

# Global existence for semilinear reaction–diffusion systems on evolving domains

Chandrasekhar Venkataraman · Omar Lakkis ·  
Anotida Madzvamuse

Received: 19 May 2010 / Revised: 5 November 2010  
© Springer-Verlag 2011

**Abstract** We present global existence results for solutions of reaction–diffusion systems on evolving domains. Global existence results for a class of reaction–diffusion systems on fixed domains are extended to the same systems posed on spatially linear isotropically evolving domains. The results hold without any assumptions on the sign of the growth rate. The analysis is valid for many systems that commonly arise in the theory of pattern formation. We present numerical results illustrating our theoretical findings.

**Keywords** Reaction–diffusion systems · Global existence · Evolving domains · Biological pattern formation

**Mathematics Subject Classification (2000)** 3K57 · 92C15 · 92B05

## 1 Introduction

Since their seminal introduction by Turing (1952), reaction–diffusion systems (RDS's) have constituted a standard framework for the mathematical modelling of pattern formation in chemistry and biology. Recent advances in mathematical modelling and developmental biology identify the important role of *domain evolution* as central in the formation of patterns, both empirically (Kondo and Asai 1995) and computationally (Crampin et al. 1999; Madzvamuse and Maini 2007; Comanici and Golubitsky 2008). In this respect, many numerical studies, such as Madzvamuse (2006) and Barrass et al. (2006), of RDS's on evolving domains are available. Yet, fundamental

---

C. Venkataraman (✉) · O. Lakkis · A. Madzvamuse  
Department of Mathematics, University of Sussex, Mantell Building, Brighton, BN1 9RF, UK  
e-mail: c.venkataraman@sussex.ac.uk

mathematical questions such as existence and regularity of solutions of RDS's on evolving domains remains an important open question (Kelkel and Surulescu 2009).

Numerous studies on the stability of solutions of RDS's on fixed domains are available, for example, Rothe (1984), Hollis et al. (1987), Wei and Winter (2008), but very little literature regarding the stability of solutions of RDS's on evolving domains. Madzvamuse et al. (2010) provides a linear stability analysis of RDS's on continuously evolving domains, and Labadie (2008) examines the stability of solutions of RDS's on monotonically growing surfaces. Our discussion here differs from all these studies in that we focus on planar evolving domains and we show existence, uniqueness and stability, for an entire class of RDS's on evolving domains independently of the rate of evolution. In this article we prove the stability of solutions of RDS's on a particular, but fundamentally important, class of time-evolving domains: that of *bounded spatially linear isotropically evolving domains*.

We show that if a RDS fulfils a restricted version of certain *stability conditions*, introduced by Morgan (1989) for fixed domains, then the RDS fulfils the same stability conditions on any bounded spatially linear isotropic evolution of the domain. We thus prove that, under certain conditions, the existence and uniqueness for a RDS on a fixed domain implies the existence and uniqueness for the corresponding RDS on an evolving domain. This is, to our best knowledge, the first result that holds independently of the growth rate and is thus valid on growing or contracting domains as well as domains that exhibit periods of growth and periods of contraction. Our analysis rigorously justifies computations for this type of domain evolution, and we illustrate our results with benchmark computations using a moving finite element (Lagrangian) approach.

The outline of our discussion goes as follows: In Sect. 2 we state our model problem together with the form of domain evolution that we consider, and present a transformation of our model system to the Lagrangian framework that helps in proving global existence of solutions. In Sect. 3 we review the existence results for RDS's on fixed domains which will form the basis of our analysis. In Sect. 4 we state and prove the central results of this work; in particular, we extend the existence results cited in Sect. 3 to problems posed on evolving domains. In Sect. 5 we illustrate some specific applications of our results, in particular those of significance in the field of biological pattern formation. We focus on growth functions commonly encountered in the field of developmental biology for which our analysis is valid and show the applicability of our analysis to some of the important reaction kinetics encountered in the theory of biological pattern formation. In Sect. 6 we present numerical results for a RDS posed on a periodically evolving domain. We present a moving finite element scheme and a fixed domain finite element scheme to approximate the solution of a RDS posed on the evolving and the Lagrangian frame respectively. In Sect. 7 we summarise our findings and indicate future research directions.

## 2 RDS's on continuously evolving domains

Let  $\mathbf{u}(\mathbf{x}, t)$  be a  $(m \times 1)$  vector of concentrations of chemical species, with  $\mathbf{x} \in \mathbb{R}^n$ , the time-dependent spatial variable and  $t \in [0, T]$ ,  $T > 0$ , the time variable.

The model problem we wish to consider is a semilinear RDS posed on a continuously evolving domain (see Madzvamuse (2000) for details of the derivation), given by,

$$\begin{aligned} \partial_t \mathbf{u}(\mathbf{x}, t) + [\nabla \cdot (\mathbf{a} : \mathbf{u})](\mathbf{x}, t) &= \mathbf{f}(\mathbf{u}(\mathbf{x}, t)) + \mathbf{D}\Delta \mathbf{u}(\mathbf{x}, t) \\ \text{for } \mathbf{x} \in \Omega_t \text{ and } t \in (0, T], \end{aligned} \tag{2.1}$$

where  $\Omega_t \subset \mathbb{R}^n$  ( $n < \infty$ ) is a  $C^{2+\gamma}(\Omega)$ , simply connected, bounded and continuously deforming domain with respect to  $t$ . The function  $\mathbf{f}$  is a  $(m \times 1)$  vector of nonlinear coupling terms that is locally Lipschitz,  $\mathbf{D}$  is a diagonal matrix with strictly positive entries on the diagonal,  $\mathbf{a}$  is a flow velocity generated by the evolution of the domain and  $(\mathbf{a} : \mathbf{u}) := (\mathbf{a}u_1, \dots, \mathbf{a}u_m)^T$  by definition.

**Assumption 2.1** (*Flow velocity*) We assume that the flow velocity  $a_i(\mathbf{x}, t)$  is identical to the domain velocity, i.e.,

$$a_i = \partial_t x_i \quad i = 1, \dots, n,$$

as is standard in the derivation of RDS’s on evolving domains on application of Reynold’s Transport Theorem (Acheson 1990).

