



Directionality of Stripes Formed by Anisotropic Reaction–Diffusion Models

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Turing mechanism explains the formation of striped patterns in a uniform field in which two substances interact locally and diffuse randomly. In a twin paper, to explain the directionality of stripes on fish skin in closely related species, we studied the effect of anisotropic diffusion of the two substances on the direction of stripes, in the cases in which both substances have high diffusivity in the same direction. In this paper, we study the direction of stripes in more general situations in which the diffusive direction may differ between the two substances. We derive a formula for the direction of stripes, based on a heuristic argument of unstable modes of deviation from the uniform steady state. We confirm the accuracy of the formula by computer simulations. When the diffusive direction is different between two substances, the directions of stripes in the spatial pattern change smoothly with the magnitude of anisotropy of two substances. When the diffusive direction of the two substances is the same, the stripes are formed either parallel or perpendicular to the common diffusive direction, depending on the relative magnitude of the anisotropy. The transition between these two phases occurs sharply.

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Introduction

The developmental pattern formation of animal coating has been studied mathematically using reaction–diffusion models (e.g. Murray, 1989). Turing (1952) and Gierer & Meinhardt (1972) studied a pair of partial differential equations for the dynamics of two substances, called an activator and an inhibitor. They interact with each other locally—the activator enhances the production of itself and the inhibitor, whilst the inhibitor suppresses both the activator and the inhibitor. They both engage in diffusion, but the diffusion rate of the inhibitor is much larger than that for the activator. The local dynamics given by the reaction terms are stable, but the

uniform stationary state is unstable in a spatially structured model with diffusion if the diffusivity is different in an appropriate manner. Starting from an initial distribution close to uniformity, spatial heterogeneity emerges spontaneously and a non-uniform stationary pattern is formed. Schnackenberg (1979) and Prigogine & Lefever (1968) also studied reaction–diffusion models for two diffusive substances, but their models have reaction terms in which two substances cannot be regarded as an activator and an inhibitor. In all of these models for Turing mechanism, the less diffusive substance tends to form clearer spatial pattern, and the more diffusive substance mediates the spatial interaction between neighboring areas, maintaining the inhomogeneity.

When these models are analysed on a two-dimensional plane, instead of a one-dimensional line, striped patterns in addition to spotted

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patterns often emerge (Maini *et al.*, 1997), which is considered as the basic mechanism explaining many examples of stripes observed in animal coating (Murray, 1989). Meinhardt (1982) also developed many examples of pattern formation in biology based on the Gierer–Meinhardt model. In these examples, however, the spatial patterns are formed in the early stage of development, and once the pattern is created, they remain unchanged while the body size increases.

In contrast, the skin of tropical fishes shows continuous rearrangement of spatial patterns as the body size increases. Kondo & Asai (1995) demonstrated that the pattern formation and change can be predicted very well by a simple reaction–diffusion model of Turing type. After their work, many theoreticians began to study this phenomenon (e.g. Painter *et al.*, 1999). In most species of tropical fishes, the stripes run in parallel either to the anterior–posterior axis or to the dorso-ventral axis, the direction of which is characteristic to each species. The direction of stripes is considered to be of behavioral ecological importance—in the case of African cichlid fishes, the vertical stripes tend to be associated with living in rocky substrate or structured vegetation, whilst the horizontal stripes are associated with schooling behavior (Seehausen *et al.*, 1999). However, the spatial pattern of many stripes generated by the standard reaction–diffusion model of Turing type on a two-dimensional plane does not have a fixed direction.

In a twin paper (Shoji *et al.*, 2001), we studied the directionality of stripes of tropical fishes. After examining two hypotheses previously proposed for the directionality of the pattern (Dillon *et al.*, 1994; Lacalli *et al.*, 1988; Maini & Myerscough, 1997), we proposed that anisotropic diffusion (directional difference in diffusion rate) might be responsible for the contrasting difference in the directionality of stripes. Fish skin has clear directional structures because most scales are arranged parallel to the anterior–posterior axis. This suggests that the substances controlling the pattern formation may diffuse along the anterior–posterior axis at a speed different from that along the dorso-ventral axis. In Shoji *et al.* (2001), we studied the effect of anisotropy on the direction of the stripes generated by reaction–diffusion models. We found that stripes

have a fixed direction when the diffusion of the two substances is anisotropic in the same direction but with different magnitudes. The directions of stripes depend on the difference in the strength of anisotropy between the two substances. Only when the values of anisotropy are almost the same between the two substances, the specificity of stripe direction disappears. Interestingly, a small difference in the relative magnitude of anisotropy of the two substances can create vastly different final patterns (vertical stripes vs. horizontal stripes).

In the present paper as a sequel, we study the effect of anisotropic diffusion on the direction of stripes in more detail. In Shoji *et al.* (2001), both substances are assumed to have the highest diffusivity in the same direction. In contrast, we study here the general case in which the direction of maximum diffusivity can be different between the two substances. We derived a formula predicting the direction of stripes in the final patterns based on a heuristic mathematical argument of unstable modes of stripe patterns. We then confirm the accuracy of the formula by computer simulations.

Model

Turing (1952) showed that two diffusive chemicals reacting with each other locally can generate a spatially heterogeneous pattern in a uniform field. The system is written as

$$\frac{\partial u}{\partial t} = \nabla^2 u + \gamma f(u, v), \quad (1a)$$

$$\frac{\partial v}{\partial t} = d \nabla^2 v + \gamma g(u, v), \quad (1b)$$

where u and v are the concentrations of two substances which differ in diffusivity. By rescaling the space variable, we made the diffusion coefficient of u equal to 1. On the other hand, the reaction terms are multiplied by a common factor γ , and the diffusion coefficient for v is replaced by the ratio of diffusion coefficient of the two substances, denoted by d . Here we assume that v diffuses faster than u , and hence d is larger than 1.

First, we consider the equilibrium (u_0, v_0) of ordinary differential equations corresponding to

the reaction terms in eqn (1). It satisfies $f(u_0, v_0) = 0$, and $g(u_0, v_0) = 0$. Since the steady state is stable in the ordinary differential equations given by the reaction terms, we have

$$\frac{\partial f}{\partial u} + \frac{\partial g}{\partial v} < 0, \quad (2a)$$

$$\frac{\partial f}{\partial u} \frac{\partial g}{\partial v} - \frac{\partial f}{\partial v} \frac{\partial g}{\partial u} > 0, \quad (2b)$$

where the partial derivatives are evaluated at equilibrium (u_0, v_0) . Since the steady-state solution $u = u_0$, and $v = v_0$ becomes unstable in the partial differential equations given by eqn (1),

$$d \frac{\partial f}{\partial u} + \frac{\partial g}{\partial v} > 0, \quad (2c)$$

$$\left(d \frac{\partial f}{\partial u} + \frac{\partial g}{\partial v} \right)^2 - 4d \left(\frac{\partial f}{\partial u} \frac{\partial g}{\partial v} - \frac{\partial f}{\partial v} \frac{\partial g}{\partial u} \right) > 0. \quad (2d)$$

The model equation (1) satisfying these conditions is called Turing system (Murray, 1989).

