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Gierer-Meinhardt Model: Bifurcation Analysis and Pattern Formation

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Abstract: The roles of diffusion and Turing Instability in the formation of spot and stripe patterns in the Gierer-Meinhardt Activator Inhibitor model are investigated by performing a Nonlinear Bifurcation Analysis. The diffusion ratio is chosen to be the only bifurcation parameter in the analysis. Two dimensional Hexagonal Lattice is used as the geometrical argument in the construction of this analysis and the Fortran Programming Language is used to do the pattern simulations. The bifurcation diagrams are seen to be able to predict the morphology that is observed for the specific patterns.

Key words: Gierer-meinhardt model, nonlinear bifurcation analysis, diffusion ratio, hexagonal lattice, pattern formation

INTRODUCTION

The formation of patterns by Turing instability has been investigated in different models to explain how these can emerge from a merely uniform environment. The interaction of two biochemical substances with different diffusion rates having the capacity to generate biological patterns was introduced by Turing (1952). Some twenty years later, Gierer and Meinhardt found that the two substances, in fact, opposed the action of each other giving rise to the activator-inhibitor model (Gierer and Meinhardt, 1972). Which can be used to explain the formation of polar, symmetric and periodic structures (spots on animals). The study of the system in 2 and 3 dimensions using the topological degree method (Pinto *et al*., 2002) showed that for small diffusion of the activator and large diffusion of the inhibitor a solution to the system exists in the form of boundary spikes. The spike solutions to the Gierer-Meinhardt model has in fact been much explored through different approaches Iron (2002), Kolokolnikov and Ward (2003), Ward *et al*. (2002) and Ward and Wei (2003). The modeling of spots and stripes in biology has shown that stripes versus spots is seen to depend on the nonlinear terms of the reaction diffusion equation (Ermentrout, 1991). In this study we aim at performing a non linear bifurcation analysis as applied to the Brusselator model by Callahan and Knobloch (1999) that revealed that stripes and spots can be simulated for specific values of the model parameters, in the Gierer-Meinhardt model. We concentrate upon identifying the main parameters in the Gierer- Meinhardt model which will differentiate between a stripe and a spot pattern in two dimensions and show their effects through a simulation process. This analysis is analogous to the work done by Ermentrout (1991) however with the specificity to the Gierer-Meinhardt model, a unique bifurcation parameter (the diffusion ratio), which reduces the number of parameters required for differentiating between the two patterns.

GIERER-MEINHARDT ACTIVATOR-INHIBITOR MODEL

Consider the simple Gierer-Meinhardt model given by:

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$$\frac{\partial u}{\partial t} = \frac{k_3 u^2}{v} - k_2 u + k_1 + D_u \nabla^2 u$$
$$\frac{\partial v}{\partial t} = k_3 u^2 - k_4 v + +D_v \nabla^2 v \quad (1)$$

where, D_u and D_v are the diffusion constants for the activator u and the inhibitor v, respectively. Equation 1 can be nondimensionalised into

$$\frac{\partial u}{\partial \tau} = \eta \frac{u^2}{v} - \varsigma u + \rho + \nabla^2 u, \quad (2)$$

$$\frac{\partial v}{\partial \tau} = \eta u^2 - \xi v + d \nabla^2 v, \quad (3)$$

where, $\rho = \frac{L^2 k_1}{D_u}$, $\eta = \frac{L^2 k_3}{D_u}$, $\zeta = \frac{L^2 k_2}{D_u}$, $\xi = \frac{L^2 K_4}{D_u}$, $\tau = \frac{D_u}{L^2} t$ and $d = \frac{D_v}{D_u}$.

For the self-organisation of spatial patterns the zero flux boundary condition is considered. We further consider the initial conditions as small deviations (δu and δv) from the steady state concentration (u_0, v_0). The mathematical problem is thus obtained as:

$$\frac{\partial u}{\partial t} = f(u, v) + \nabla^2 u,$$

$$\frac{\partial v}{\partial t} = g(u, v) + d \nabla^2 v \quad (4)$$

with zero flux and initial conditions given by $(\hat{n} \cdot \nabla)\begin{pmatrix} u \\ v \end{pmatrix} = 0$, $u(x, 0) = u_0 + \delta u$ and $v(x, 0) = v_0 + \delta v$, respectively. Our aim is to find the conditions that guarantee the steady state solution (u_0, v_0) to give rise to Turing Instability.