To simplify the exposition we take boundary conditions to be of homogenous Neumann type. Morgan (1989) considers a much wider class of boundary conditions and our analysis may be extended to this more general setting. We are primarily interested in patterns that arise as a result of self-organisation prompting the consideration of homogenous Neumann boundary conditions. We take the initial condition for each  $u_i$  to be bounded and nonnegative. Our model problem thus takes the form (2.1), equipped with the following boundary and initial conditions:

$$\begin{cases} [\mathbf{v} \cdot \nabla \mathbf{u}](\mathbf{x}, t) = 0, & \mathbf{x} \in \partial\Omega_t, t > 0, \\ \mathbf{u}(\mathbf{x}, 0) = \mathbf{u}_0(\mathbf{x}), & \mathbf{x} \in \Omega_0. \end{cases} \tag{2.2}$$

### 2.2 Lagrangian transformation

For our analysis it is more convenient to work with problems defined on a time-independent domain. Therefore, we introduce a transformation that maps our model problem (2.1) from a time-dependent domain to a fixed domain (see Baines 1994 for a more detailed discussion of this approach). In order to do this, without too many technical complications, we will restrict our attention to special evolutions of the domain, described next.

**Assumption 2.3** (*Isotropic domain evolution*) We assume the domain  $\Omega_t$  to evolve by obeying a bounded spatially linear isotropic domain deformation, i.e.,

$$\mathbf{x} = \rho(t)\boldsymbol{\xi} \quad \text{for all } (\boldsymbol{\xi}, t) \in \Omega_0 \times [0, T] \text{ and } \text{all } \mathbf{x} \in \Omega_t, \tag{2.3}$$

with  $\rho \in C^2([0, T]; 0, \infty)$  and where  $\xi$  represents the spatial coordinates of the initial domain. This assumption and Assumption 2.1 imply that

$$\mathbf{a}(\mathbf{x}, t) = \dot{\rho}(t)\xi, \quad (2.4)$$

where  $\dot{\rho} := \frac{d\rho}{dt}$ .

Hence, we obtain the following transformed problem on the initial domain (see Madzvamuse and Maini 2007 for details), with

$$\hat{\mathbf{u}}(\xi, t) = \mathbf{u}(\rho(t)\xi, t) \quad \text{for } t \in [0, T] \quad \text{and} \quad \xi \in \Omega_0, \quad (2.5)$$

we have

$$\begin{cases} \partial_t \hat{\mathbf{u}} + n \frac{\dot{\rho}}{\rho} \hat{\mathbf{u}} = \mathbf{f}(\hat{\mathbf{u}}) + \frac{D}{\rho^2} \Delta \hat{\mathbf{u}} & \text{on } \Omega_0 \times (0, T], \\ [\mathbf{v} \cdot \nabla \hat{\mathbf{u}}](\xi, t) = 0 & \text{on } \partial\Omega_0, t > 0, \\ \hat{\mathbf{u}}(\xi, 0) = \hat{\mathbf{u}}_0(\xi) & \xi \in \Omega_0, \\ 0 \leq \hat{\mathbf{u}}_0(\xi) < \infty, & \end{cases} \quad (2.6)$$

where  $\Omega_0$  is the initial spatial domain,  $n$  is the spatial dimension and the Laplacian is now taken with respect to  $\xi$ . The local and global existence results that we utilise from the existing literature require the coefficients on our diffusion term to be independent of time; to this end we introduce the following proposition:

**Proposition 2.4** (Time rescaling Labadie (2008)) *Let  $\mathbf{u}$  be a solution of (2.1), rescaling time via the change of variables*

$$s(t) := \int_0^t \frac{dr}{\rho(r)^2}, \quad (2.7)$$

and denoting  $S := s(T)$ . We have,  $\mathbf{u}(\rho(t)\xi, t) = \tilde{\mathbf{u}}(\xi, s)$ , where  $\tilde{\mathbf{u}}$  satisfies

$$\begin{cases} \partial_s \tilde{\mathbf{u}} + n\rho \dot{\rho} \tilde{\mathbf{u}} = \rho^2 \mathbf{f}(\tilde{\mathbf{u}}) + D \Delta \tilde{\mathbf{u}} & \text{on } \Omega_0 \times (0, S], \\ [\mathbf{v} \cdot \nabla \tilde{\mathbf{u}}](\xi, s) = 0 & \xi \in \partial\Omega, s > 0, \\ \tilde{\mathbf{u}}(\xi, 0) = \tilde{\mathbf{u}}_0(\xi) & \xi \in \Omega. \end{cases} \quad (2.8)$$

Furthermore, if  $\mathbf{f}(\mathbf{u})$  is locally Lipschitz in  $\mathbf{u}$  then  $\tilde{\mathbf{f}}(\tilde{\mathbf{u}}(\xi, s), s) = \rho^2(s) \mathbf{f}(\tilde{\mathbf{u}}(\xi, s)) - n\rho(s)\dot{\rho}(s)\tilde{\mathbf{u}}(\xi, s)$ , is locally Lipschitz in  $\tilde{\mathbf{u}}$ .

*Proof* We note that with domain evolution of the form considered in this study, there exist  $C_1, C_2$  such that  $0 < \rho \leq C_1 < \infty$  and  $\|\dot{\rho}\|_{L^\infty[0, T]} \leq C_2 < \infty$ . Applying the rescaling (2.7), we see that for any function  $g \in C^1[0, T]$

$$\partial_s g(t) = \partial_s t(s) \partial_t g(t) = \rho^2(t) \partial_t g(t). \quad (2.9)$$

Defining  $\tilde{\mathbf{u}}(\boldsymbol{\xi}, s) := \mathbf{u}(\rho(t)\boldsymbol{\xi}, t)$  and multiplying problem (2.6) by  $\rho^2$ , we obtain problem (2.8). Clearly since  $\mathbf{f}(\mathbf{u})$  is locally Lipschitz in  $\mathbf{u}$ , Assumption 2.3 implies  $\tilde{\mathbf{f}}(\tilde{\mathbf{u}}, s)$  is locally Lipschitz in  $\tilde{\mathbf{u}}$  and globally Lipschitz in  $s$ .  $\square$

### 3 Basic theoretical setting for RDS’s on fixed domains

We now summarise the existing results for RDS’s on fixed domains which will form the basis of our analysis on evolving domains. The following result is a straightforward generalisation of Hollis et al. (1987, Prop. 1).