Schnackenberg (1979) chose the following reaction terms:

$$f(u, v) = a - u + u^2 v, \quad (3a)$$

$$g(u, v) = b - u^2 v. \quad (3b)$$

There are several other choices of reaction terms, such as the Gierer–Meinhardt model (Meinhardt, 1982), and the linear model with truncation (Kondo & Asai, 1995; Asai *et al.*, 1999), which show behavior similar to the Schnackenberg model (Shoji *et al.*, 2001). In the following we first study the cases with the Schnackenberg model, given by eqn (3), but later we discuss other choices of reaction terms.

ANISOTROPIC DIFFUSION

Since fish epidermis has morphological directionality due to the presence of scales, it is plausible to assume directionality in diffusion speed. Shoji *et al.* (2001) focused on the case in which the most diffusive direction is the same between the two substances, though the magnitude of anisotropy may differ. Here we examine the general case in which the diffusive direction can be different between the two substances.

We consider the following dynamics:

$$\frac{\partial u}{\partial t} = \nabla \cdot (D_u(\theta_u) \nabla u) + \gamma f(u, v), \quad (4a)$$

$$\frac{\partial v}{\partial t} = d \nabla \cdot (D_v(\theta_v) \nabla v) + \gamma g(u, v). \quad (4b)$$

The diffusion coefficients of the two substances are

$$D_u(\theta_u) = \frac{1}{\sqrt{1 - \delta_u \cos(2(\theta_u - \psi_u))}}, \quad (5a)$$

$$D_v(\theta_v) = \frac{1}{\sqrt{1 - \delta_v \cos(2(\theta_v - \psi_v))}}, \quad (5b)$$

where θ_u and θ_v indicate the angle of the gradient vectors of u and v , respectively. These are written as

$$\theta_u = \arctan\left(\frac{\partial u}{\partial y} / \frac{\partial u}{\partial x}\right) \quad \text{and} \quad \theta_v = \arctan\left(\frac{\partial v}{\partial y} / \frac{\partial v}{\partial x}\right). \quad (5c)$$

The flux of each substance is proportional to the gradient vector, but the multiplication coefficient depends on the angle of the vector. Equation (5a) implies that the diffusivity of u is the largest for $\theta = \psi_u$ and its opposite direction $\theta = \psi_u + \pi$, and that it is the smallest for directions perpendicular to these ($\theta = \psi_u + \pi/2$ and $\theta = \psi_u + 3\pi/2$). Similarly, ψ_v is the direction of the highest diffusivity for v . In the following we call ψ_u and ψ_v as the “diffusive direction” of u and v , respectively. δ_u and δ_v are the magnitude of anisotropy for u and v , respectively. These satisfy $0 \leq \delta_u < 1$ and $0 \leq \delta_v < 1$. A special case of $\delta_u = 0$ and $\delta_v = 0$ implies the isotropy in diffusion. This form of anisotropic diffusion was adopted by Kobayashi (1993) in his study of dendritic crystal formation, but the functional

forms of $D_u(\theta)$ and $D_v(\theta)$ he adopted were different from ours. In modelling the image processing in the visual cortex, Bressloff *et al.* (2001) introduced anisotropic neural connection in an integro-differential equation model.

Spatial Patterns Generated

We calculated the model given by eqns (4) and (5) numerically. In most of the analysis, we adopted the reaction terms by Schnackenberg (1979), given in eqns (3), because it was more robust in forming striped spatial patterns than other choices of reaction terms (Ermentrout, 1991). We also have done some analyses with different reaction terms, as explained later.

In most simulations we chose parameters as: $a = 0.025$, $b = 1.550$, $\gamma = 10\,000$, and $d = 20.0$, which are the ones studied in Shoji *et al.* (2001). We also examined different parameter values, but the result remained qualitatively the same as far as stripes formed in the final pattern. All the simulations were performed with the periodic boundary condition in a square domain of size: 2.0×2.0 (grid size: 200×200). A simple explicit scheme was adopted. When both δ_u and δ_v were less than 0.4, the mesh size was 10^{-6} . Otherwise, the mesh size was 5×10^{-7} . These were chosen to satisfy the stability condition for numerical analysis. We tested three initial conditions in which u and v were the equilibrium values perturbed by small random deviations. The results concerning the directionality of obtained stripe patterns were the same in the three trials. To obtain the final spatial distribution, we ran the model for a sufficiently long time. From a given spatial distribution of u , we calculated the direction of stripes using an algorithm explained in Appendix A.

THE DIFFUSIVE DIRECTION IS THE SAME FOR THE TWO SUBSTANCES: $\psi_u = \psi_v$

Figure 1 shows stripe patterns generated by eqns (3)–(5) when $\psi_u = \psi_v = \pi/3$. The anisotropic diffusion of u and isotropic diffusion of v produced stripes parallel to the common diffusive direction [Fig. 1(a)]. In contrast, the anisotropic diffusion of v and isotropic diffusion of u make stripes perpendicular to the diffusive direction [Fig. 1(b)]. Shoji *et al.* (2001) studied the case

with $\psi_u = \psi_v$ in which both u and v are anisotropic in their diffusion but can be of different magnitudes. The direction of stripes to be formed depends critically on the relative magnitude of anisotropy: when anisotropy of u is stronger than that of v ($\delta_u > \delta_v$), stripes are formed parallel to the diffusive direction, whilst, if anisotropy of v is larger than that of u ($\delta_u < \delta_v$), the stripes are formed perpendicular to the diffusive direction.

In Fig. 2, the directionality of stripes in the spatial pattern is indicated by a short line passing through an open circle that is located at (δ_u, δ_v) . Two axes are for the magnitude of anisotropy of the two substances. This phase plane is separated into a domain in which stripes were parallel to the diffusive direction and another domain in which stripes were perpendicular to the diffusive direction. In between these two, there is a narrow band in which the direction of stripes was not determined by using the algorithm in Appendix A [e.g. in Fig. 1(c)], indicated by circles without line in Fig. 2.

