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Morphogenesis and Pattern Formation in Biological Systems

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The Moving Grid Finite Element Method Applied to Biological Problems

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Summary. This paper presents a novel numerical technique, the moving grid finite element method, to solve generalised Turing [20] reaction-diffusion type models on continuously deforming growing domains. Applications to the development of bivalve ligaments and pigmentation colour patterns in the wing of the butterfly *Papilio dardanus* will be considered, by way of examples.

5.1 Introduction

It is half a century since the appearance of Turing's seminal paper [20] on the chemical basis of morphogenesis which gave rise to the emergence of reaction-diffusion theory in developmental biology. He considered a system of two reacting and diffusing chemicals (which he termed morphogens) and demonstrated the possibility that, although in the absence of diffusion, the system tends to a linearly stable uniform steady state, in the presence of diffusion, the system evolves, due to diffusion driven instability, to a spatially non-uniform pattern. Since then, many nonlinear reaction-diffusion models have been proposed [10] and analysed, mainly on geometrically simple fixed domains.

Nature is more complicated, however. For example, butterfly wing pigmentation patterns, animal coat markings [10] and shell pigmentation patterns [8] occur on geometrically complex growing surfaces. Kondo and Asai [6] have shown that domain growth can play an important role in pattern formation. To compute the outcome of a pattern generator operating on a continuously deforming and growing domain requires novel applications of numerical computational methods. Of particular interest is the moving grid finite element method [1]. We employ this method to compute solutions of a general Tur-

ing system of two chemical morphogens on fixed, complicated and growing domains in one and two dimensions.

In section 5.2 we present the theory behind the moving grid finite element method applied to a generalised Turing reaction-diffusion model on a continuously deforming domain. Two biological applications are considered. Section 5.3 analyses the essentially one-dimensional growth patterns of certain bivalve ligaments. Section 5.4 considers the two-dimensional wing colour patterning in the butterfly *Papilio darndanus*. Finally, in section 5.5 we discuss future research.

5.2 Moving grid finite element method

We write the non-dimensional form of the two species Turing reaction-diffusion model on a continuously deforming domain $\Omega(t)$ in the form [3]:

$$\frac{\partial u}{\partial t} + \nabla \cdot (\mathbf{a}u) = \gamma f(u, v) + p_3(u, v) + \nabla^2 u, \quad (5.1)$$

$$\frac{\partial v}{\partial t} + \nabla \cdot (\mathbf{a}v) = \gamma g(u, v) + q_3(u, v) + d \nabla^2 v, \quad (5.2)$$

where $u(\mathbf{x}, t)$ and $v(\mathbf{x}, t)$ are chemical concentrations at spatial position \mathbf{x} and time t . We define $\mathbf{a}(\mathbf{x}, t)$ as the velocity field. The kinetic functions f , p_3 , g and q_3 describe the nonlinear reaction between the chemicals, with p_3 and q_3 bivariate cubic polynomials. Here f and g encode some of the familiar and often used reaction schemes:

(see website¹ for more details and a freely downloadable software). The parameter values γ and d represent the reaction timescale and ratio of diffusion coefficients respectively. Typically, boundary conditions on the spatial domain are either zero flux (Neumann) or fixed (Dirichlet) or both.

The model equations (5.1) and (5.2) assume that the domain $\Omega(t)$ deforms continuously and uniformly in time. This enables us to solve the system numerically by use of moving grid finite elements [1]. We first derive an equivalent weak form over a space V . Multiplying (5.1) and (5.2) by $w \in V$ and applying Green's theorem we seek to find $u, v \in V$ such that:

$$\left(\frac{\partial u}{\partial t}, w \right) + (\nabla \cdot (\mathbf{a}u), w) = (\gamma f(u, v) + p_3(u, v), w) + (\nabla^2 u, w), \quad (5.3)$$

$$\left(\frac{\partial v}{\partial t}, w \right) + (\nabla \cdot (\mathbf{a}v), w) = (\gamma g(u, v) + q_3(u, v), w) + d (\nabla^2 v, w), \quad (5.4)$$

where $(u, w) = \int_{\Omega(t)} u w \, d\Omega(t)$ is the L_2 -inner product. Let $V^h \subset V$ be a finite-dimensional space consisting only of simple functions depending only

