PATTERN FORMATION IN NOISY SELF-REPLICATING SPOTS

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Among reaction-diffusion systems showing Turing patterns, the diffusive Gray-Scott model [Pearson, J. A., 1993, Science 261, 189] stands out by showing self-replicating patterns (spots), which makes it the ideal simple model for developmental research. A first study of the influence of noise in the Gray-Scott model was performed by Lesmes et al. [2003 Phys. Rev. Lett. 91, 238301] concluding that there exits an optimal noise intensity for which spot multiplication is maximal. Here we show in details the transition from non-spotlike to spotlike pattern, with the identification of a wide range of noise intensities instead of an optimal value for which this transition occurs. Additional studies also reveal that noise produces a shift and a shrinkage of the regions of spatial patterns in the phase diagram, without introducing qualitative changes to the diagram.

Keywords: Turing patterns, reaction-diffusion, noise, self-replication, prebiotic evolution

The major step forward in the modern theory of pattern formation was given by Turing [1952], who used the linear analysis to determine the conditions necessary for the creation of spatial patterns in two-component reaction-diffusion systems. More recently, Gierer and Meinhardt [2000], Koch and Meinhardt [1994] and independently Segel and Jackson [1972] postulated that the interplay between two antagonistic feedbacks is essential for pattern formation. On one hand, the positive feedback should consist in the self-enhancement or autocatalysis of one of the chemical components - generally called activator -, a reaction necessary for small perturbations to be amplified. On the other hand, the increase in activator's concentration must be complemented by a fast-diffusing response in order to obtain pattern formation. According to the nature of the antagonistic response, the resulting systems are either of activator-inhibitor type - an inhibitory substance is produced by the activator that slows down the latter's production, or of activator-substrate type - a substrate substance is consumed during autocatalysis leading to a depletion of the activator and the relaxation of the self-enhancement.

Two well-known examples of the two types of reaction-diffusion systems are the Meinhardt system [Gierer and Meinhardt 2000] and the diffusive Gray-Scott system [Pearson 1993], respectively (see Cross and Hohenberg 1993 for a review). The interplay between activator and inhibitor under a spatially-extended scenario creates most startling spatio-temporal patterns, such as spots, stripes, travelling waves, spot replication, and spatio-temporal chaos. The Turing patterns are characterized by the active role that diffusion plays in destabilizing the homogeneous steady state of the system. They emerge spontaneously as the system is driven into a state where it is unstable towards the growth of finite-wavelength stationary perturbations.

A remarkable feature of these structures and particularity of those emerging from the diffusive Gray-Scott model, is that they provide a model for the unfolding development of a simple proto-organism. In this case, cell-like localized structures grow, deform and make replicas of themselves until they occupy the entire space. Somehow, the self-replicating spots formed under the nonlinear spatial dynamics of the Gray-Scott model retain some key features of replicating higher-order entities beyond pure chemical replicators (see Boerlijst 2000 and references therein). It thus makes it of high interest in exploring tentative steps towards life forms beyond well-mixed chemical replicators.

The Turing patterns from the work of Pearson [1993] on the diffusive Gray-Scott model were confirmed experimentally by Lee et al. [1993], the spot replication too [Lee et al. 1994]. Theoretically, extensive work exist in the literature on the dynamics of this model concerning the spot-replication pattern in one, two and three dimensions [Muratov and Osipov 2000]. Recently, a first study of the influence of noise in the Gray-Scott model was performed by Lesmes et al. [2003] (see also Hochberg et al. 2003) concluding that there is an optimal noise intensity for which spot multiplication is maximal. Here we show in details the transition from non-spotlike to spotlike pattern, with the identification of a wide range of noise intensities for which this transition occurs. We have studied also the effect of noise on the entire phase diagram including all spatial patterns. The study shows that the noise does not produce qualitative changes of the diagram, but rather a shrinkage of the Turing regions, and thus the importance of noise is to be considered relative to specific values of the parameters and not to the entire parameters space.