THE DIFFUSIVE DIRECTION IS DIFFERENT $\psi_u \neq \psi_v$

Now we consider the cases in which the direction of the fastest diffusion is different between the two substances. Figure 3 shows the stripe patterns of simulation results of eqns (3)–(5), when $\psi_u = \pi/3$, $\psi_v = \pi/6$. When only u is anisotropic in diffusion, stripes were formed parallel to the diffusive direction of u [Fig. 3(a)]. When only v is anisotropic in diffusion, the stripes were formed perpendicular to the diffusive direction of v [Fig. 3(b)]. If both u and v are anisotropic, the stripes were formed in the direction intermediate between these two, as shown in Fig. 3(c). Figure 4 illustrates the phase diagram in which the direction of stripes is indicated by a short line passing through an open circle located at (δ_u, δ_v) . The direction of stripes changes smoothly with anisotropy of u and v (δ_u and δ_v).

Search for Unstable Modes—A Heuristic Approach

To know an approximate direction of stripes to be formed by the model, we developed a heuristic argument. We consider a small deviation from the uniform equilibrium of striped spatial

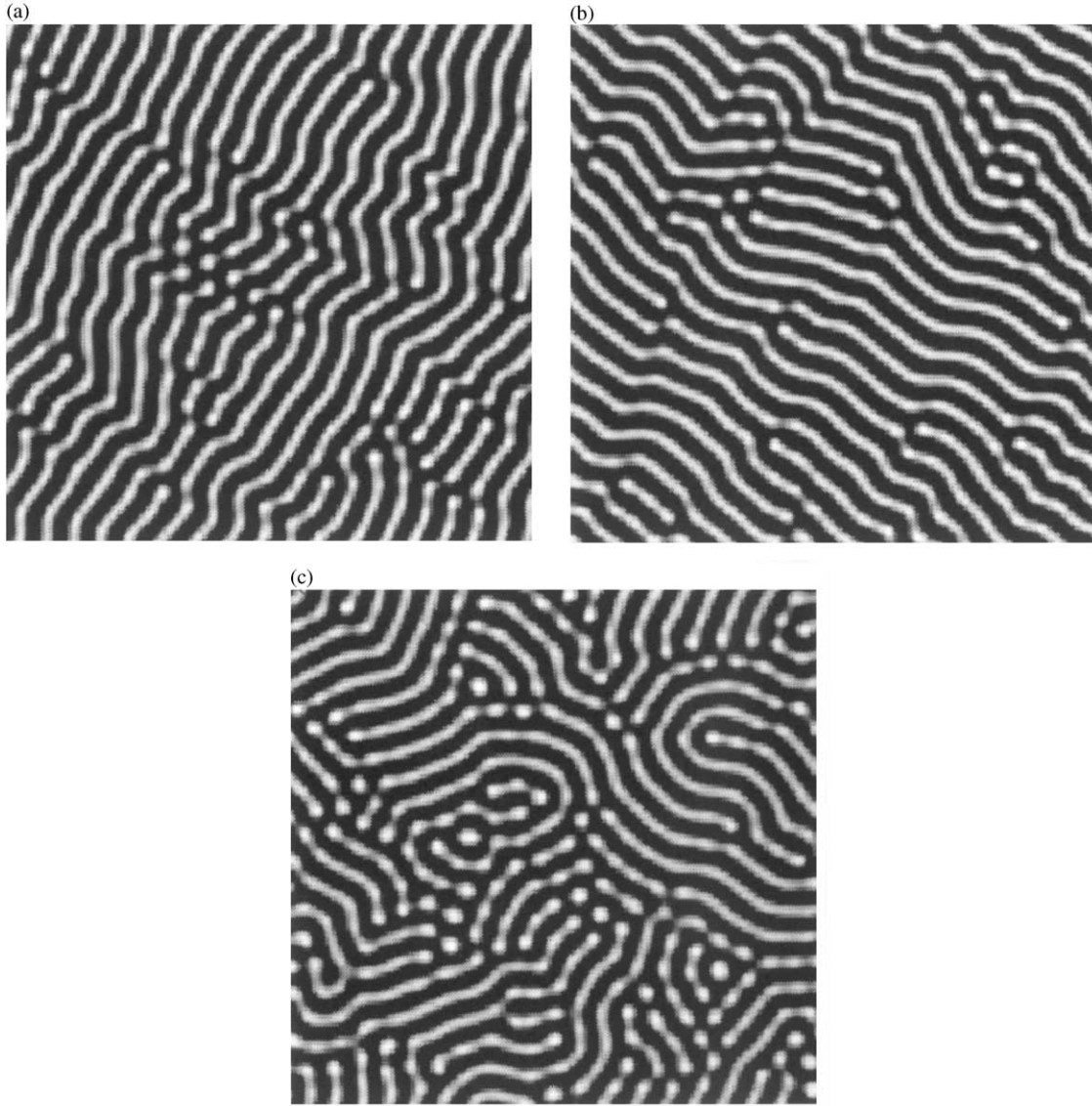


FIG. 1. The stripe patterns generated by eqns (3)–(5). Both substances have the fastest diffusion in the same direction: $\psi_u = \psi_v = \pi/3$. The magnitudes of anisotropy of two substances are: (a) $\delta_u = 0.2$, $\delta_v = 0.0$; (b) $\delta_u = 0.0$, $\delta_v = 0.2$; (c) $\delta_u = \delta_v = 0.1$. Other parameters are: $a = 0.025$, $b = 1.550$, $d = 20.0$, and $\gamma = 10\,000$. The anisotropic diffusion of u makes stripes form parallel to the diffusive direction. In contrast, the anisotropic diffusion of v makes stripes form perpendicular to the diffusive direction. However, when the values of anisotropy are the same between u and v , the specificity of stripe direction disappears.

pattern that grows exponentially with time. Let (u_0, v_0) be the equilibrium of the ordinary differential equations given by reaction terms. We consider a small deviation from the uniform steady state $(u, v) = (u_0, v_0)$, as follows:

$$u = u_0 + A \cos(k_x x + k_y y) e^{\lambda t}, \quad (6a)$$

$$v = v_0 + B \cos(k_x x + k_y y) e^{\lambda t}, \quad (6b)$$

where A and B are small constants. Equation (6) indicates a spatial pattern with stripes having normal vector equal to (k_x, k_y) . If $\lambda < 0$, the mode given by eqn (6) decreases in size. In contrast, if $\lambda > 0$, the mode grows exponentially with time. We replace eqn (6) in the linearized dynamics of eqn (4) calculated around $(u, v) = (u_0, v_0)$. For any given (k_x, k_y) , we can construct a solution of the form (6) by choosing λ at an appropriate