In Fig. 1, the positive intersection of the null clines f(u, v) = 0 and g(u, v) = 0 give rise to the steady state solution (u_0, v_0), which is evaluated to:

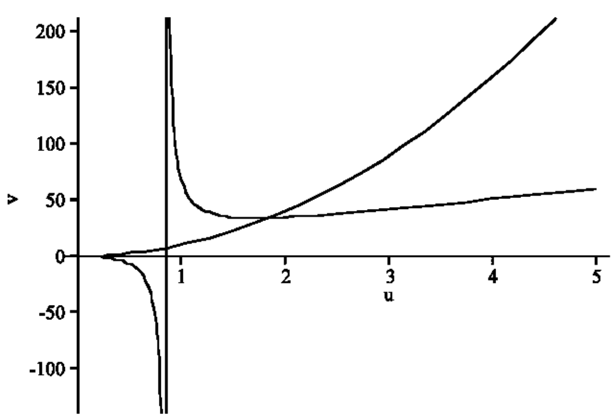

Fig. 1: The positive intersection of the null clines for the steady state solution (u_0, v_0). $\eta = 1$, $\xi = 0.1$, $\rho = 0.085$ and $\zeta = 0.65$

$$u_0 = \frac{\xi+\rho}{\zeta}, \quad v_0 = \frac{\eta(\xi+\rho)^2}{\xi\zeta^2}$$

where, $\eta = 1$, $\xi = 0.1$, $\rho = 0.085$, $\zeta = 0.65$. We now look for a system which is very close to Eq. 4 when (u, v) is near (u_0, v_0). This is done by approximating the real valued functions f(u, v) and g(u, v) by their tangents around the equilibrium point (u_0, v_0). Using Taylor's expansion and knowing that $f(u_0, v_0) = 0$ and $g(u_0, v_0) = 0$ yields the two linear functions:

$$f(u,v) = \frac{\partial f}{\partial u}(u_0, v_0)(u-u_0) + \frac{\partial f}{\partial v}(u_0, v_0)(v-v_0) \tag{5}$$

$$g(u,v) = \frac{\partial g}{\partial u}(u_0, v_0)(u-u_0) + \frac{\partial g}{\partial v}(u_0, v_0)(v-v_0) \tag{6}$$

TURING INSTABILITY

Turing instability is known to be of primeval importance in the generation of biological patterns (Murray, 1994) and in this context we investigate the restriction on the parameters of the Gierer-Meinhardt model for the generation of 2-Dimensional spot and stripe patterns.

Absence of Diffusion

In the absence of diffusion, Eq. 4 can be linearised into

$$\frac{\partial R}{\partial t} = AR \qquad R = \begin{bmatrix} u - u_0 \\ v - v_0 \end{bmatrix}, \tag{8}$$

where, A is the 2×2 stability matrix of the reaction terms f(u, v) and g(u, v) at (u_0, v_0). Upon differentiation and substitution, the stability matrix is found to be

$$A = \begin{pmatrix} \frac{\zeta(\xi-\rho)}{(\xi+\rho)} & -\frac{\xi^2\zeta^2}{(\xi+\rho)^2} \\ \frac{2\eta(\xi+\rho)}{\zeta} & -\xi \end{pmatrix}.$$

The linearised system (8) is known to have solutions of the form:

$$R \propto \exp(\lambda t), \tag{9}$$

where, $\lambda = -\mu^2$ is an eigenvalue of A.

Conditions for Linear Stability

The conditions for linear stability in the absence of diffusion as given by Perko (2000) are given by:

$$\text{tr } A < 0, \tag{10}$$

$$|A| > 0 \tag{11}$$

which for the Gierer-Meinhardt model yields:

$$\xi\left(\frac{\xi+\rho}{\xi-\rho}\right) > \zeta, \qquad \zeta > 0.$$

Presence of Diffusion

In the presence of diffusion consider the linear system,

$$\frac{\partial R}{\partial t} = AR + D\nabla^2 R, \qquad D = \begin{pmatrix} 1 & 0 \\ 0 & d \end{pmatrix}, \tag{12}$$

with the trial solution of the form:

$$R(x,t) = \sum_{\mu} E_{\mu} e^{\lambda t} R_{\mu}. \tag{13}$$

Applying the specified zero flux boundary conditions on Eq. 13, the 2-D solution becomes:

$$R(x,t) = \sum_{M,N} E_{M,N} e^{\lambda_{M,N} T} \cos\left(\frac{mpx}{p}\right)\cos\left(\frac{npy}{q}\right) \tag{14}$$

where, $0<x<p$, $0<y<q$ and the coefficients $E_{m,n}$ are determined from the Fourier expansion of the initial conditions. In biological formulation, it is important to ensure that all the $E_{m,n}$ are non-zero, therefore, the values of m and n are chosen such that all the terms in Eq. 14 contains all possible unstable Fourier modes (Murray, 1994) since they are responsible for the emergence of spatial patterns.