1. The Model

The model was originally introduced in Gray and Scott [1985] as an isothermal system with chemical feedback in a continuously fed, well-stirred tank reactor, where the last property implied the lack of diffusion. The analysis of the system revealed stationary states, sustained oscillations and even chaotic behavior. The model considers the chemical reactions

$$U + 2V \; \rightarrow \; U + 3V \tag{1}$$
$$V \; \rightarrow \; P, \tag{2}$$

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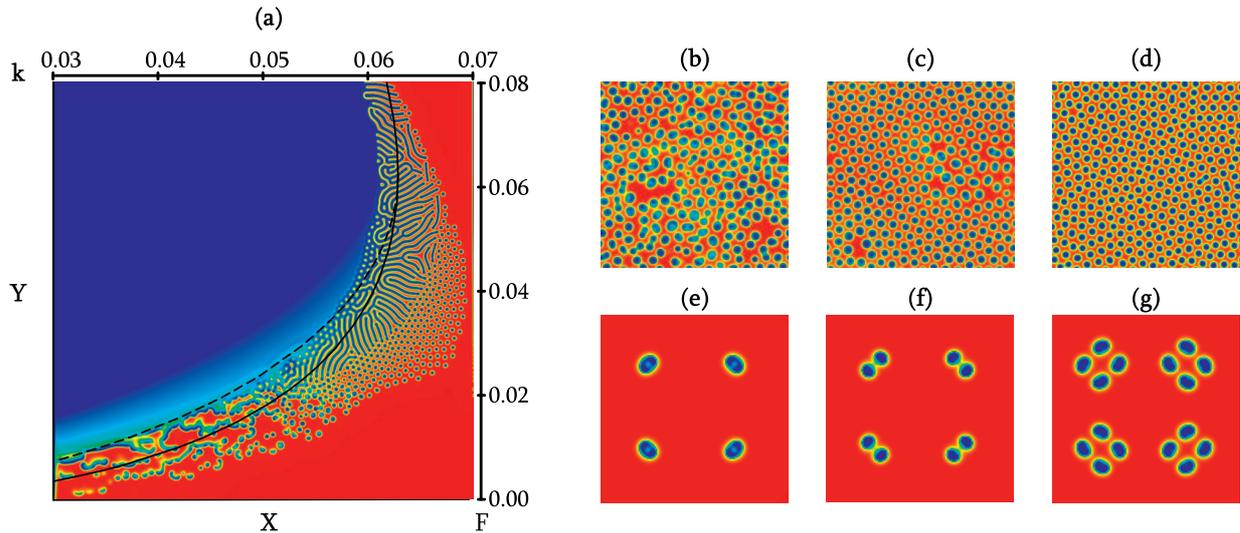
FIG. 1 Pearson model. *(a)* Illustrative static version of the final patterns produced by the system. The bifurcation curves are drawn: the saddle-node *(solid line)* and the Hopf bifurcation curve *(dashed line)*. The spot-multiplication patterns as classified in Pearson [1993]: the *(b)* ϵ, *(c)* ζ and *(d)* λ patterns. Panels *(e)*, *(f)* and *(g)* illustrate the spot-multiplication process.

describing the autocatalytic growth of an activator V on the continuously fed substrate, U and the decay of the former in the inert product P, subsequently removed from the system. A major development was performed by Pearson [1993] who introduced the role of space by relaxing the constraint of a well-stirred tank and studied the system in two dimensions, in the limit of small diffusion. In two dimensions, the concentrations of the two chemical components, $u(x, y, t)$ and $v(x, y, t)$ are given by

$$\frac{\partial u}{\partial t} = D_u \nabla^2 u - uv^2 + F(1 - u) \qquad (3)$$

$$\frac{\partial u}{\partial t} = D_v \nabla^2 u + uv^2 - (F + k)v, \qquad (4)$$

where D_u and D_v are the diffusion coefficients, F is the dimensionless flow rate (the inverse of the residence time) and k is decay constant of the activator, V. The original study involved fixed diffusion coefficients, $D_u = 2 \times 10^{-5}$ and $D_v = 10^{-5}$, with F and k being the control parameters.