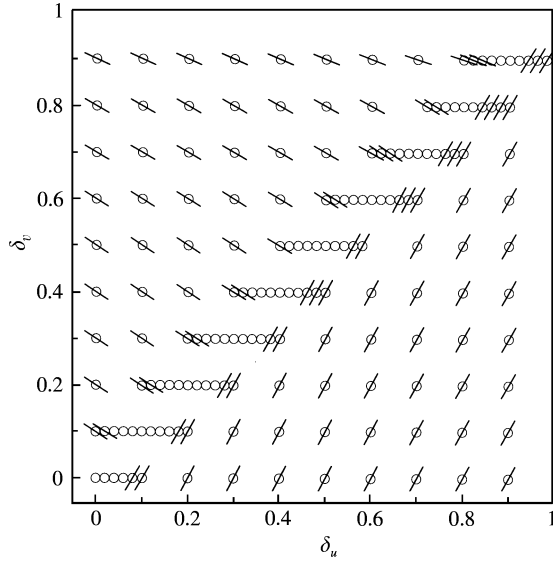


FIG. 2. The diagram illustrating the directionality of stripes. A short line passing through an open circle indicates the direction parallel to the stripes formed in the final spatial pattern when anisotropy of the two substances is given by the location of the circle (δ_u, δ_v) . The direction of stripes is calculated from the algorithm explained in Appendix A. The spatial patterns were generated from eqns (3)–(5). The direction for the fastest diffusivity was the same between two substances: $\psi_u = \psi_v = \pi/3$.

value. If all the solutions of form (6) have a negative λ , the uniform steady state is stable against these modes of deviation with stripes. If instead there are many solutions of the form given by eqn (6) with different (k_x, k_y) and $\lambda > 0$, the mode with the largest positive λ is the one that grows at the fastest rate. We may compare the direction of this most unstable stripe calculated from linear analysis with the stripe in the final spatial pattern formed by the nonlinear dynamics equation (4). Note that the stripes to be formed are perpendicular to vector (k_x, k_y) , because it is a normal vector.

From eqn (6), we can derive $\theta_u = \theta_v = \arctan(k_y/k_x)$, which implies that the gradient vectors of both u and v take a fixed direction that is perpendicular to vector (k_x, k_y) . In Appendix B, we search for the squared length of the vector, $\sqrt{k_x^2 + k_y^2}$, and the angle of the vector, $\theta = \arctan(k_y/k_x)$, which realize an approximately maximum positive λ . Then the length of the vector is related (inversely) to the distance between adjacent stripes and the angle corresponds to the

(perpendicular) direction of stripes in the pattern. We can show that the mode of deviation (k_x, k_y) that achieves an approximately maximum λ has angle $\theta = \arctan(k_y/k_x)$ that maximizes the following quantity:

$$\eta(\theta) = \frac{D_v(\theta)}{D_u(\theta)} = \sqrt{\frac{1 - \delta_u \cos(2(\theta - \psi_u))}{1 - \delta_v \cos(2(\theta - \psi_v))}}. \quad (7)$$

See Appendix B for the argument leading to this result. In the following we examine the angle that maximizes eqn (7), denoted by $\theta_{\text{predicted}}$.

CASE 1. THE DIFFUSIVE DIRECTION IS THE SAME:

$$\psi_u = \psi_v$$

Consider first the case in which the diffusive direction of two substances is the same, which was the situation numerically studied by Shoji *et al.* (2001). In such a case, we should examine the maximum of $\eta^2 = (1 - \delta_u w)/(1 - \delta_v w)$, when $-1 \leq w \leq 1$, by setting $w = \cos(2(\theta - \psi))$. By drawing the graph of this function, we can conclude that

If $\delta_u > \delta_v$, the maximum is attained when $w = -1$,

$$\text{i.e. } \theta_{\text{predicted}} = \psi + \frac{\pi}{2} + n\pi \quad (n = \text{integer}). \quad (8a)$$

If $\delta_u < \delta_v$, the maximum is attained when $w = 1$,

$$\text{i.e. } \theta_{\text{predicted}} = \psi + n\pi \quad (n = \text{integer}). \quad (8b)$$

If $\delta_u = \delta_v$, $\eta(\theta) = D_v(\theta)/D_u(\theta)$ becomes perfectly independently of θ , and there is no special direction in which stripes are more likely to be formed than in other directions. Noting that θ gives the direction of the normal vector \mathbf{k} , which is perpendicular to the direction of stripes, we can conclude as follows.

If $\delta_u > \delta_v$, stripes are formed parallel to the diffusive direction.

If $\delta_u < \delta_v$, stripes are formed perpendicular to the diffusive direction.

If $\delta_u = \delta_v$, there is no specific direction for stripes.