**Theorem 3.1** (Local existence) *Let Assumption 2.3 hold. Problem (2.8) admits a unique local solution. Furthermore, defining the unique maximal solution of (2.8) by*

$$\tilde{\mathbf{u}} : \Omega_0 \times [0, T_{\max}) \rightarrow \mathbb{R}^m, \tag{3.1}$$

there exists a function  $\mathbf{N} \in C([0, T_{\max}); \mathbb{R}^m)$  such that,

$$\|\tilde{\mathbf{u}}_i(\cdot, s)\|_{L_\infty(\Omega_0)} \leq N_i(s) \quad \text{for } i \in [1, \dots, m] \text{ and } s \in [0, T_{\max}). \tag{3.2}$$

Finally, if  $T_{\max} < \infty$ ,

$$\lim_{s \rightarrow T_{\max}} \left( \sum_{i=1}^m \|\tilde{\mathbf{u}}_i(\cdot, s)\|_{L_\infty(\Omega_0)} \right) = \infty. \tag{3.3}$$

#### 3.2 Global existence on fixed domains

If  $\rho(t) = 1$  for all  $t \in [0, T]$ , Problem (2.8) becomes, find  $\tilde{\mathbf{u}} : \Omega_0 \times (0, T] \rightarrow \mathbb{R}^m$  such that,

$$\begin{cases} \partial_t \tilde{\mathbf{u}} = \mathbf{f}(\tilde{\mathbf{u}}) + \mathbf{D}\Delta \tilde{\mathbf{u}}, & \text{on } \Omega_0 \times (0, T], \\ [\mathbf{v} \cdot \nabla \tilde{\mathbf{u}}](\boldsymbol{\xi}, t) = 0, & \boldsymbol{\xi} \in \partial\Omega_0, t > 0, \\ \tilde{\mathbf{u}}(\boldsymbol{\xi}, 0) = \tilde{\mathbf{u}}_0(\boldsymbol{\xi}), & \boldsymbol{\xi} \in \Omega_0, \end{cases} \tag{3.4}$$

where we have used the fact that  $s(t) = t$  (cf. (2.7)).

**Definition 3.3** (Invariant region)  $\Sigma \subset \mathbb{R}^m$  is called an invariant region for the solution of the reaction–diffusion system (3.4) if for any solution  $\mathbf{u}$ ,

$$\mathbf{u}(\boldsymbol{\xi}, 0) \in \Sigma \implies \mathbf{u}(\boldsymbol{\xi}, t) \in \Sigma \quad \text{for all } t \in (0, T]. \tag{3.5}$$

**Assumption 3.4** (Positive solutions) We assume hereon that

$$f_i(\mathbf{u})|_{u_i=0} \geq 0 \quad \text{for all } t \in [0, T], \tag{3.6}$$

and for  $f \notin C^1(\mathbb{R}_+^m; \mathbb{R}^m)$ , the strict inequality

$$f_i(\mathbf{u})|_{u_i=0} > 0 \quad \text{for all } t \in [0, T]. \quad (3.7)$$

Assumption 3.4 together with the positivity of our initial data, implies  $\mathbb{R}_+^m$  which we refer to as the positive quadrant, is an invariant region for the solutions of problem (3.4) (see Smoller 1994, Th.14.7,14.11, pp. 200–203).

*Remark 3.5 (General invariant regions)* Assumption 3.4 may be relaxed. The proof of our existence results only requires bounded initial data and the existence of an invariant region. Furthermore, consideration of the positive quadrant alone is sufficient for our studies.

### 3.6 Lyapunov stability conditions

We now introduce a Lyapunov function for the dynamical system defined by (3.4) when the initial condition  $\tilde{\mathbf{u}}_0$  varies which is used to prove global existence and a restricted version of the conditions it is required to fulfil (Morgan 1989).

Suppose  $f$  is as defined in problem (3.4) and that there exists a function  $H \in C^2(\mathbb{R}_+; \mathbb{R})$  and  $h_i \in C^2(\mathbb{R}_+; \mathbb{R})$  for each  $i = 1, \dots, m$ , such that

$$H(\mathbf{z}) = \sum_{i=1}^m h_i(z_i) \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m, \quad (3.8)$$

$$h_i(z_i), h_i''(z_i) \geq 0 \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m, \quad (3.9)$$

$$H(\mathbf{z}) \rightarrow \infty \iff \mathbf{z} \rightarrow \infty \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m. \quad (3.10)$$

Suppose there exists  $A = (a_{ij}) \in (\mathbb{R})^{m \times m}$  satisfying  $a_{ij} \geq 0$ ,  $a_{ii} > 0$  with  $1 \leq i, j \leq m$  such that for some  $r, k_1, k_2 \in \mathbb{R}_+$  independent of  $j$ , we have

$$\sum_{i=1}^j a_{ij} h_i'(z_i) f_i(\mathbf{z}) \leq k_1 (H(\mathbf{z}))^r + k_2 \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m, j \leq m. \quad (3.11)$$

Suppose there exist  $q, k_3, k_4 \in \mathbb{R}_+$  such that for  $1 \leq i \leq m$ , we have

$$h_i'(z_i) f_i(\mathbf{z}) \leq k_3 (H(\mathbf{z}))^q + k_4, \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m. \quad (3.12)$$

Suppose there exist  $k_5, k_6 \geq 0$  such that

$$\nabla H(\mathbf{z}) \cdot f(\mathbf{z}) \leq k_5 H(\mathbf{z}) + k_6 \quad \text{for all } \mathbf{z} \in \mathbb{R}_+^m. \quad (3.13)$$

**Theorem 3.7** (A priori estimates (Morgan 1989)) *Let conditions (3.8), (3.9) and (3.13) hold and let  $\tilde{\mathbf{u}}$  be a solution of problem (3.4). The following a priori estimates hold,*

$$\left\| \int_{\tau}^t H(\tilde{\mathbf{u}}(\cdot, s)) ds \right\|_{L_{\infty}(\Omega_0)} \leq g(t) \quad \text{for } 0 \leq \tau < t < T_{\max}, \tag{3.14}$$

$$\int_0^t \int_{\Omega_0} H(\tilde{\mathbf{u}}(\xi, s))^2 d\xi ds \leq \tilde{g}(t) \quad \text{for } 0 \leq t < T_{\max}, \tag{3.15}$$

where  $g, \tilde{g} \in C[0, \infty)$ .