As a typical Turing pattern, the system has a steady state stable with respect to homogeneous temporal oscillations which becomes unstable towards standing, space-periodic perturbations when diffusion is taken into account (see Mazin et al. 1996 for a detailed linear analysis of the Gray-Scott model). The linear analysis indicates the existence of a trivial homogeneous steady state $(u_\mathrm{R}, v_\mathrm{R}) = (1, 0)$ - referred to as the red stage - which is stable for any pair of (F, k) and reflects the continuously supplied substrate. For certain values of F and k, namely when $1 - 4\delta^2 F \geq 0$, other two steady states exist, $(u_\mathrm{B}, v_\mathrm{B})$ and $(u_\mathrm{I}, v_\mathrm{I})$, with $u_\mathrm{B,I} = (1 \pm \sqrt{1 - 4\delta^2 F})/2$ and $v_\mathrm{B,I} = (1 \mp \sqrt{1 - 4\delta^2 F})/2\delta$.

When these two steady states exist, it can be shown that $(u_\mathrm{I}, v_\mathrm{I})$ is always unstable, while $(u_\mathrm{B}, v_\mathrm{B})$ - the blue state -

may be either stable or unstable, with the stability conditions given by $Tr(A) = -v_0^2 + k < 0$ and $|A| = (v_0^2 - F)(F + k) > 0$. More precisely, for the values of (F, k) for which $Tr^2(A) - 4|A| < 0$, the blue state crosses a Hopf bifurcation [Strogatz 1994] when the condition $TrA = 0$ is fulfilled, that is when $F_\mathrm{H} = \frac{1}{2}[\sqrt{k} - 2k - \sqrt{(2k - \sqrt{k})^2 - 4k^2}]$.

In order for the system to present Turing structures, it must cross a Turing bifurcation point in the (F, k) space such that a stable steady state of the system becomes unstable to standing, space-periodic perturbations [Rovinsky and Menzinger 1992]. With the introduction of the diffusion terms, the non-diffusive stability conditions become:

$$[\sigma(F + k) - (v_\mathrm{B}^2 + F)]^2/4\sigma > (F + k)(V_\mathrm{B}^2 - F) \quad (5)$$

$$\sigma(F + k) - (v_\mathrm{B}^2 + F) > 0, \qquad (6)$$

with $\sigma \equiv D_u/D_v$, the diffusion coefficient ratio. The previous inequalities define the domain in the parameters space (F, k, σ) – called Turing space – for which spatial patterns grow (see Fig.1a). Mazin et al. [1996] delimitate this domain: the regions in the (F, k) space where the blue state is unstable towards the growth of standing spatial perturbations, for several values of σ.

2. Pattern Formation

For the numerical study of the partial differential equations we used the initial conditions and resolution employed in Pearson [1993] and consisting in a system size of $R \times R$, with $R = 2.5$ discretized through $x \to (x_0, x_1, x_2, ..., x_N)$ and $y \to (y_0, y_1, y_2, ..., y_N)$, with $N = 256$. We have used the standard five-point approximation for the 2D Laplacian

with periodic boundary conditions. More precisely, the concentrations $(u_{i,j}^{n+1}, v_{i,j}^{n+1})$ at the moment $(n+1)\tau$ at the mesh position (i, j) are given by

$$u_{i,j}^{n+1} = u_{i,j}^n + \tau D_u \Delta_h u_{i,j}^n + \tau \mathcal{F}_1(u_{i,j}^n, v_{i,j}^n) \quad (7)$$

$$v_{i,j}^{n+1} = v_{i,j}^n + \tau D_v \Delta_h v_{i,j}^n + \tau \mathcal{F}_2(u_{i,j}^n, v_{i,j}^n), \quad (8)$$

with the Laplacian defined by

$$\Delta_h u_{i,j}^n = \frac{u_{i+1,j}^n + u_{i,j+1}^n + u_{i-1,j}^n + u_{i,j-1}^n - 4u_{i,j}^n}{h^2}. \quad (9)$$

