growing patterns shown in Fig. 7 resemble very much the actual pattern on the real fish.

Summarizing, we have performed a set of numerical calculations using the Turing system in Ref. [7] in a two-

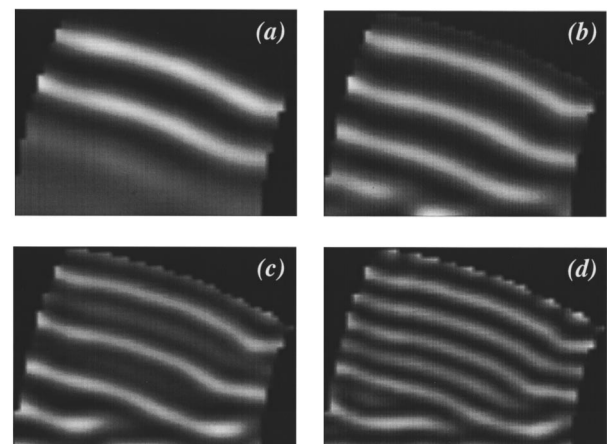


FIG. 7. Calculation modeling the growth of the fish *Pomacanthus imperator* with Eq. (2), with a source field only at the upper curved boundary.

dimensional finite lattice. We have introduced two important concepts. (i) The influence of the boundary conditions on the pattern is readily put forth by assuming that there is an enhanced source at some of the boundaries. This idea is sensible in biological systems because of their small size and compatible with recent findings [6] that show the possible existence of such sources in well-defined parts of the body of an animal. (ii) The role of the initial conditions in the shape of the stable pattern is of paramount importance when considering a system that changes shape and size with time.

Our calculations were centered in modeling the shape of the angelfish, recently studied by Kondo and Asai [4], who made the important point that in this fish the conservation of wavelength in the pattern while the fish grows is an indicator that a Turing system might be appropriate to model the pattern, particularly the merging of new stripes. We also modeled the dynamic growth of the fish in the case when the ratio between the two time scales of the system is not negligible. This is very interesting because it really can tell if the evolution of stripes is influenced by departing from the uniform state used in the static calculations since it is obvious

that a stable pattern at a given time does not start from the uniform state. This could allow one to draw some conclusions not only about the diffusion rates, but also about the locality of the system.

We are conscious that our calculations are far from being exhaustive, but the results exposed here look promising and encouraging. We are aware that very limited conclusions can be drawn concerning the actual processes in living organisms such as fish. For instance, the truly three-dimensional character of the fish skin, which could probably affect the diffusion of chemicals, was not addressed here. Also, it is not clear that our method of growing is the most appropriate since one lacks information about how the newborn cells in the skin acquire their coloring. However, we are implicitly assuming that the features studied here are general to a wide variety of models.

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- [1] A. M. Turing, *Philos. Trans. R. Soc. London, Ser. B* **237**, 37 (1952).
- [2] Q. Ouyang, J. Boissonade, J. C. Roux, and P. de Kepper, *Phys. Lett. A* **134**, 282 (1989).
- [3] V. Castets, E. Dulos, J. Boissonade, and P. de Kepper, *Phys. Rev. Lett.* **64**, 2953 (1990).
- [4] S. Kondo and R. Asai, *Nature (London)* **376**, 765 (1995).
- [5] T. Höfer and P. K. Maini, *Nature (London)* **380**, 678 (1996).
- [6] D. St. Johnston and C. Nüsslein-Volhard, *Cell* **68**, 201 (1992).
- [7] R. Dillon, P.K. Maini, and H.G. Othmer, *J. Math. Biol.* **32**, 345 (1994).
- [8] See, for instance, H. Meinhardt, *Nature (London)* **376**, 722 (1995), and references therein.
- [9] M. C. Cross and P. C. Hohenberg, *Rev. Mod. Phys.* **65**, 1045 (1993).
- [10] R. Kapral and K. Showalter, *Chemical Waves and Patterns* (Kluwer, Dordrecht, 1995).
- [11] A. J. Koch and H. Meinhardt, *Rev. Mod. Phys.* **66**, 1481 (1994).