Condition for Instability

Using Eq. 14, 12 and proper substitutions, the eigenvalues corresponding to the instability conditions are obtained by solving the characteristic equation:

$$\left|\lambda I - A + D\mu^2\right| = 0.$$

The values of λ are found by solving:

$$\begin{aligned} &\lambda^2 + \lambda\left[\mu^2(1+d) - \operatorname{tr} A\right] + F(\mu^2) = 0, \\ &F(\mu^2) = d\mu^4 - (da_{11} + a_{22})\mu^2 + |A|. \end{aligned} \tag{15}$$

According to Murray (1994), the conditions for instability (real part of the eigenvalues should be positive) are given by:

$$da_{11} + a_{22} > 0$$

and

$$\frac{(da_{11} + a_{22})^2}{4d} > |A|.$$

At bifurcation, there is a transition between stability and instability and this occurs when $F(\mu^2) = 0$, that is, when $\operatorname{Re}(\lambda) = 0$. This further gives,

$$|A| = \frac{(d_c a_{11} + a_{22})^2}{4d_c} \tag{16}$$

where d_c is the critical value of the diffusion ratio calculated from Eq. 16. Furthermore, the critical wavenumber as stated by Murray (1994) is obtained as:

$$w = \mu_c^2 = \frac{(d_c a_{11} + a_{22})}{2d_c} \tag{17}$$

The conditions for instability in the presence of diffusion can thus be summarized to:

$$\xi\left(\frac{\xi+\rho}{\xi-\rho}\right) < d\zeta,$$

$$d > d_c = \frac{\xi(\xi+\rho)(3\xi+\rho) + 2\sqrt{2}\xi^{\frac{3}{2}}(\xi+\rho)^{\frac{3}{2}}}{\zeta(\xi-\rho)^2}.$$

For the initiation of spatial patterns from Turing Instability, the value of the diffusion ratio d should be much larger than the critical value d_c.

BIFURCATION ANALYSIS

Generally, the concept of bifurcation analysis is to approximate the changes that may subsequently occur in the dynamics of a system of differential equations when one or more parameters are varied. In the present context, the nonlinear analysis will determine the stability of the two pattern morphologies - spots and stripes. The bifurcation parameter under consideration is the diffusion ratio d and ζ is chosen to be the parameter that accounts for the shape of the patterns. We begin the analysis as proposed by Callahan and Knobloch (1999), by first writing the activator-inhibitor concentration field $\vec{\omega} = (r_1, r_2)^T$ in terms of the active Fourier modes as described by Leppanen (2004), that is:

$$\vec{\omega} = \vec{\omega}_0 \sum \left[W_j \exp(i\vec{\mu}_j \times r) + W_j^* \exp(-i\vec{\mu}_j \times r) \right]$$

where, $\vec{\omega}_0$ gives the direction of the modes μ_j and $-\mu_j$ with amplitudes W_j and W_j*, respectively.

The complete nonlinear bifurcation analysis is performed in the following three steps:

- Derivation of the general form of the amplitude equation.
- Determination of the parameters of the amplitude equations using the technique of Center Manifold Reduction.
- Stability analysis of stripe and spot patterns.

The Amplitude Equation

The two dimensional hexagonal lattice is adopted for which the amplitude equation is given by:

$$\frac{dW_j}{dt} = \lambda_d W_j + XW_{j+1}^* W_{j+2}^* - YW_j\left[|W_j|^2 + Z\left(|W_{j+1}|^2 + |W_{j+2}|^2\right)\right], \quad j = 1, 2, 3. \tag{18}$$

where it is assumed that saturation occurs at the third order (Leppanen, 2004). The coefficients in the amplitude equation can be calculated using Center Manifold Reduction.

Center Manifold Reduction

Performing a CMR consists of projecting the dynamics of a system of differential equations onto the center manifold such that the properties of the dynamics remain nearly unchanged. The CMR limits the nonlinear effects in the Reaction Diffusion system to the center manifold which helps in approximating the stability of the different morphologies (stripes and spots). We have used the approach proposed by Callahan and Knobloch (1999) to obtain the coefficients in the amplitude equation. Due to the complexity of the CMR, the Mathematical software *Mathematica*© was used to find the parameters X, Y and Z. The coefficient λ_d evaluated from the eigenvalue λ gives:

$$\lambda_d = \left(\frac{\zeta w + w^2 - \dfrac{2\zeta w \xi}{(\rho+\xi)}}{\dfrac{2\zeta\xi}{(\rho+\xi)} - \zeta - \xi - w - d_c w} \right)(d - d_c)$$

where, d is the value of the diffusion ratio under consideration, d_c is its critical value and

$$w = \mu_c^2 = \frac{\zeta(\xi-\rho)}{2(\xi+\rho)} - \frac{\zeta(\xi-\rho)^2}{2\left((\xi+\rho)(3\xi+\rho) + 2\sqrt{2\xi}(\xi+\rho)^{\frac{3}{2}}\right)}.$$

Stability Analysis of the Two Dimensional Patterns

We perform a linear analysis to study the stability of the amplitudes. The stationary states of the amplitude system which are denoted by $W_c = (W_1^c, W_2^c, W_3^c)$ are found and the system is linearised to obtain the linearised matrix as:

$$B_{ij} = \left| \frac{dF_i}{d|W_j|} \right|_{(W_1^c, W_2^c, W_3^c)}, \tag{19}$$

where, F_i represents the right-hand side of the corresponding amplitude equation *I* given by Eq. 18. The eigenvalues of the Jacobian matrix B is worked out to determine the stability of the different structures when the parameter d, the diffusion ratio is varied. The parameter ζ is chosen to be the one responsible for the shape that the forming patterns will admit. For computer simulations of reaction diffusion equations, two dimensional hexagonal lattice was chosen to be the appropriate geometrical argument to be used for the analysis.