**Theorem 3.8** (Global existence on fixed domains (Morgan 1989)) *If conditions (3.8)–(3.12) hold, with  $r$  from condition (3.11) satisfying  $r < (1+a)$ ,  $a \in \mathbb{R}_+$ ,  $\tilde{\mathbf{u}}$  is a solution of problem (3.4) and if there exists  $g \in C[0, \infty)$  such that*

$$\left\| \int_{\tau}^t |H(\tilde{\mathbf{u}}(\cdot, s))|^a ds \right\|_{L_{\infty}(\Omega_0)} \leq g(t) \quad \text{for } 0 \leq \tau < t < T_{\max}, \tag{3.16}$$

then  $T_{\max} = \infty$ . Alternatively, if conditions (3.8)–(3.12) hold, with  $r$  from condition (3.11) satisfying  $r < (1 + \frac{2b}{n+2})$ ,  $b > 0$  and where  $n$  represents the spatial dimension,  $\tilde{\mathbf{u}}$  solves a problem of the form (3.4) and if there exists  $\tilde{g} \in C[0, \infty)$  such that

$$\int_0^t \int_{\Omega_0} |H(\tilde{\mathbf{u}}(\xi, s))|^b d\xi ds \leq \tilde{g}(t) \quad \text{for } 0 \leq t < T_{\max}, \tag{3.17}$$

then  $T_{\max} = \infty$ .

Specifically if  $r$  from condition (3.11) satisfies  $r < 2$  or if  $\Omega_0 \subset \mathbb{R}$  with  $r < \frac{7}{3}$  and the remaining conditions (3.8)–(3.13) are satisfied then  $T_{\max} = \infty$ .

### 4 Global existence on evolving domains

In this section we show that, if the stability conditions in Sect. 3.6 are valid for Problem (3.4) then they remain valid under any evolution of the domain fulfilling Assumption 2.3, given a suitable assumption on the structure of  $H$ . We also extend the previous a priori estimates and existence results of Morgan (1989) to problems with time dependent  $f$ .

**Assumption 4.1** (Polynomial Lyapunov function) We assume the Lyapunov function introduced in Sect. 3.6 is of the following form

$$H(\mathbf{z}) = \sum_{i=1}^m z_i^{p_i}, \quad p_i \geq 1 \quad \text{for } i = 1, \dots, m. \quad (4.1)$$

**Remark 4.2** (*Polynomial growth restriction*) Assumption 4.1 is somewhat natural. Condition (3.12) is essentially a polynomial type growth restriction on the zero order terms (Morgan 1989). Assumption 4.1 can be viewed as the explicit analogue of the polynomial growth restriction on the zero order terms implicit in (3.12).

**Lemma 4.3** (*Equivalence of Lyapunov functions*) Suppose Assumptions 2.3, 3.4 and 4.1 hold. Let the Lyapunov stability conditions in Sect. 3.6 be satisfied by  $H$  and  $\mathbf{f}$ . Then the conditions in Sect. 3.6 with  $r$  (cf. (3.11)) replaced by  $\tilde{r} := \max(1, r)$ , are satisfied by  $H$  and  $\tilde{\mathbf{f}}$  (cf. (4.2)) in place of  $\mathbf{f}$ .

*Proof* We denote the zero order term in Problem (2.8) by

$$\tilde{\mathbf{f}}(\tilde{\mathbf{u}}(\boldsymbol{\xi}, s), s) := \rho^2(s) \mathbf{f}(\tilde{\mathbf{u}}(\boldsymbol{\xi}, s)) - n \dot{\rho}(s) \rho(s) \tilde{\mathbf{u}}(\boldsymbol{\xi}, s). \quad (4.2)$$

The positive quadrant remains an invariant region for the solutions of our evolving domain problem since

$$\tilde{f}_i(\tilde{\mathbf{u}}(\boldsymbol{\xi}, s), s) |_{u_i=0} = \rho^2(s) f_i(\tilde{\mathbf{u}}(\boldsymbol{\xi}, s)) |_{u_i=0}, \quad (4.3)$$

thus Assumption 3.4 implies  $\mathbb{R}_+^m$  is an invariant region for the solutions of problem (2.8). Let  $k_i, i = 1, \dots, 6, q, r$  and  $\mathbf{A}$  be as defined in Sect. 3.6, for which conditions (3.8)–(3.13) hold for problem (3.4). Denote  $C_1 := \|\rho\|_{L_\infty[0, T]}$  and  $C_2 := \|\dot{\rho}\|_{L_\infty[0, T]}$ ; these are well defined real numbers thanks to Assumption 2.3. We now show that conditions (3.8)–(3.13) hold with the same  $H, \mathbf{f}$  replaced by  $\tilde{\mathbf{f}}$  and  $r$  from (3.11) replaced by  $\tilde{r}$ , where  $\tilde{r} = \max(1, r)$ .

Clearly conditions (3.8)–(3.10) are still satisfied as they depend only on  $H$  which is unchanged. Condition (3.11) holds since

$$\sum_{i=1}^j a_{ij} h'_i \tilde{f}_i = \sum_{i=1}^j a_{ij} h'_i (\rho^2 f_i - n \dot{\rho} \rho \tilde{u}_i) \leq (k_1(H)^r + k_2) C_1^2 + n C_1 C_2 \sum_{i=1}^j a_{ij} h'_i \tilde{u}_i, \quad (4.4)$$

by the stability of the fixed domain problem. Assumption 4.1 gives,

$$\begin{aligned} \sum_{i=1}^j a_{ij} h'_i \tilde{f}_i &\leq (k_1(H)^r + k_2) C_1^2 + n C_1 C_2 \sum_{i=1}^j a_{ij} p_i h_i \\ &\leq (k_1(H)^r + k_2) C_1^2 + k_7 H \leq (k_1 C_1^2 + k_7)(H)^{\tilde{r}} + k_8, \end{aligned} \quad (4.5)$$



where

$$\tilde{r} = \max(1, r) \quad \text{and} \quad k_8 := \begin{cases} k_2 C_1^2 + k_1 C_1^2, & \text{if } r < 1, \\ k_2 C_1^2, & \text{if } r = 1, \\ k_2 C_1^2 + k_7, & \text{if } r > 1. \end{cases}$$