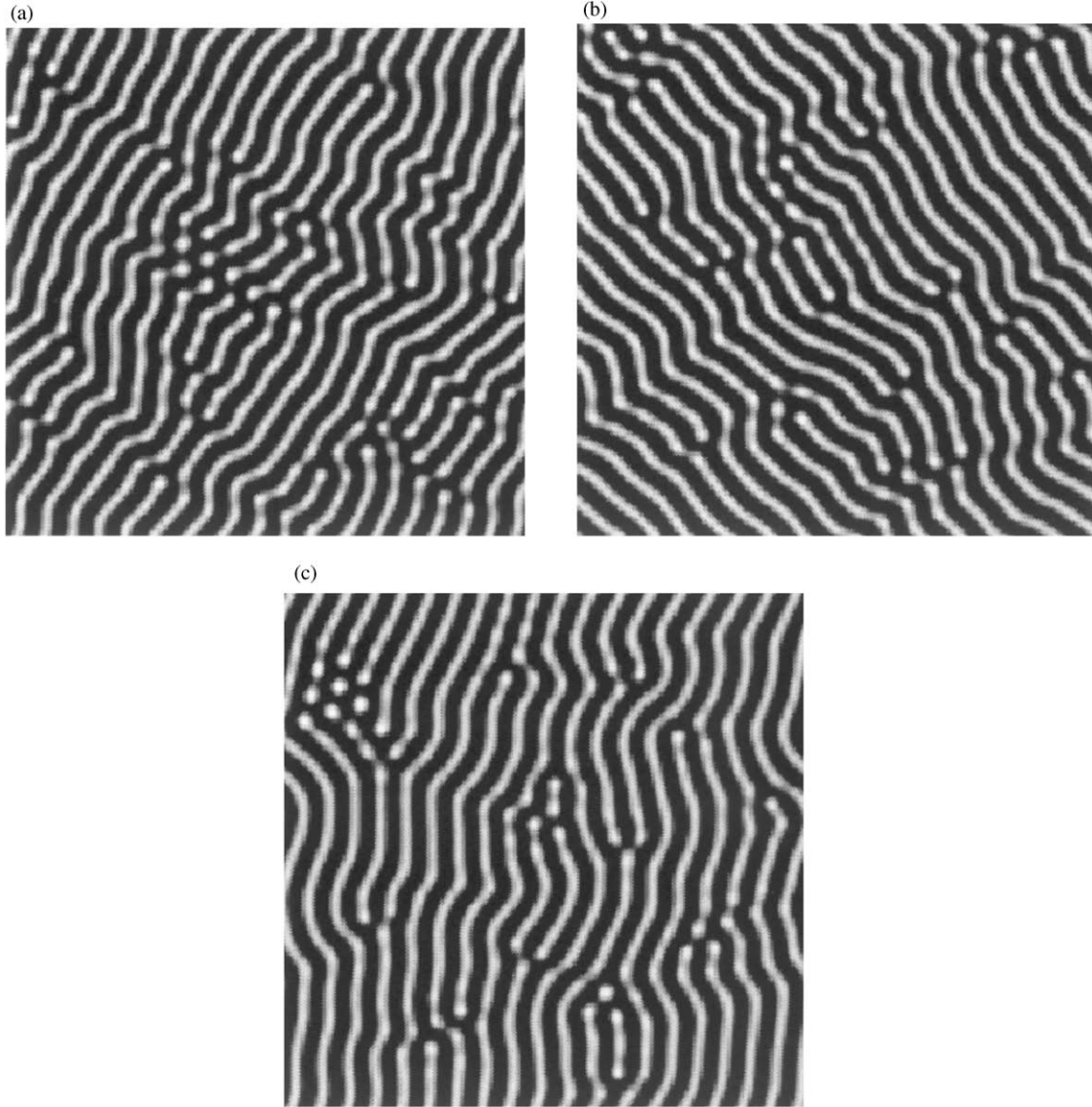


FIG. 3. The stripe patterns generated by eqns (3)–(5). Two substances have the fastest diffusion in different directions: $\psi_u = \pi/3$, $\psi_v = \pi/6$. Magnitudes of anisotropy of two substances are: (a) $\delta_u = 0.2$, $\delta_v = 0.0$; (b) $\delta_u = 0.0$, $\delta_v = 0.2$; (c) $\delta_u = \delta_v = 0.1$. Other parameters are: $a = 0.025$, $b = 1.550$, $d = 20.0$ and $\gamma = 10\,000$. As in Fig. 1, anisotropic diffusion of u and isotropic diffusion of v generate a spatial pattern with stripes parallel to the diffusive direction, and the anisotropic diffusion of v makes stripes form perpendicular to the diffusive direction. However, when the values of anisotropy are the same between u and v , the stripe pattern formed in the middle between the diffusive direction of u and perpendicular to diffusive direction of v .

This is consistent with the conclusion by Shoji *et al.* (2001).

CASE 2. THE DIFFUSIVE DIRECTION IS DIFFERENT:

$$\psi_u \neq \psi_v$$

When anisotropy is small for both substances ($\delta_u \ll 1$, and $\delta_v \ll 1$), we can expand squared $\eta(\theta)$

as follows:

$$\begin{aligned} \eta(\theta)^2 &= 1 - \delta_u \cos 2(\theta - \psi_u) + \delta_v \cos 2(\theta - \psi_v) \\ &\quad + [\text{higher-order terms}], \\ &= 1 - R \cos 2\left(\theta - \frac{\chi}{2}\right) + [\text{higher-order terms}], \end{aligned} \tag{9a}$$

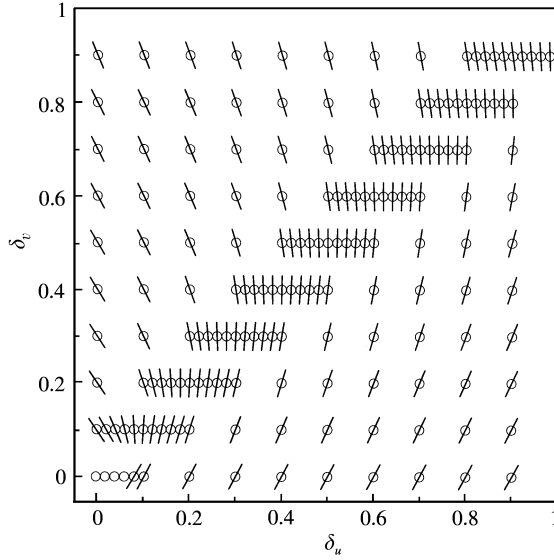


FIG. 4. The diagram illustrating the directionality of stripes. A short line passing through an open circle indicates the direction parallel to the stripes formed in the final spatial pattern when anisotropy of the two substances is given by the location of the circle (δ_u, δ_v) . The direction of stripes is calculated from the algorithm explained in Appendix A. The spatial patterns were generated from eqns (3)–(5). The direction for the fastest diffusivity was different between two substances: $\psi_u = \pi/3$, $\psi_v = \pi/6$.

where

$R =$

$$\sqrt{(\delta_u \cos 2\psi_u - \delta_v \cos 2\psi_v)^2 + (\delta_u \sin 2\psi_u - \delta_v \sin 2\psi_v)^2}, \quad (9b)$$

$$\cos \chi = \frac{1}{R} (\delta_u \cos 2\psi_u - \delta_v \cos 2\psi_v), \quad (9c)$$

$$\sin \chi = \frac{1}{R} (\delta_u \sin 2\psi_u - \delta_v \sin 2\psi_v). \quad (9d)$$

Hence, the minimum of $\eta(\theta)^2$ is attained when $\theta = \frac{1}{2}(\chi + \pi)$, $\theta = \frac{1}{2}(\chi + \pi) + n\pi$ (n is any integer). Then we predict that the stripe patterns to be formed should have a normal vector with the angle given by

$$\theta_{\text{predicted}} = \frac{1}{2} \arctan \left[\frac{\delta_u \sin 2\psi_u - \delta_v \sin 2\psi_v}{\delta_u \cos 2\psi_u - \delta_v \cos 2\psi_v} \right] + \frac{\pi}{2}. \quad (10)$$

Comparison between Predicted and Observed Directions

In the last section, we searched for an unstable mode with an approximately largest positive λ , with the hope that this mode of fast growth rate is likely to be selected and stripes tend to be formed in the direction specified by this mode. However, a fast-growing mode of deviation from the uniform steady state obtained from linear analysis can be different from the direction of stripes formed in the final stationary pattern of nonlinear dynamics. Hence, the argument leading to the predicted direction of stripes $\theta_{\text{predicted}}$, which is the one that maximizes eqn (7), is no more than a heuristic one. To check whether this prediction is useful in explaining observed patterns, we compared the directions predicted by the analysis in the previous section and the direction of stripes generated by numerical analysis of the nonlinear dynamics.