For stripes, the eigenvalues of the stability matrix B are given by $\mu_1 < \lambda_d$, $\mu_2 = -X\sqrt{\frac{\lambda_d}{Y}} + \lambda_d(1-Z)$ and $\mu_3 = X\sqrt{\frac{\lambda_d}{Y}} + \lambda_d(1-Z)$. Since $\lambda_d > 0$, we have $\mu_1 < 0$ and also $\mu_3 > \mu_2$. Therefore, it follows that the stability of 2D stripes can be determined by the sign of μ_3.

In the case of hexagonally arranged spots, the eigenvalues of the Jacobian matrix are given as $\mu_2^* = \lambda_d - W_c^\pm(X + 3YW_c^\pm)$ and $\mu_3^* = \lambda_d + W_c^\pm(2X - 3Y(1+2Z)\,W_c^\pm)$ where $W_c^\pm$ is given by:

$$W_c^\pm = \frac{X \pm \sqrt{X^2 + 4\lambda_d Y(1+2Z)}}{2Y(1+2Z)} \tag{20}$$

The eigenvalues of the linearised system are plotted against the parameter ζ to obtain the bifurcation diagrams which are in turn used to predict the pattern that we might expect to see for different values of the parameters.

RESULTS AND DISCUSSION

Traditionally, a parameter from the reaction term in the Reaction Diffusion System is chosen as the bifurcation parameter when doing the nonlinear bifurcation analysis. In this study, we are using the diffusion ratio d as the only bifurcation parameter and thus d determines how the amplitudes of activator concentration will grow over a 2D Hexagonal domain. In the bifurcation diagrams that follow from the analysis, the parameters are able to predict the shape of the patterns that might be formed. From numerical simulations of the GM model, we obtain patterns in the form of spots and stripes depending on the value of the parameters being used. All the parameter values have been chosen such that they satisfy Turing Instability, which is the required condition for pattern initiation.

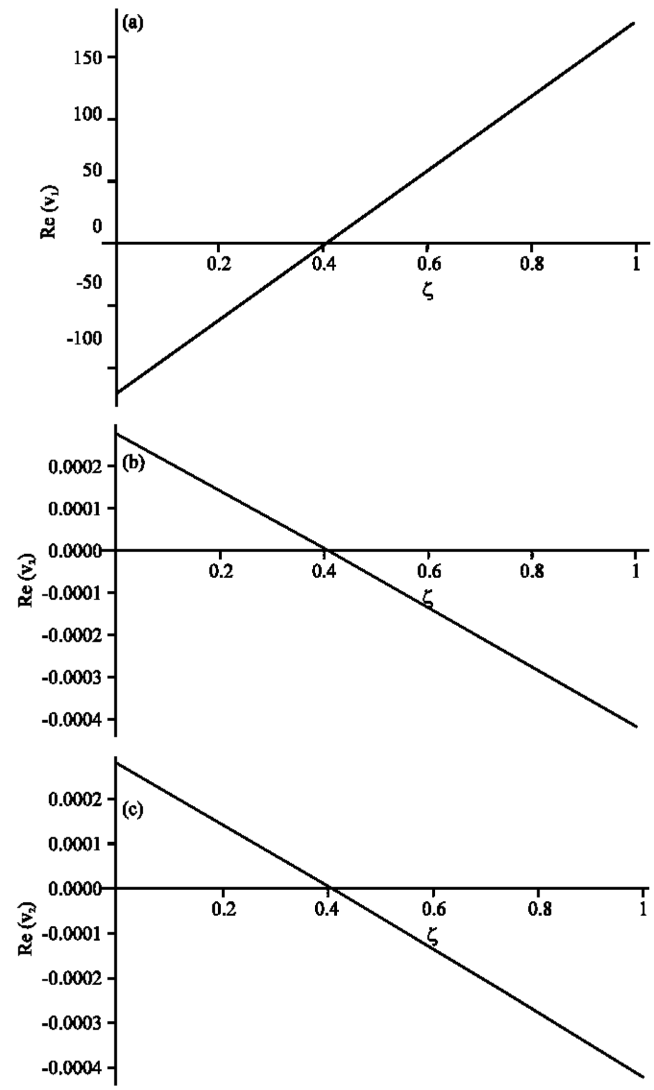

Fig. 2: Bifurcation diagrams for stripes (a) and spots (b), (c). Real part of eigenvalues with respect to the bifurcation parameter ζ. $\eta = 1$, $\xi = 0.08$, $\rho = 0.069$ and $d = 150$