Condition (3.12) holds since

$$\begin{aligned} h'_i \tilde{f}_i &\leq C_1^2 h'_i f_i + n C_1 C_2 p_i h_i \\ &\leq k_3 C_1^2 (H)^q + k_4 C_1^2 + n C_1 C_2 \max_i(p_i) H \\ &\leq k_{10} H^{\tilde{q}} + k_{11}, \end{aligned} \tag{4.6}$$

where

$$\tilde{q} = \max(1, q) \quad \text{and} \quad k_{11} := \begin{cases} k_4 C_1^2 + k_3 C_1^2, & \text{if } q \leq 1, \\ k_4 C_1^2, & \text{if } q = 1, \\ k_4 C_1^2 + k_9, & \text{if } q > 1. \end{cases}$$

Condition (3.13) holds since

$$\nabla H \cdot \tilde{\mathbf{f}} \leq \sum_{i=1}^m C_1^2 h'_i f_i + n C_1 C_2 p_i h_i \leq (k_5 H + k_6) C_1^2 + k_{12} H. \tag{4.7}$$

Thus the positive quadrant remains an invariant region for the solutions of problem (2.8) and the Lyapunov stability conditions in Sect. 3.6 are satisfied, completing the proof.  $\square$

*Remark 4.4* (Applicability of Morgan (1989) to systems with time dependent zero order terms) Suppose the reaction function  $\tilde{\mathbf{f}}(\tilde{\mathbf{u}}(\boldsymbol{\xi}, t), t)$  is locally Lipschitz with respect to  $\tilde{\mathbf{u}}$  and  $t$ , and suppose that the Lyapunov function  $H$  depends only on  $\tilde{\mathbf{u}}$ . Then, Theorems 3.7 and 3.8 remain applicable (Morgan 1989, (5.5); Morgan and Hollis 1995, Th. 1.1 and Bendahmane and Saad 2010, Th. 4). Thus, the Lipschitz result of Proposition 2.4, the structural Assumption 4.1 and the equivalence of Lyapunov functions proved in Lemma 4.3 imply that Theorems 3.7 and 3.8 are applicable for solutions of (2.8).

For completeness, we include a proof of Theorems 3.7 and 3.8 for solutions of Problem (2.8), in Appendices A and B respectively. To remain concise we prove a sufficient existence result for the examples presented in Sect. 5 and briefly sketch the full proof of Theorems 3.7 and 3.8.

The results of Morgan and Hollis (1995) apply for systems with time dependent diffusion. This may allow treatment of more general domain evolution where the rescaling carried out in Sect. 2 yields a system with time dependent diffusion. We leave this generalisation for future studies.

**Theorem 4.5** (Global existence of solutions on evolving domains) *Let Assumptions 2.3, 3.4 and 4.1 hold and suppose  $H$ ,  $f$  and  $r$  satisfy the conditions in Sect. 3.6 with  $r < 2$  or if  $\Omega \subset \mathbb{R}$ ,  $r < \frac{7}{3}$  (cf. (3.11)). Then, Problem (2.1) admits a global classical solution.*

*Proof* Application of the results in Sect. 2.2 allows us to show existence for the transformed Problem (2.8) defined on a fixed domain. Theorem 3.1 gives the existence of a unique non-continuable classical solution. From Lemma 4.1 the stability conditions in Sect. 3.6 hold with  $\tilde{f}$  (cf. (4.2)),  $H$  and  $r < 2$  or if  $\Omega \subset \mathbb{R}$ ,  $r < \frac{7}{3}$ . Theorem 3.7 gives an a priori estimate for  $H$ . Theorem 3.8 implies  $T_{\max} = \infty$  (cf. (3.1)) completing the proof.  $\square$

## 5 Applications

In this section we illustrate some applications of Theorem 4.5. We present different forms of admissible domain evolution that fulfil Assumption 2.3. We show that Assumption 4.1 is applicable to some commonly encountered models in chemistry and biology. We concentrate on RDS's which admit Turing instabilities, as the main focus of our research is biological pattern formation. We identify and describe Lyapunov functions and constants that imply global existence for the fixed domain problem and thus for the evolving domain problem by Theorem 4.5.

### 5.1 Admissible domain evolution

We now provide some commonly encountered examples of domain evolution in developmental biology for which Assumption 2.3 holds:

- Logistic evolution on any finite positive time interval

$$\rho(t) = \frac{e^{r_g t}}{1 + \frac{1}{K}(e^{r_g t} - 1)}, \quad t \in [0, T], \quad (5.1)$$

where  $r_g \geq 0$  is the growth rate and  $K > 1$  is the carrying capacity (limiting size of the evolving domain).

- Exponential evolution on any finite positive time interval

$$\rho(t) = e^{r_g t}, \quad t \in [0, T]. \quad (5.2)$$

- Linear evolution on any finite positive time interval

$$\rho(t) = 1 + r_g t, \quad t \in [0, T], \quad (5.3)$$

where  $r_g > -\frac{1}{T}$ .

### 5.2 Admissible kinetics

We now present some of the commonly encountered reaction kinetics of problem (2.1) for which the analysis of Morgan (1989) implies global existence of solutions on fixed domains. We first consider the problem (2.1) with this general reaction term

$$f_i(\mathbf{u}) = \sum_{j=1}^m c_{ij}u_j + (-1)^i g(\mathbf{u}) + b_i, \tag{5.4}$$

with the following restrictions

$$c_{ij} \geq 0, \quad \text{for } i \neq j. \tag{5.5}$$

$$b_i \geq 0, \quad i = 1, \dots, m. \tag{5.6}$$

$$g(\mathbf{u})|_{u_i=0} = 0, \quad i = 1, \dots, m. \tag{5.7}$$

$$g(\mathbf{u}) \leq \left( \sum_{i=1}^m u_i \right)^p, \quad \text{for all } \mathbf{u} \in \mathbb{R}_+^m. \tag{5.8}$$

$$g \in C^1(\mathbb{R}_+^m; \mathbb{R}). \tag{5.9}$$

The motivation of this type of kinetics, as discussed by Murray (2003), is their role in the theory of biological oscillators due to a feedback mechanism.