¹ <http://web.comlab.ox.ac.uk/oucl/work/andy.wathen/software.html>

on finitely many parameters. The Galerkin Formulation [12] seeks to find $u^h, v^h \in V^h$ such that

$$\begin{aligned} \left(\frac{\partial u^h}{\partial t}, w^h \right) + (\nabla \cdot (\mathbf{a}u^h), w^h) &= (\gamma f(u^h, v^h) + p_3(u^h, v^h), w^h) - (\nabla u^h, \nabla w^h), \\ \left(\frac{\partial v^h}{\partial t}, w^h \right) + (\nabla \cdot (\mathbf{a}v^h), w^h) &= (\gamma g(u^h, v^h) + q_3(u^h, v^h), w^h) - d (\nabla v^h, \nabla w^h), \end{aligned}$$

for all $w^h \in V^h$ where zero-flux boundary conditions have been applied. Here u^h and v^h are the finite element approximations to u and v respectively, defined as

$$u^h(\mathbf{x}, t) = \sum_{i=0}^{N+1} u_i^h(t) \alpha_i(\mathbf{x}, \mathbf{s}(t)) \quad \text{and} \quad v^h(\mathbf{x}, t) = \sum_{i=0}^{N+1} v_i^h(t) \alpha_i(\mathbf{x}, \mathbf{s}(t))$$

where $\mathbf{x} \in \mathbb{R}^m$ indicates the spatial coordinates and $\mathbf{s}(t)$ represents the moving grid in time. The time derivative of u^h (or similarly v^h) is given by ([2, 5])

$$\frac{\partial u^h}{\partial t} = \sum_{i=0}^{N+1} [\dot{u}_i^h - \dot{x}_i u_x^h] \alpha_i(\mathbf{x}, \mathbf{s}(t)) \quad (5.5)$$

in one dimension and

$$\frac{\partial u^h}{\partial t} = \sum_{i=0}^{N+1} [\dot{u}_i^h - (\dot{x}_i u_x^h + \dot{y}_i u_y^h)] \alpha_i(\mathbf{x}, \mathbf{s}(t)) \quad (5.6)$$

in two dimensions. The effect of domain growth on the finite element formulation is to add extra terms as illustrated in (5.5) and (5.6). The spatial discretisation gives rise to a semi-discrete system of nonlinear ordinary differential equations. We use the Backward Euler finite difference scheme to discretise the ordinary differential equations in time. In one dimension the discretisation gives rise to symmetric, tridiagonal and diagonally dominant systems which can be solved using the Thomas algorithm [9]. In two dimensions we use a preconditioned Conjugate Gradient method [13].

5.3 Growth patterns in bivalve ligaments

The bivalve ligament is the uncalcified, elastic part of the bivalve shell which joins the two valves dorsally (Fig. 5.1, top panel). In the family Arcidae, these ligaments typically consist of oblique lamellar and fibrous sheets, alternating along the hinge so that their attachments on the two valves form characteristic chevron patterns. New elements are added at or near the middle of the growth zone as the ligament expands ventrally (see [7, 18] for more details). In the family Noetiidae, new elements are added to each end of the ligament,

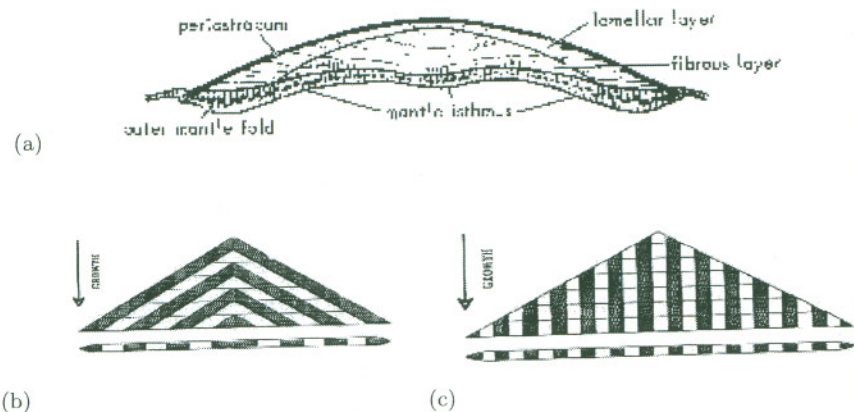


Fig. 5.1. (a): Bivalve ligament in longitudinal section (Adapted from Fig. 51, Truman [19]). Schematic showing growth patterns of the duplivincular ligament typical of (b) *Glycymeris* (arcoid) and (c) the noetioid ligament showing a cross-sectional view of the ligament as it is inserted on the attachment area of each valve [18].

anteriorly and posteriorly (see Fig. 5.1). By solving numerically the Schnakenberg [14] reaction-diffusion model on a one-dimensional growing domain with fixed parameter values we generate a variety of patterns consistent with those observed in nature (see Fig. 5.2 top panel). Similar results can be obtained in two dimensions as illustrated in Fig. 5.2 (bottom panel). This investigation shows that the noetioid growth pattern can be derived from the chevron pattern by simply fixing the value of one of the morphogens at the centre of the domain. These results suggest that the noetioid growth pattern could have evolved independently more than once, and not necessarily from a single common ancestor as the existing classification implies.