The Nonlinear Bifurcation Analysis identified which range of values of ζ can favour the formation of stable spots or stripes given that the other parameters in the GM model are kept constant whilst satisfying the Diffusion Driven Instability. This results confirms the work of Ermentrout but in addition brings out the specificity of the diffusion rates and confirms the original of Gierer-Meinhardt, but with more precision in the diffusion ratio.

In Fig. 2a and 3a, the real part of the eigenvalue corresponding to the stability of stripes is plotted against the parameter ζ. Fig. 2b,c, 3b,c and 4a,b give the stability range of the two eigenvalues for the formation of spots. Analytically, these two eigenvalues should have a common region of negative real parts for some values of ζ so that stable spots can be simulated.

Three different sets of parameters are chosen so that each corresponding set of figures predicts a different pattern morphology from the other two sets. Thus, Fig. 2 illustrates that either spots or stripes, are expected to be generated, when we do the numerical simulations for some specific values

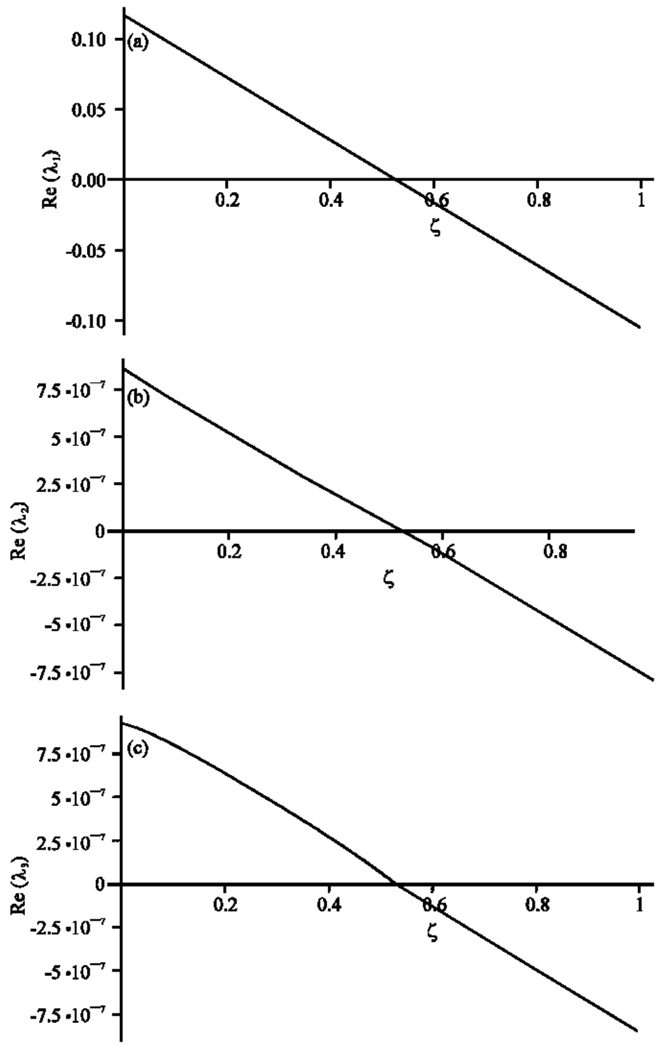

Fig. 3: Bifurcation diagrams for stripes (a) and spots (b), (c). Real part of eigenvalues with respect to the bifurcation parameter ζ. $\eta = 1$, $\xi = 0.1$, $\rho = 0.085$ and $d = 120$