**Proposition 5.3** (Lyapunov function) *We show that problem (2.1) equipped with kinetics (5.4) is well posed, with Lyapunov function  $H(\mathbf{z}) := \sum_{i=1}^m z_i$ .*

*Proof* Recalling that the initial data is bounded and nonnegative (2.2), we show that Assumption 3.4 is fulfilled, which implies  $\mathbb{R}_m^+$  is an invariant region for the solutions. Indeed, from (5.7) we have

$$f_i(\mathbf{u})|_{u_i=0} = \sum_{j=1}^m c_{ij}u_j + b_i = \sum_{j=1}^{i-1} c_{ij}u_j + \sum_{j=i+1}^m c_{ij}u_j + b_i. \tag{5.10}$$

Conditions (5.5) and (5.5) imply

$$f_i(\mathbf{u})|_{u_i=0} \geq b_i \geq 0 \quad \text{for all } \mathbf{u} \in \mathbb{R}_+^m. \tag{5.11}$$

Thus Assumption 3.4 is fulfilled due to (5.9). Now we show conditions (3.8)–(3.13) are fulfilled with  $r = 1$ . Clearly conditions (3.8)–(3.10) hold. Condition (3.11) holds with

$$a_{ij} := \begin{cases} 1 & \text{if } j = i, \\ 1 & \text{if } j = 1 \text{ and } i \text{ is even,} \\ 0 & \text{otherwise,} \end{cases}$$

$k_1 = \max_{i,j}(c_{ij}), k_2 = \sum_{i=1}^m b_i$  and  $r = 1$ . Condition (3.12) holds since

$$h'_i f_i = f_i \leq \max_{i,j}(c_{ij}) \sum_{i=1}^m u_i + \max_i(b_i) + g(\mathbf{u}). \tag{5.12}$$

Using (5.8) we have

$$\begin{aligned} h'_i f_i &\leq \max_{i,j}(c_{ij}) \sum_{i=1}^m u_i + \max_i(b_i) + \left(\sum_{i=1}^m u_i\right)^p \\ &\leq \max_{i,j}(c_{ij})H(u) + H(u)^p + \max_i(b_i) \leq kH(u)^q + b, \end{aligned} \tag{5.13}$$

where  $k, q, b \in \mathbb{R}_+$  represent constants that depend on the value of  $p$  in (5.8). Condition (3.13) holds since

$$\nabla H \cdot \mathbf{f} = \sum_{i=1}^m f_i \leq \max_{i,j}(c_{ij}) \sum_{i=1}^m u_i + \sum_{i=1}^m b_i \leq kH(u) + b, \tag{5.14}$$

where  $k = \max_{i,j}(c_{ij})$  and  $b = \sum_{i=1}^m b_i$ . A straightforward application of Theorem 4.5 thus completes the proof.  $\square$

*Example 5.4* The generic problem for which we showed global existence of solutions actually encompasses some of the more widely studied models in the theory of pattern formation such as the Gray-Scott model and the Brussellator. Below we present two examples of two species reaction terms for which our analysis implies global existence of solutions, the first of which is a restriction of the reaction term above.

- *Activator-depleted substrate model:* We consider the *activator-depleted* substrate model (Schnakenberg 1979; Gierer and Meinhardt 1972; Lefever and Prigogine 1968) also known as the Brusselator model:

$$\begin{cases} f_1(u_1, u_2) = \gamma(a - u_2^2 u_1), \\ f_2(u_1, u_2) = \gamma(b - u_2 + u_2^2 u_1), \end{cases} \tag{5.15}$$

where  $0 < a, b, \gamma < \infty$ . The assumption of nonnegative initial data implies that the positive quadrant is invariant for our problem due to the fact that  $a, b > 0$ . If we take  $H(\mathbf{u}) = u_1 + u_2$ , then conditions (3.8)–(3.13) are fulfilled with  $r = 0$  which implies global existence of solutions on evolving domains via Theorem 4.5. The remaining constants for which conditions (3.8)–(3.13) hold are given in Table 1.

- *Thomas reaction kinetics:* The following model, proposed and studied experimentally by Thomas (1975), is based on a specific reaction involving the substrates oxygen and uric acid which react in the presence of the enzyme uricase:

$$\begin{cases} f_1(u_1, u_2) = \gamma(a - u_1 - g(u_1, u_2)), \\ f_2(u_1, u_2) = \gamma(b - \alpha u_2 - g(u_1, u_2)), \end{cases} \tag{5.16}$$

**Table 1** Terms from Sect. 3 for which conditions (3.8)–(3.13) hold for the kinetics defined in (5.15) and (5.16) respectively

Parameters	Activator-depleted substrate model	Thomas model
$a_{11}$	1	1
$a_{12}$	0	0
$a_{21}$	1	0
$a_{22}$	1	1
$k_1$	0	0
$k_2$	$\gamma(a + b)$	$\gamma(a + b)$
$k_3$	$\frac{\gamma}{2}$	0
$q$	3	0
$k_4$	$\gamma(\max(a, b))$	$\gamma(\max(a, b))$
$k_5$	0	0
$k_6$	$\gamma(a + b)$	$\gamma(a + b)$

where

$$g(u_1, u_2) = \frac{\kappa u_1 u_2}{1 + u_1 + \beta u_1^2}, \tag{5.17}$$

and  $0 < \gamma, a, \alpha, b, \kappa, \beta < \infty$ . Once again the assumption of nonnegative initial data implies that the positive quadrant is invariant for our problem due to the fact that  $a, b > 0$ . If we again take  $H(\mathbf{u}) = u_1 + u_2$ , then conditions (3.8)–(3.13) are fulfilled with  $r = 0$  which implies global existence of solutions on evolving domains via Theorem 4.5. The remaining constants for which conditions (3.8)–(3.13) hold are given in Table 1.

*Remark 5.5 (Invariant rectangles for the Thomas model)* It can be shown, utilising the techniques of Smoller (1994), that there exist bounded invariant rectangles for the solutions of the Thomas model defined in (5.16). This implies global existence of solutions via Theorem 3.1. However the authors can show that it is possible to construct growth functions that fulfil Assumption 2.3, for which the bounded invariant rectangle can be made arbitrarily large. This necessitates the Lyapunov function approach to show existence and uniqueness of solutions.

*Remark 5.6 (Further applications)* The analysis can be applied to a large number of problems unrelated to the theory of pattern formation. Garvie and Trenchea (2009) provide an example applicable to ecology and the aforementioned paper of Morgan (1989) contains further examples as well as the numerous citations of said paper that use the approach on various problems.

## 6 Numerical experiments

In this section we present numerical results on two-dimensional evolving domains to back-up the theoretical results of the previous sections. The numerical simulation of

RDS's on growing domains is an extensive research area. Crampin et al. (2002) and Madzvamuse and Maini (2007) study mode doubling and tripling behaviour of the *activator-depleted* substrate model on one- and two-dimensional growing domains. The theoretical results derived above apply for any evolution that fulfils Assumption 2.3. We present numerical results on a periodically evolving domain that exhibit spot splitting as well as spot annihilation and merging, which to the authors knowledge is as yet an unstudied area.