As in Pearson [1993], a colormap for the U-concentration was used for visualization, with the red color representing the (u_R, v_R) steady state and the blue one, a value in the vicinity of the (u_B, v_B) state, e.g. $(u, v) = (0.3, 0.25)$. We numerically integrated Eqs. (3)-(4) and the resulting phase diagram is shown in Fig. 1a, where the bifurcation curves are also drawn (see Rovinsky and Menzinger 1992). Once a spot of high V is formed, it is maintained by the concentration difference between its center and the surroundings of the spot. As the concentrations are limited to the $[0, 1]$ interval, the spot can grow until the central concentration can no longer achieve the necessary gradient and thus its V-value starts to decrease. This induces the spot-division phase.

As examples of patterns implying spots multiplication and following Pearson terminology, we have represented in Fig. 1b,c,d a selection sharing this property, while in panels e,f,g we illustrate a typical spot-replication process. For all of them, the process of spot multiplication continues until they fill the entire space. While the λ pattern reaches a stationary state of completely packed spots, the other two patterns present a continuous formation and disappearance of spots, the latter being due to over-crowding and leading to the creation of extended red areas [Pearson 1993]. More precisely, the ϵ pattern is formed through the continuous disordered breaking of randomly spread filiform structures into spots, while for the ζ pattern, the area occupied by spots forms in the center and grows outward spherically.

3. The Influence of Noise

In order to analyze the role of noise in the outcome of the Gray-Scott model, Lesmes et al. [2003] have carried out the first study of the noise-controlled pattern formation in the Pearson model, with emphasis on the self-replicating patterns. They found that for the chosen value of the pair $(F, k) = (0.05, 0.0655)$, the noise drives the system from the non-multiplicative, stripe-like pattern (κ pattern) to the spot-multiplication one (λ pattern) – Fig. 2.

The noise included in this analysis is (following Lesmes et al. 2003) an additive Gaussian one with zero-mean and standard deviation controlled by the parameter A as $\sigma^2 = 2A$. Specifically, we have random fluctuations such that the additive noise terms, $\eta_u(\mathbf{x}, t)$ and $\eta_v(\mathbf{x}, t)$ satisfy
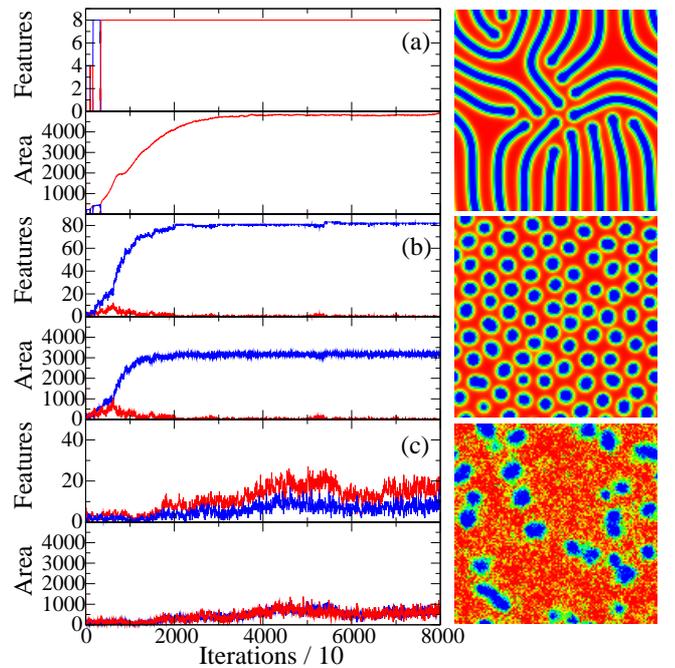