THE DIFFUSIVE DIRECTION IS THE SAME: $\psi_u = \psi_v$

Figure 2 shows the results of computer simulation when the most diffusive direction is the same between two substances ($\psi_u = \psi_v = \pi/3$). The directions of stripes are determined by the relative magnitude of anisotropy between the two substances (u and v). When the anisotropy of u is larger than that of v , the stripes are formed in parallel to the most diffusive direction [Fig. 1(a)], whereas when the anisotropy of v is larger than that of u , stripes are formed in the direction perpendicular to the diffusive direction [Fig. 1(b)]. When the magnitude of anisotropy of the two substances is almost the same, clear stripes were not formed [Fig. 1(c)]. This exactly fits the prediction by the heuristic approach in the last section. The direction of stripes changed discontinuously on the border of parameter regions in which the magnitude of anisotropy is the same between two substances ($\delta_u = \delta_v$).

THE DIFFUSIVE DIRECTION IS DIFFERENT: $\psi_u \neq \psi_v$

When the most diffusive direction is different (not parallel) between the two substances, the direction of stripes changes smoothly from the diffusive direction of u to the direction perpendicular to the diffusive direction of v as the anisotropy of

u and v changes smoothly. Figure 4 illustrates the direction of the stripes in the final spatial pattern when $\psi_u = \pi/3$ and $\psi_v = \pi/6$. The heuristic argument in the previous section suggests that stripes are likely to be formed in the direction given by θ that maximizes eqn (7).

Figure 5 showed the comparison of the predicted direction and the direction of the stripes in simulation results when $\psi_u = \pi/3$, $\psi_v = \pi/6$. In Fig. 5, the horizontal axis indicates the direction predicted by eqn (10) and the vertical axis stands for the direction of stripes in the spatial pattern generated by direct computer simulations. In Fig. 5, we indicated the results for $\delta_u < 0.4$ and $\delta_v < 0.4$ and others by different symbols; they both lie close to the diagonal line, implying a very good match between these two, showing the usefulness of the heuristic approach in the last section.

Other Models of Turing Type

In this paper, we mainly used the Schnackenberg model given by eqn (3). To examine whether

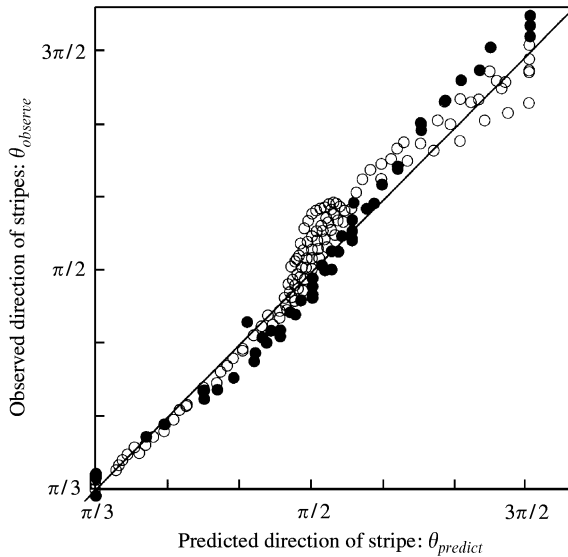


FIG. 5. The comparison between the direction predicted by the mathematical analysis and the direction of stripes formed in computer simulations. Parameters are: $\psi_u = \pi/3$, $\psi_v = \pi/6$. Circles are the results for different values of δ_u and δ_v . Solid circles are the results for $\delta_u < 0.4$ and $\delta_v < 0.4$, and open circles are those for either $\delta_u > 0.4$ or $\delta_v > 0.4$. Diagonal line indicates perfect matching of the prediction and the observation. We can conclude that the prediction by the heuristic method is quite close to the observed direction of stripes.

the same conclusion holds for other choices of reaction terms, we examined two alternative models.

GIERER-MEINHARDT MODEL

This model describes the activator-inhibitor mechanism first proposed by Gierer & Meinhardt (1972), and extensively studied by Meinhardt (1982). In this model, u is the activator concentration, which encourages the production of itself (autocatalysis). Activator promotes the production of inhibitor v , which suppresses the production of u . The reaction terms are

$$f(u, v) = A - Bu + \frac{u^2}{v}, \quad (11a)$$

$$g(u, v) = u^2 - v, \quad (11b)$$

where A and B are constants. In computer simulation we used: $A = -0.14$, $B = 0.74$ and diffusion coefficient $d = 5.00$.

LINEAR MODEL

In Kondo & Asai (1995) and Asai *et al.* (1999), the model with linear kinetics was used to explain the change in skin patterns of tropical fishes as they grow. To prevent the indefinite growth of the deviation of two quantities from the uniform equilibrium, a ceiling was introduced beyond which the variable cannot grow. The reaction terms are

$$f(u, v) = Au - v + C, \quad (12a)$$

$$g(u, v) = Bu - v + 1, \quad (12b)$$

where A and B are constants with truncation. In computer simulation, we used: $A = 0.90$, $B = 1.20$, $C = 0.16$, and diffusion coefficient $d = 5.0$. Upper and lower limits are set as $u = v = 10.0$ and $u = v = 0.0$, respectively.

In both cases we obtained very similar results as in the case with Schnackenberg's model for reaction terms (results not shown). From these, we conclude that the choice of the functional forms of reaction does not affect strongly the directionality of stripes.