5.4 Colour patterning in *Papilio dardanus*

For many decades scientists have been fascinated by the spectacular colour patterns of butterfly wings. On the basis of the pioneering work of Schwabwitsch [15] and Süffert [17] on the nymphalid ground plan, the seemingly complicated colour patterns on butterfly wings can now be understood as a composite of a relatively small number of pattern elements. A number of mathematical models have been put forward to account for the diversity of colour patterning (see [10, 11] for review). Nijhout [11] proposed a specific ground plan for *Papilio dardanus*, a species known for its spectacular phenotypic polymorphism in females. Recently, Sekimura *et al.* [16] proposed a global wing

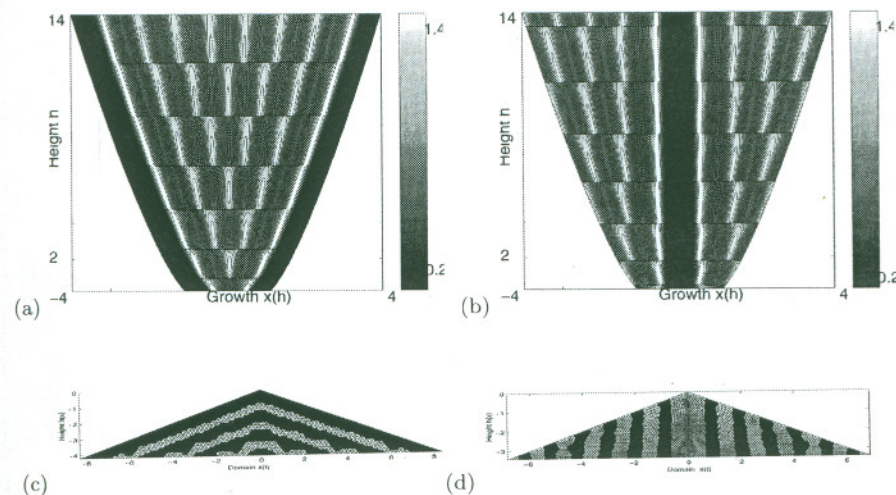


Fig. 5.2. (a), (b): Numerically computed results for u corresponding to the Schnakenberg reaction scheme with the boundaries (a) $v = 0.7$, $u_n = 0$ along $x = -1$ and $x = 1$. (b) $v_n = 0$, $u_n = 0$ along $x = -1$ and $x = 1$ with $v = 0$ along $x = 0$. (a) is consistent with arcoid patterning, while (b) is similar to the patterning observed in the noetioids (compare with Fig 5.1 (b) and (c)). (c), (d): Two-dimensional results consistent with the patterns observed in one dimension.

colouration hypothesis due to stripe-like patterns of some pigment inducing morphogens. By solving the Gierer-Meinhardt [4] reaction diffusion model on a geometrically accurate (fixed) wing shape, we can capture the details of the diverse colour patterns exhibited in the wing of *Papilio dardanus* (Fig. 5.3) by simply modifying the gradient threshold above which pigmentation occurs.

5.5 Discussion

Although we have illustrated results for the Schnakenberg and Gierer-Meinhardt reaction models, similar results can be obtained for other common kinetic models. The power of the moving grid finite element method applied to biological problems is that dynamically deforming complex geometries can be dealt with easily and efficiently without many changes in the numerical code. By solving the paradigm Turing model on continuously deforming domains we have shown that when a particular species exhibits morphological diversity, such diversity may arise through a simple modification of a basic ground plan. The generality of our numerical method allows us to study other biological patterns observed experimentally. We are currently carrying out computational

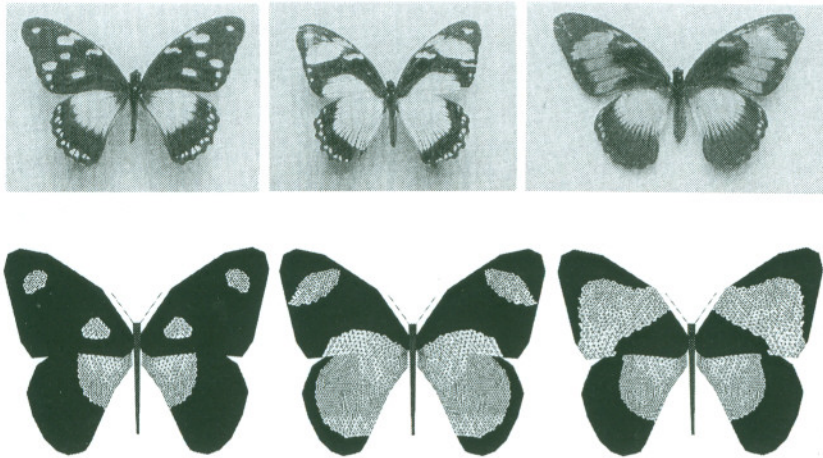


Fig. 5.3. Top panel: Some mimetic forms of females of *Papilio dardanus*. From left to right: cenea, hippocoon, and planemoides. (Courtesy of Dr. A. P. Volger and Dr. A. Cieslak of the Natural History Museum, London and Imperial College, Silwood Park). Bottom panel: Numerical results of the Gierer-Meinhardt model [4], showing patterns corresponding to hippocoon, cenea and planemoides respectively (see [16] for full details).

studies of wing development in *Papilio dardanus* from the larval imaginal disc to the adult wing, and will use our model and numerical scheme to make predictions on the effects of experimental manipulation.

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