FIG. 2 The influence of noise on pattern formation for $(F, k) = (0.05, 0.0655)$ and: (a) $A = 0.0$;(b) $A = 0.0005$; (c) $A = 0.003$. Temporal evolution of the number of lines (red) and spots (blue) – upper panel – and of the total area encompassed by them – lower panels. R.h.s. panels show the spatial pattern obtained after 80000 iterations.

$$\langle \eta_u(\mathbf{x}, t) \, \eta_u(\mathbf{x}', t') \rangle = 2A_u \, \delta^2(\mathbf{x} - \mathbf{x}') \, \delta(t - t') \quad (10)$$

$$\langle \eta_v(\mathbf{x}, t) \, \eta_v(\mathbf{x}', t') \rangle = 2A_v \, \delta^2(\mathbf{x} - \mathbf{x}') \, \delta(t - t'). \quad (11)$$

In their analysis, Lesmes et al. argue in favor of an optimal noise intensity for which the number of spots is maximal, after a sufficiently long integration time. This is an interesting observation, pointing towards a possible target of selection based on maximization in the number of higher-order spatial structures (the spots) under prebiotic conditions. In other words, under a given noise level, appropriate kinetic parameters might enhance the formation of spatial, cell-like structures that are not present when noise is absent.

We reproduce their results in Fig. 3d obtained from a statistics of 20 experiments and 100000 iterations for every (F, k, A) chosen. Supplementary to their analysis, we included also the evolution of the number of lines/spots (upper panels) and the total normalized area occupied by spots and lines, respectively (lower panels). As suggested also by Fig. 3, we consider the latter as a better tracer of the effect of noise on pattern formation. As component cells of a spot were considered those characterized by a value of $u < 0.1$, while the total area was scaled to the real space by multiplying the number of spot's or line's cells with the scale factor h^2.

In comparison with the results of Lesmes et al., ours suggest the existence of an interval of optimum noise-intensity values leading to a maximum number of spots, rather than
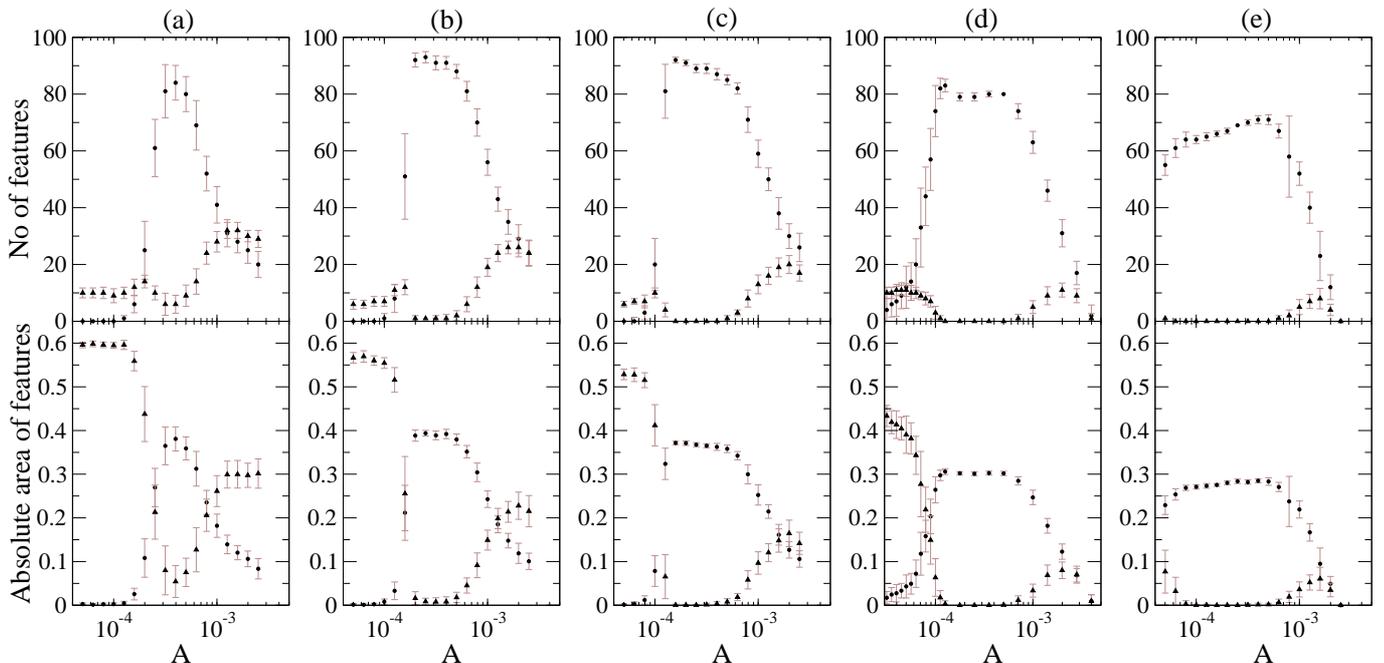
FIG. 3 The number of spots *(upper panels – dots)* and lines *(upper panels – triangles)* as a function of noise intensity. The area occupied by spots *(lower panels – dots)* and lines *(lower panels – triangle)* as a function of noise intensity. The parameters are $F = 0.05$ and *(a)*: $k = 0.064$,*(b)*: $k = 0.0645$, *(c)*: $k = 0.065$,*(d)*: $k = 0.0655$, *(e)*: $k = 0.066$.