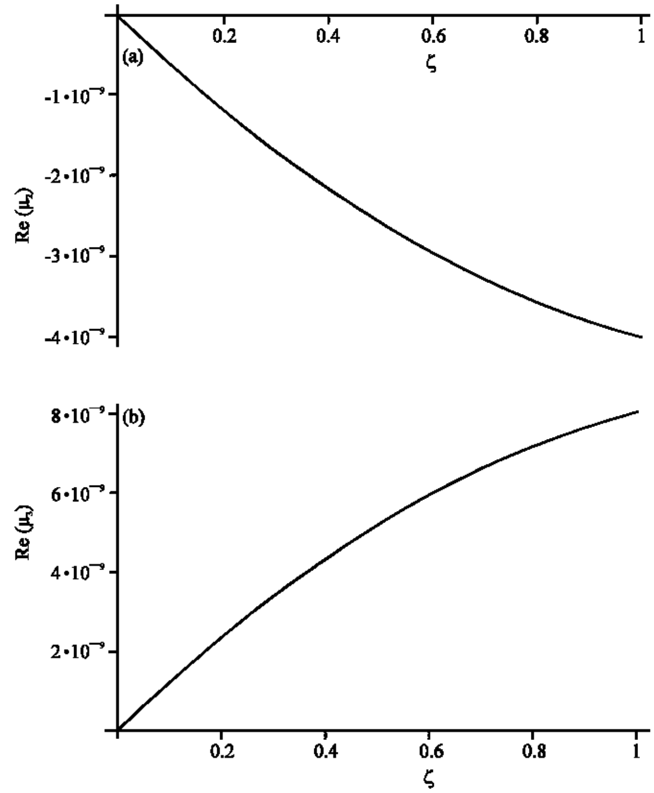

Fig. 4: Bifurcation diagrams for spots (a), (b). Real part of eigenvalues with respect to the bifurcation parameter ζ. $\eta = 1$, $\xi = 0.0065$, $\rho = 0.006$ and $d = 400$

of ζ between 0 and 1. In fact, the graphs show clearly that stripes can be obtained for values of ζ tending to zero and spots for values tending to one. Both spots and stripes could be stable (region of bistability) for $0.52 < \zeta < 1.00$. Therefore, it is difficult to predict what pattern morphology could possibly emerge (Fig. 3).

Figure 4, on the other hand, gives a region in which neither spots nor stripes would be expected though the parameters that are being used satisfy Turing Instability.

Figures 5 and 6 are simulation patterns for stripes and spots. The pattern gives the distribution of activator concentration over the 2D array. The activator concentration is above a threshold level and represented as a positional information in terms of a symbol in the simulation. The changing characteristic of the activator concentration over the simulation domain is displayed after several iterations. The parameter values used in the pattern simulations were chosen from the sets of values corresponding to Fig. 3 and it was found that the parameter ζ does differentiate between the two morphologies. The same values are considered for $\xi = 0.1$, $\eta = 1$, $\rho = 0.085$ and $d = 120$ while the value for ζ is 0.8 for spots and 0.55 for stripes.

The numerical simulations of activator patterns reveal that Turing Instability is a necessary condition for the generation of chemical patterns but it is not sufficient as far as the Gierer-Meinhardt Model is concerned. This can be confirmed by considering the set of values used in Fig. 4, which is Turing unstable but cannot generate patterns as predicted by the bifurcation diagrams.