Discussion

When the direction of the fastest diffusion is different between the two substances, the direction of stripes in the final spatial pattern changes smoothly with the relative magnitude of anisotropy of two substances. This direction can be predicted well by $\theta_{\text{predicted}}$ that maximizes eqn (7), which was derived from a heuristic argument based on the search for the unstable modes of small deviations in u and v from the uniform steady state in Appendix B. When the most diffusive direction is the same between the two substances in the model, a discontinuous change in the direction of stripes occurs when $\delta_u = \delta_v$. In this special case, a small difference in the relative size of anisotropy can create a big difference in the directionality of the striped patterns (transition between horizontal and vertical stripes), as studied in a twin paper (Shoji *et al.*, 2001).

Most fish species with stripe patterns on their skin have stripes either parallel or perpendicular to their anterior–posterior axis. Very few species have stripes of random direction. The results of this paper suggest that the diffusive direction of all the substance to make stripes is the same between the two substances. Shoji *et al.* (2001) described two closely related species of fish (*Genicanthus melanospilos* and *G. watanabei*), which are very similar in size, morphology and ecology except that the direction of stripes that appear as they change sex is vertical in one species and horizontal in the other. If the anisotropy of diffusion of the two substances is responsible for the contrasting difference between these two species, a small difference in the magnitude of anisotropy can explain a very large difference in the direction of stripes on fish skin. According to the study in this paper, such a discontinuous change in the direction of stripes can be observed only when the directions of anisotropy of the two substances coincide. If the diffusive directions of the two substances are different, we should observe a continuous change in the directionality of stripes caused by smooth change in parameters. Considering the strong similarity of the two species in genus *Genicanthus*, the theoretical study suggests that anisotropy of the two substances expressed in reaction–diffusion model is responsible for determining the direction of stripes and that the

diffusive direction of the two substances must be the same.

In addition, the theory indicates that the most diffusive direction should be either parallel or perpendicular to the anterior–posterior axis. In Shoji *et al.* (2001), we conjectured that the anisotropy might be caused by the morphological structure of epidermis with scales arranged along the same direction. This conjecture is consistent with the theoretical study of this idea in more general situations in the present paper.

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APPENDIX A

Let $u(\mathbf{x})$ be the magnitude of u at location \mathbf{x} . To know whether a spatial pattern has stripes with a fixed direction and to quantify the direction in which these stripes are formed, we define the spatial autocorrelation function.

$$I(r, \theta) = \frac{1}{A\sigma^2} \int \{u(\mathbf{x}) - \bar{u}\} \{u(\mathbf{x} + \mathbf{r}) - \bar{u}\} d\mathbf{x}, \quad (\text{A.1})$$

where $\mathbf{r} = (r \cos \theta, r \sin \theta)$. \bar{u} and σ^2 are the mean and the variance of $u(\mathbf{x})$, and A is the total area of the region. $I(r, \theta)$ is the correlation between two sites separated by distance r and with the relative directional angle θ . To focus on the effect of relative directional angle θ , we calculated $I_R(\theta)$, the integral of $I(r, \theta)$ with respect to r from R_1 to R_2 . To obtain the clearest result, we chose R_1 a little less than half and R_2 a little more than twice the distance between adjacent stripes. Then we searched for the angle which attains the maximum of $I_R(\theta)$. Let us denote this by ψ . If we calculate the Fourier series of $I_R(\theta)$:

$$I_R(\theta) \sim a + b \cos(2(\theta - \psi)) + [\text{other components}]. \quad (\text{A.2})$$

If the stripe pattern is clear, the second term should be much larger than all the other components. Hence, we can obtain ψ by the same method to calculate the Fourier series:

$$\begin{aligned} \int_0^{2\pi} I_R(\theta) \cos 2\theta d\theta &= b\pi \cos 2\psi \quad \text{and} \\ \int_0^{2\pi} I_R(\theta) \sin 2\theta d\theta &= b\pi \sin 2\psi. \end{aligned} \quad (\text{A.3})$$

From the ratio of these two quantities, we can calculate ψ , the direction in which the stripes run. The amplitude b in this expression, also obtained by Fourier series, implies the importance of the component, or clearness of the stripe pattern.

How this method works can be illustrated by considering an idealized case of clear stripes:

$$u(\mathbf{x}) = u_0 + \sum_{n=1} u_n \cos(n\mathbf{k} \cdot \mathbf{x} - \delta_n) + \varepsilon(\mathbf{x}), \quad (\text{A.4})$$

where $\varepsilon(\mathbf{x})$ is a small deviation that is not periodic with mean zero. Equation (A.4) implies that there is a wave-like pattern with normal vector of \mathbf{k} and periodic with respect to that direction. Let θ_k be the directional angle of vector \mathbf{k} . Then after some arithmetics, we have

$$\begin{aligned} \int_0^{2\pi} I_R(\theta) \cos 2\theta d\theta &\propto \cos 2\left(\theta_k - \frac{\pi}{2}\right) \quad \text{and} \\ \int_0^{2\pi} I_R(\theta) \sin 2\theta d\theta &\propto \sin 2\left(\theta_k - \frac{\pi}{2}\right). \end{aligned} \quad (\text{A.5})$$

From the ratio of these two values, we can calculate the directional angle of the wave θ_k . Comparing eqns (A.5) and (A.3), the direction of stripes ψ corresponds to $\theta_k + \pi/2$, which is plausible as θ_k is the normal vector of waves.

APPENDIX B

If eqns (6) and (4a, b) are combined, and if the terms of higher order with respect to A and B are neglected, we have the following equations:

$$\begin{aligned} \lambda \begin{pmatrix} u \\ v \end{pmatrix} &= \begin{pmatrix} -D_u(\theta)(k_x^2 + k_y^2) & 0 \\ 0 & -D_v(\theta)(k_x^2 + k_y^2) \end{pmatrix} \\ &\times \begin{pmatrix} u \\ v \end{pmatrix} + \gamma \begin{pmatrix} \frac{\partial f}{\partial u} & \frac{\partial f}{\partial v} \\ \frac{\partial g}{\partial u} & \frac{\partial g}{\partial v} \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix}. \end{aligned}$$

To obtain a non-trivial solution $(u, v) \neq (0, 0)$, λ needs to satisfy

$$\det \begin{vmatrix} \lambda + D_u(\theta)(k_x^2 + k_y^2) - \gamma \frac{\partial f}{\partial v} & -\gamma \frac{\partial g}{\partial u} \\ -\gamma \frac{\partial f}{\partial u} & \lambda + dD_v(\theta)(k_x^2 + k_y^2) - \gamma \frac{\partial g}{\partial v} \end{vmatrix} = 0. \quad (\text{B.1})$$