## 6.1 Domain evolution

We consider periodic domain evolution defined by

$$\rho(t) = 1 + 9 \sin\left(\frac{\pi t}{T}\right), \quad t \in [0, 1,000 = T], \quad (6.1)$$

with the initial domain defined as  $\Omega_0 = [-0.25, 0.25]^2$  which grows to  $\Omega_{500} = [-2.5, 2.5]^2$  before contracting back to the original domain.

## 6.2 Continuous problems

We present results for the aforementioned *activator-depleted* model considered on a periodically evolving domain and its equivalent transformed system on a fixed domain as in Sect. 2.2. For example, on a periodically evolving domain the problem is stated as follows:

$$\begin{cases} \partial_t u_1(\mathbf{x}, t) + [\nabla \cdot (\mathbf{a}u_1)](\mathbf{x}, t) - \Delta u_1(\mathbf{x}, t) \\ \quad = 0.1 - [u_2^2 u_1](\mathbf{x}, t), & \text{for } \mathbf{x} \in \Omega_t \\ \partial_t u_2(\mathbf{x}, t) + [\nabla \cdot (\mathbf{a}u_2)](\mathbf{x}, t) - 0.01 \Delta u_2(\mathbf{x}, t) \\ \quad = 0.9 - u_2(\mathbf{x}, t) + [u_2^2 u_1](\mathbf{x}, t), & \text{and } t \in (0, T], \\ [\mathbf{v} \cdot \nabla \mathbf{u}](\mathbf{x}, t) = 0, & \mathbf{x} \in \partial\Omega_t, t > 0, \end{cases} \quad (6.2)$$

where  $\mathbf{x} = \rho(t)\boldsymbol{\xi}$  and  $a_i(\mathbf{x}, t) = \dot{\rho}(t)\boldsymbol{\xi}$ ,  $i = 1, 2$ . Equivalently, the following transformed equations are obtained on a fixed domain,

$$\begin{cases} \partial_t u_1 + 2\frac{\dot{\rho}}{\rho}u_1 - \frac{1}{\rho^2}\Delta u_1 = 0.1 - u_2^2 u_1, \\ \partial_t u_2 + 2\frac{\dot{\rho}}{\rho}u_2 - \frac{0.01}{\rho^2}\Delta u_2 = 0.9 - u_2 + u_2^2 u_1, & \text{on } \Omega_0 \times (0, T], \\ [\mathbf{v} \cdot \nabla \mathbf{u}](\boldsymbol{\xi}, t) = 0, & \boldsymbol{\xi} \in \partial\Omega_0, t > 0. \end{cases} \quad (6.3)$$

In both cases we take identical initial conditions as small perturbations around the homogenous steady state of (0.9, 1.0) obtained in the absence of domain evolution.

### 6.3 Numerical schemes

We employ a Galerkin finite element method for the spatial approximation and an implicit-explicit modified backward Euler scheme for the time integration. Discretising in time we divide the time interval  $[0, T]$  into a partition of  $N$  uniform subintervals,  $0 = t_0 < \dots < t_N = T$  and denote by  $\tau := t_n - t_{n-1}$  the time step. For the spatial discretisation we introduce a regular triangulation  $\mathcal{T}^0$  of  $\Omega_0$  with  $K \in \mathcal{T}^0$  an open simplex. We define the following shorthand for a function of time,  $f(t_n) =: f^n$ .

We define the finite element space on the initial domain  $\mathbb{V}^0 \subset H^1(\Omega_0)$  as,

$$\mathbb{V}^0 := \{\Phi \in H^1(\Omega_0) : \Phi|_K \in \mathbb{P}^1 \text{ for all } K \in \mathcal{T}^0\}, \tag{6.4}$$

where  $\mathbb{P}^1$  denotes the space of polynomials no higher than degree 1. For the numerical simulation of Eq. (6.2) we require finite element spaces defined on the evolving domain. We construct the finite element spaces  $\mathbb{V}^n$  according to the following relation between the basis functions of  $\mathbb{V}^n$  and  $\mathbb{V}^0$ .

$$\Psi^n = \Psi(\rho^n \xi, t_n) = \Phi(\xi) \quad n = 1, \dots, N. \tag{6.5}$$

Thus the family of finite element spaces on the evolving domain  $\mathbb{V}^n \subset H^1(\Omega_{t_n}) \quad n = 1, \dots, N$  may be defined as,

$$\mathbb{V}^n := \{\Psi^n \in H^1(\Omega_{t_n}) : \Psi^n|_K \in \mathbb{P}^1 \text{ for all } K \in \mathcal{T}^n\}, \tag{6.6}$$

where we have used the fact that the domain evolution is linear with respect to space. We approximate the initial conditions in both schemes by

$$U^0 = \mathcal{I}u_0(\xi) \quad \text{for all } \xi \in \Omega_0, \tag{6.7}$$

where  $\mathcal{I}$  is the standard Lagrange interpolant. The finite element scheme to approximate the solution to Eq. (6.2) aims to find  $U_1^n, U_2^n \in \mathbb{V}^n, n = 1, \dots, N$  such that

$$\begin{cases} \frac{1}{\tau} \langle U_1^n, \Psi^n \rangle + \langle \nabla U_1^n, \nabla \Psi^n \rangle = \left\langle 0.1 - (U_2^{n-1})^2 U_1^n, \Psi^n \right\rangle + \frac{1}{\tau} \langle U_1^{n-1}, \Psi^{n-1} \rangle, \\ \frac{1}{\tau} \langle U_2^n, \Psi^n \rangle + 0.01 \langle \nabla U_2^n, \nabla \Psi^n \rangle = \langle 0.9 - U_2^n + U_2^{n-1} U_1^n U_2^n, \Psi^n \rangle + \frac{1}{\tau} \langle U_2^{n-1}, \Psi^{n-1} \rangle, \end{cases} \tag{6.8}$$

for all  $\Psi^n \in \mathbb{V}^n, n = 1, \dots, N$ . Similarly the finite element scheme to approximate the solution to Eq. (6.3) aims to find  $W_1^n, W_2^n \in \mathbb{V}^0, n = 1, \dots, N$  such that

$$\begin{cases} \frac{1}{\tau} \langle W_1^n - W_1^{n-1}, \Phi \rangle + \frac{1}{(\rho^n)^2} \langle \nabla W_1^n, \nabla \Phi \rangle + \frac{2\hat{\rho}^n}{\rho^n} \langle W_1^n, \Phi \rangle \\ \quad = \left\langle 0.1 - (W_2^{n-1})^2 W_1^n, \Phi \right\rangle, \\ \frac{1}{\tau} \langle W_2^n - W_2^{n-1}, \Phi \rangle + \frac{0.01}{(\rho^n)^2} \langle \nabla W_2^n, \nabla \Phi \rangle + \frac{2\hat{\rho}^n}{\rho^n} \langle W_2^n, \Phi \rangle \\ \quad = \langle 0.9 - W_2^n + W_2^{n-1} W_1^n W_2^n, \Phi \rangle, \end{cases} \tag{6.9}$$

for all  $\Phi \in \mathbb{V}^0$ .