a single optimum value. In other words, our distribution of spots shows a plateau at the level of maximum number of spots, while theirs appears to have a more bell-like shape. The plateau characteristics is more evident in the distribution of the area occupied by the two features – spots and lines - as the noise intensity varies. In order to confirm this remark, we have carried out a similar analysis for various pairs of (F, k), more precisely maintaining F constant and varying the parameter k. The chosen (F, k) pairs encompass several patterns, from completely stripe-like to completely spot-like patterns. One can see from Fig. 3 that in general there exists an optimum-noise interval that guarantees the maximum number of spots. When going to lower values of k or equivalently deeper into the stripe-like pattern region, the noise loses its constructive role and the capability of pattern switching. Additionally, one can see that, once a certain noise threshold is reached, the transition into a spot-like dynamics is extremely fast compared with the slow decay of the number of spots when the noise level becomes destructive.

From the cases considered so far, it results without any doubt that the stripe phase is actually replaced by a spot phase at high enough noise levels. In the search of a general conclusion concerning the entire parameters space, we have determined the phase diagram in the spirit of Fig. 1*a*, but for nonzero noise levels (Fig. 4). One can notice that a low noise level (Fig. 4*a*) produces little impact on the structure of the spatial phases. Comparing Fig. 1*a* with Fig. 4*a*, one can notice that a low noise level produces little impact on the structure of the spatial phases. In other words, the region of spatial patterns shrinks under the effect of noise. Moreover, for larger

noise values (Fig. 4*b*), a suppression of the stripe-like phase is found, with any pattern dissolving into ephemeral spots of short lifetime.

4. DISCUSSION

The role of noise in shaping self-organizing reaction-diffusion systems has been stressed by a number of authors over the last decade. Of particular relevance in this context are those models dealing with primitive scenarios of life formation. It is well known that spatial degrees of freedom strongly modify the predicted features exhibited by well-mixed systems. In particular, pattern-driven changes occur due to limited diffusion and interaction, thus facilitating the coexistence of molecular species (see Boerlijst 2000 and references therein).