Hence, λ is given as the root of a quadratic function:

$$\begin{aligned} \lambda^2 + & \left\{ (D_u(\theta_u) + dD_v(\theta_u))(k_x^2 + k_y^2) - \gamma \left(\frac{\partial f}{\partial u} + \frac{\partial g}{\partial v} \right) \right\} \lambda \\ & + \left\{ D_u(\theta_u)(k_x^2 + k_y^2) - \gamma \frac{\partial f}{\partial u} \right\} \\ & \times \left\{ dD_v(\theta_v)(k_x^2 + k_y^2) - \gamma \frac{\partial g}{\partial v} \right\} \\ & - \gamma \frac{\partial f}{\partial u} \frac{\partial g}{\partial v} = 0, \end{aligned} \quad (\text{B.2})$$

which depends on $k_x^2 + k_y^2$ and θ , together with the local dynamics $(\partial f/\partial u, \partial f/\partial v, \partial g/\partial u$ and $\partial g/\partial v)$. From the Routh–Hurwitz criteria, both solutions λ of eqn (B.2) have a negative real part if and only if the following two conditions are satisfied:

$$(D_u(\theta) + dD_v(\theta))(k_x^2 + k_y^2) - \gamma \left(\frac{\partial f}{\partial u} + \frac{\partial g}{\partial v} \right) > 0, \quad (\text{B.3a})$$

$$\begin{aligned} & \left\{ D_u(\theta)(k_x^2 + k_y^2) - \gamma \frac{\partial f}{\partial u} \right\} \\ & \times \left\{ dD_v(\theta)(k_x^2 + k_y^2) - \gamma \frac{\partial g}{\partial v} \right\} - \gamma^2 \frac{\partial f}{\partial v} \frac{\partial g}{\partial u} > 0. \end{aligned} \quad (\text{B.3b})$$

Equation (B.3a) is always satisfied because of eqn (2a). Then whether eqn (B.3b) holds or not determines whether the corresponding mode of deviation given by eqn (6a) disappears or grows with time.

Noting that the left-hand side of eqn (B.3b) is a quadratic function of $z = k_x^2 + k_y^2$, we can write

it as $F(z, \theta)$, which is given by

$$\begin{aligned} F(z, \theta) = & dD_u(\theta)D_v(\theta)z^2 \\ & - \gamma \left(\frac{\partial f}{\partial u} dD_v(\theta) + D_u(\theta) \frac{\partial g}{\partial v} \right) z \\ & + \gamma^2 \left(\frac{\partial f}{\partial u} \frac{\partial g}{\partial v} - \frac{\partial f}{\partial v} \frac{\partial g}{\partial u} \right). \end{aligned} \quad (\text{B.4})$$

If the left-hand side of eqn (B.4) is positive for all choices of $z = k_x^2 + k_y^2 \geq 0$ and $\theta = \arctan(k_y/k_x)$, none of the deviations in the form of eqn (6) are growing. If instead some choices of $z = k_x^2 + k_y^2$ and $\theta = \arctan(k_y/k_x)$ make the left-hand side of eqn (B.4) negative, there are unstable modes of striped shape. We consider the mode that achieves the greatest negative value on the left-hand side of eqn (B.4). This corresponds to an unstable mode of striped spatial pattern, but it is not the same as the mode that makes the largest positive λ . These two are close if the right-hand side of eqn (B.3a) does not strongly depend on θ . The search for the greatest negative value of the left-hand side of eqn (B.4) is much simpler in mathematics than the search for the mode achieving the largest positive λ . It worked very well in predicting the direction of stripes to be formed, as shown by the comparison with computer simulations in the text.

In the following we consider whether any choice of $z = k_x^2 + k_y^2$ and $\theta = \arctan(k_y/k_x)$ can make $F(z, \theta)$ negative, and if so which choice of these attains the negative $F(z, \theta)$ of the largest magnitude. The choices of $z = k_x^2 + k_y^2$ and $\theta = \arctan(k_y/k_x)$ are those of magnitude of the squared wave number and the angle of solution in eqn (6), corresponding to the distance between adjacent stripes and the (perpendicular) direction

of stripes, respectively. $F(z, \theta)$ is a quadratic function with respect to z , and it attains the minimum denoted as $F(\theta)_{min}$ when $z = z_m$:

$$z_m = \frac{\gamma(\partial f/\partial u)dD_v(\theta) + (\partial g/\partial v)D_u(\theta)}{2D_u(\theta)dD_v(\theta)}, \quad (\text{B.5a})$$

$$\begin{aligned} F(\theta)_{min} &= -d\left(\frac{\partial f}{\partial u}\right)^2 \frac{D_v(\theta)}{D_u(\theta)} - 2\left(\frac{\partial f}{\partial u}\right)\left(\frac{\partial g}{\partial v}\right) \\ &\quad - \left(\frac{\partial g}{\partial v}\right)^2 \frac{D_u(\theta)}{dD_v(\theta)} \\ &\quad + [\text{terms independent of } \theta] \\ &= -d\left(\frac{\partial f}{\partial u}\right)^2 \eta(\theta) - 2\left(\frac{\partial f}{\partial u}\right)\left(\frac{\partial g}{\partial v}\right) \\ &\quad - \frac{(\partial g/\partial v)^2}{d\eta(\theta)} + [\dots], \end{aligned} \quad (\text{B.5b})$$

where $\eta(\theta) = D_v(\theta)/D_u(\theta)$. From the form of function of eqn (B.5b) as a hyperbolic function of $\eta(\theta)$, we can conclude that $F(\theta)_{min}$ is a monotonically decreasing function of $\eta(\theta)$ for $\eta(\theta) > |\partial f/\partial u|/d|\partial g/\partial v|$. From eqns (2a) and (2c), we can derive $1/d < |\partial f/\partial u|/|\partial g/\partial v| < 1$. This implies that $|\partial f/\partial u|/d|\partial g/\partial v|$ is much smaller than 1, whilst $\eta(\theta) = D_v(\theta)/D_u(\theta)$ is constrained to take values not very different from 1 if the anisotropy in diffusion is not very large. Hence, the angle $\theta = \arctan(k_y/k_x)$ that attains the minimum of $F(\theta)_{min}$ is the one that maximizes $\eta(\theta) = D_v(\theta)/D_u(\theta)$. Thus, we can conclude that the stripes to be formed have the normal vector with the direction close to θ that maximize the following quantity:

$$\eta(\theta) = \frac{D_v(\theta)}{D_u(\theta)} = \sqrt{\frac{1 - \delta_u \cos(2(\theta - \psi_u))}{1 - \delta_v \cos(2(\theta - \psi_v))}}. \quad (\text{B.6})$$