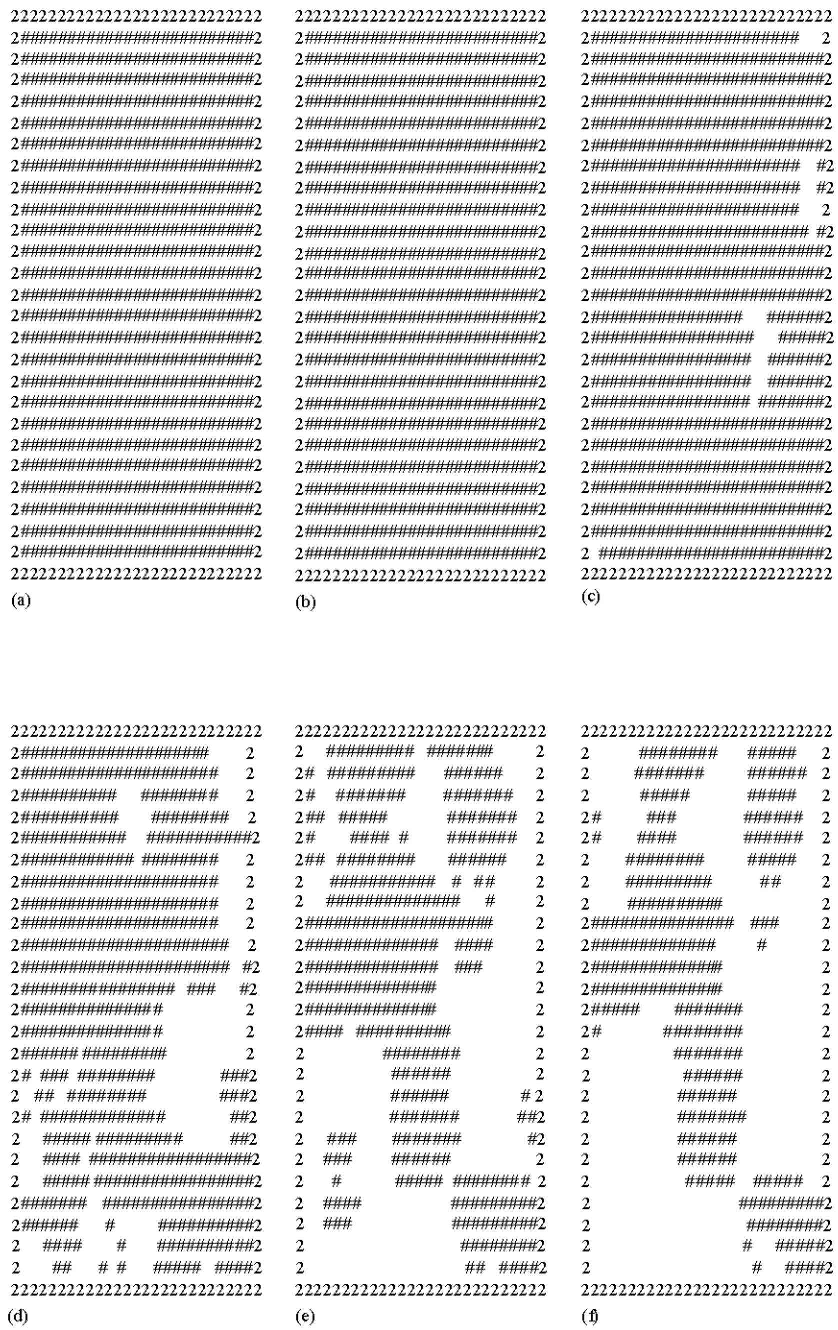

Fig. 5: Continued

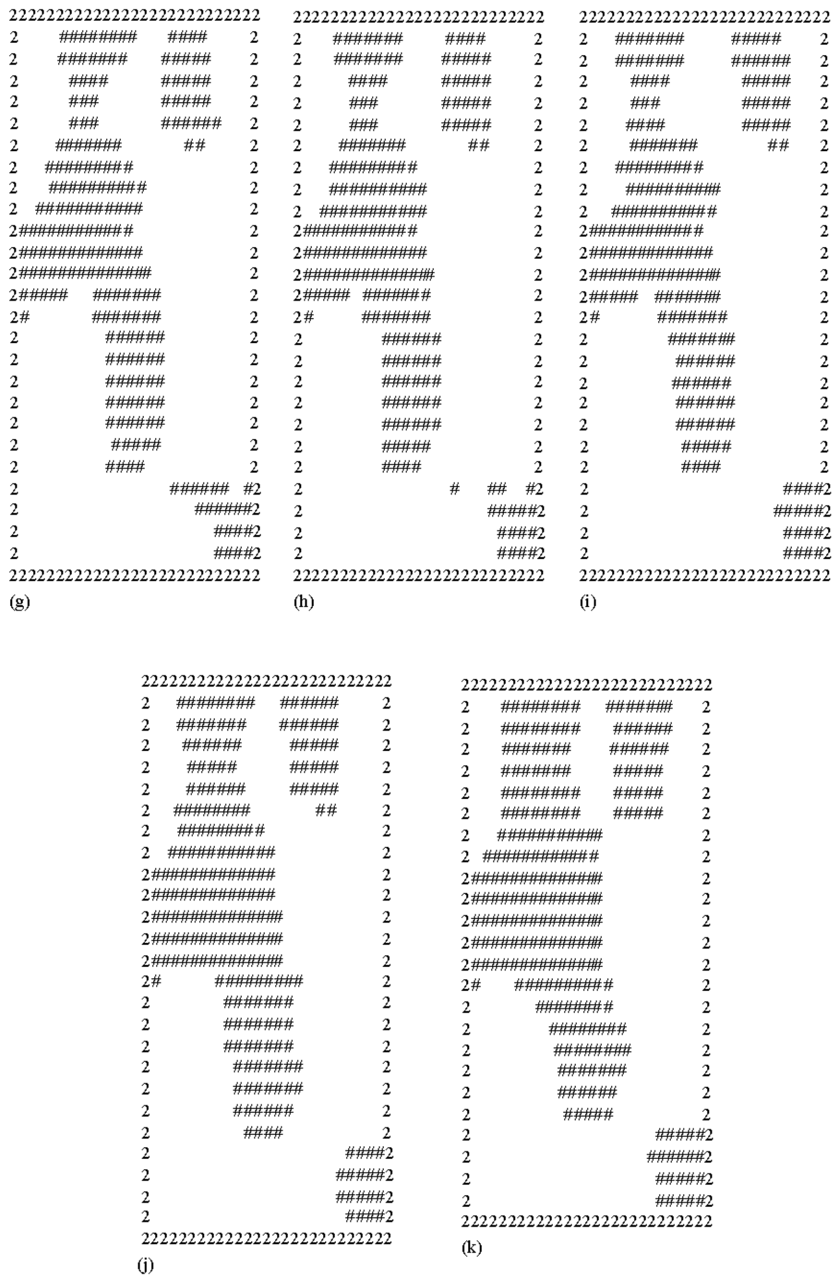

Fig. 5: Simulation patterns for stripes. (a) 1600 iterations (b) 2400 iterations (c) 3200 iterations (d) 4000 iterations (e) 4800 iterations (f) 5600 iterations (g) 6400 iterations (h) 7200 iterations (i) 8000 iterations (j) 8800 iterations (k) 9600 iterations. $\xi = 0.1$; $\eta = 1$, $\rho = 0.085$, $d = 120$, $\zeta = 0.55$