In this paper we have extended a previous numerical analysis of self-replicating spots under the presence of noise performed by Lesmes et al. [2003]. Our systematic study of the parameter space confirms their findings as they appear to be generic. More precisely, the noise-induced replicating spots appear for a range of noise levels (a plateau) instead of a single optimum. The phase diagram calculated for different values of noise suggests that the presence of even moderate levels of noise typically shrinks the pattern-forming regions of parameter space, but does not induce qualitative changes to the diagram. It becomes apparent that the stripes-pattern may turn into self-replicating spots under the effect of noise, as well as spots-pattern may disappear completely under the same effect.
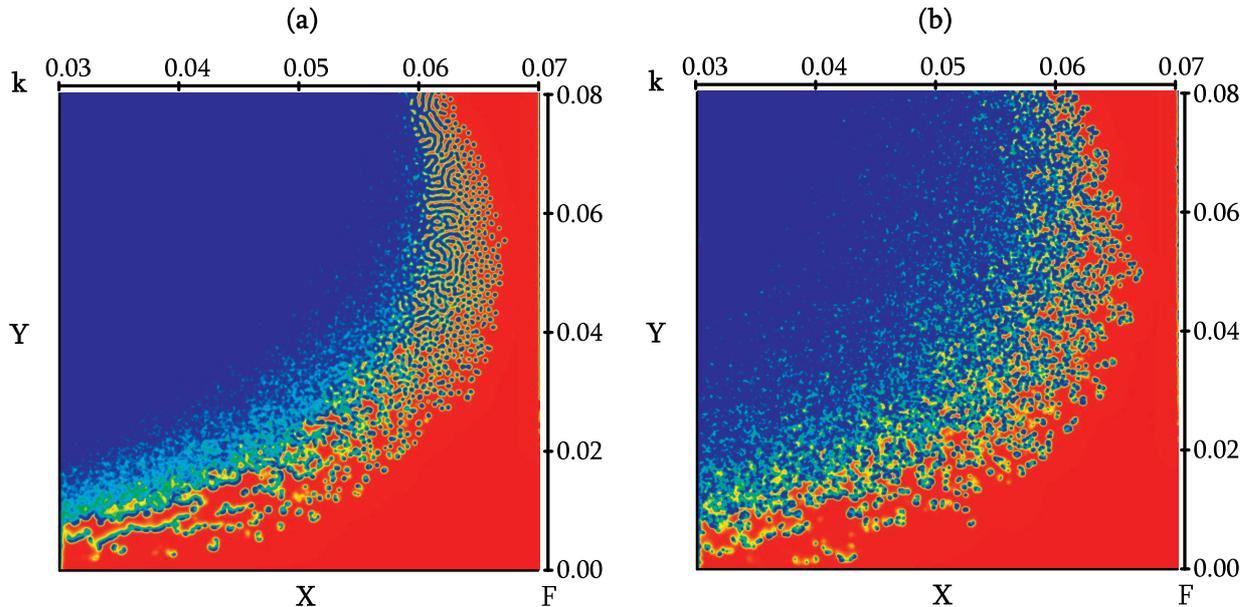
(a)

(b)

FIG. 4 Effects of noise on the parameter space of the Gray-Scott model (compare with figure 1). Here two different noise levels have been used, namely (a) $A = 5 \times 10^{-4}$ and (b) $A = 5 \times 10^{-3}$. For small noise levels (a) we have a phase space closely similar to the deterministic one, whereas larger noise levels (b) lead to a suppression of the stripe phase.

Thus, concerning the boundaries of the distinctive phases in the (F, k) space, we only detect a little expansion of the lower boundary for decreasing F values, indicating that noise can be helpful in maintaining spots that are unlikely to persist under purely deterministic conditions.

The noise is an important ingredient in the spatio-temporal context, an ingredient that was likely to be of relevance in early life. Concerning also future artificial replicators, reliable replication and evolution is likely to be favored by a two-dimensional context, and noise will be an additional factor to consider. As biological systems chemically operate within narrow parameter ranges and not for every point of the parameters space, one can envision that noise might play an important constructive role, as it has been illustrated for the (F, k) cases in this work. From this perspective, interesting results could be expected from exploring the impact of such fluctuations on the pattern dynamics of multicomponent, generalized Gray-Scott models [Takagi and Kaneko 2002].

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