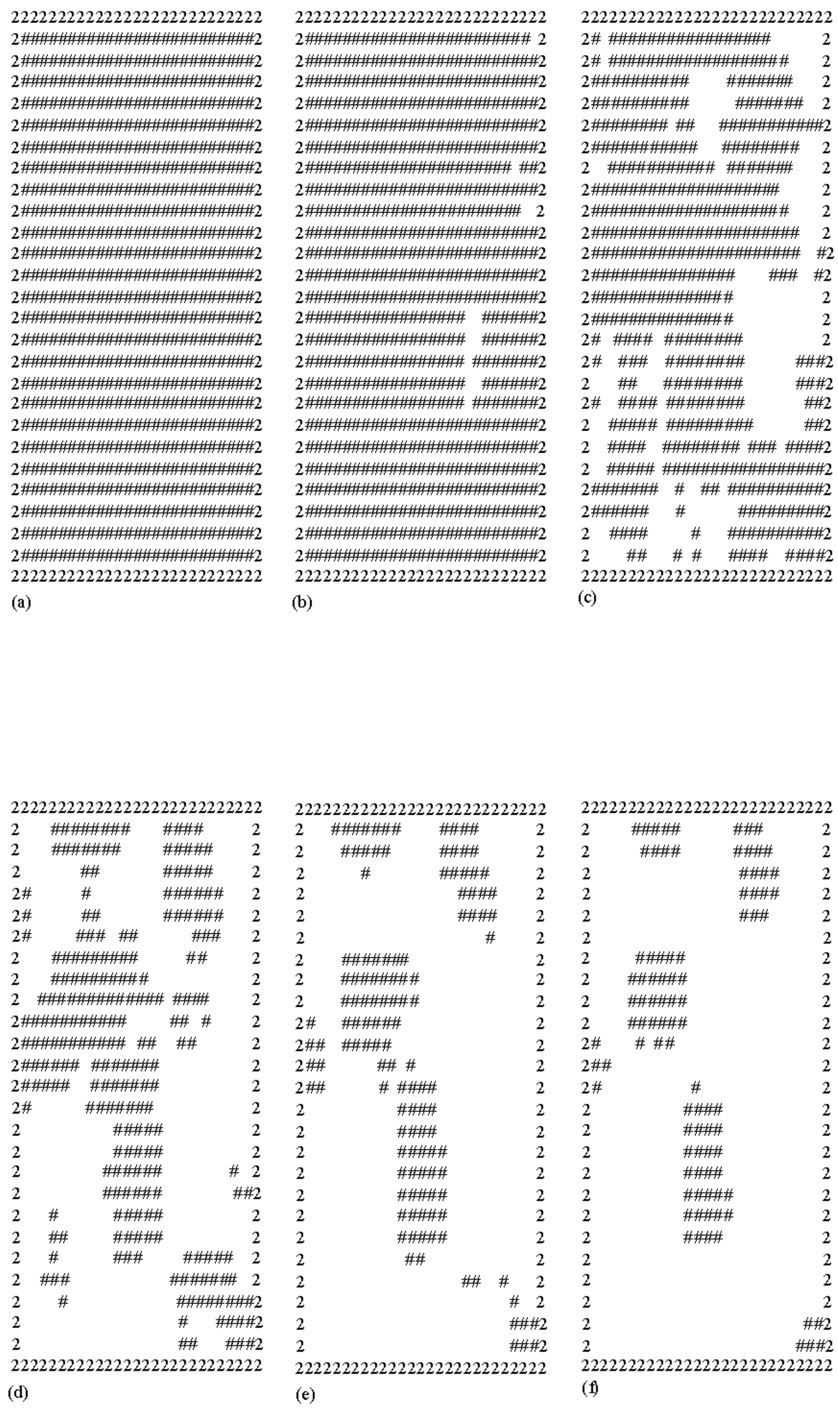

Fig. 6: Continued

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2      ###    ###         2
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2       ###               2
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(j)
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2                 ##      2
2                 ##      2
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222222222222222222222222222
(k)
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Fig. 6: Simulation patterns for spots. (a) 1600 iterations (b) 2400 iterations (c) 3200 iterations (d) 4000 iterations (e) 4800 iterations (f) 5600 iterations (g) 6400 iterations (h) 7200 iterations (I) 8000 iterations (j) 8800 iterations (k) 9600 iterations. $\xi = 0.1$; $\eta = 1$, $\rho = 0.085$; $d = 120$; $\zeta = 0.8$

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