We solved the models in C utilising the FEM library ALBERTA by Schmidt and Siebert (2005). We used the conjugate gradient solver to compute our discrete solutions. We took an initial triangulation  $\mathcal{T}^0$  with 8321 nodes, a uniform mesh diameter of  $2^{-6}$  and a fixed timestep of  $10^{-3}$ . PARAVIEW was used to display our results.

## 6.4 Results

Figures 1 and 2 show snapshots of the activator profile corresponding to the *activator-depleted* system (5.15). The inhibitor profiles have been omitted as they are  $180^\circ$  out of phase to the activator profiles. We have verified numerically that there is very little difference between the discrete solution corresponding to system (6.8) mapped to the fixed domain and the discrete solution corresponding to system (6.9) defined on a fixed domain, as is expected from the results in Sect. 2.2.

The figures illustrate the mode doubling phenomena that occurs as the domain grows as well as the spot annihilation and spot merging phenomena that occurs as the domain contracts. In Fig. 3 we present in more detail the novel spot merging phenomena observed on the contracting domain. It is still unclear whether the spot merging phenomenon is in fact a special case of the spot annihilation phenomenon, that occurs when the modes are of sufficient proximity to influence each other.

We note that the mode transition sequence, i.e., the number of spots, is different when the domain grows to when it contracts. The difference in the mechanism of mode transitions on growing and contracting domains is an area in which very little work has been done and these initial numerical results indicate the need for further exploration of this area.

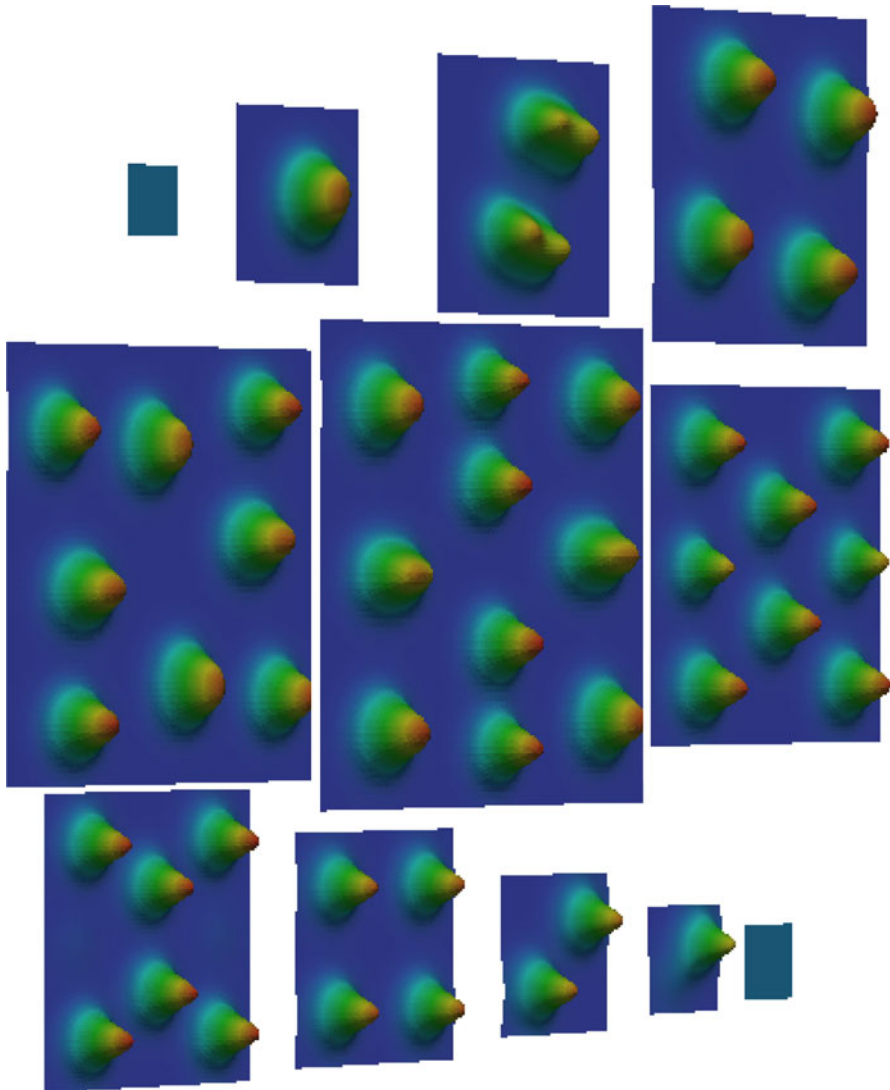
## 7 Conclusion

Many problems in biology and biomedicine involve growth. In developmental biology recent advances in experimental data collection allow experimentalists to capture the emergence of pattern structure formation during growth development of the organism or species. Such experiments include the formation of spot patterns on the surface of the eel, patterns emerging on the surface of the Japanese flounder and butterfly wing patterns forming during the growth development of the imaginal wing disc. In all these examples, patterns form during growth development.

Since the seminal paper by Turing (1952) which considered linear models that could give rise to spatiotemporal solutions on fixed domains due the process of diffusion-driven instability, a lot of theoretical results on global existence of such solutions have been derived and proved for highly nonlinear mathematical models (Smoller 1994; Rothe 1984). Only recently, mathematical models on growing domains have been derived from first principles in order to incorporate the effects of domain evolution into the models (Madzvamuse 2000; Crampin et al. 1999). In all these studies, very little analysis has been done up to now to extend the theoretical global existence results to models defined on evolving domains.

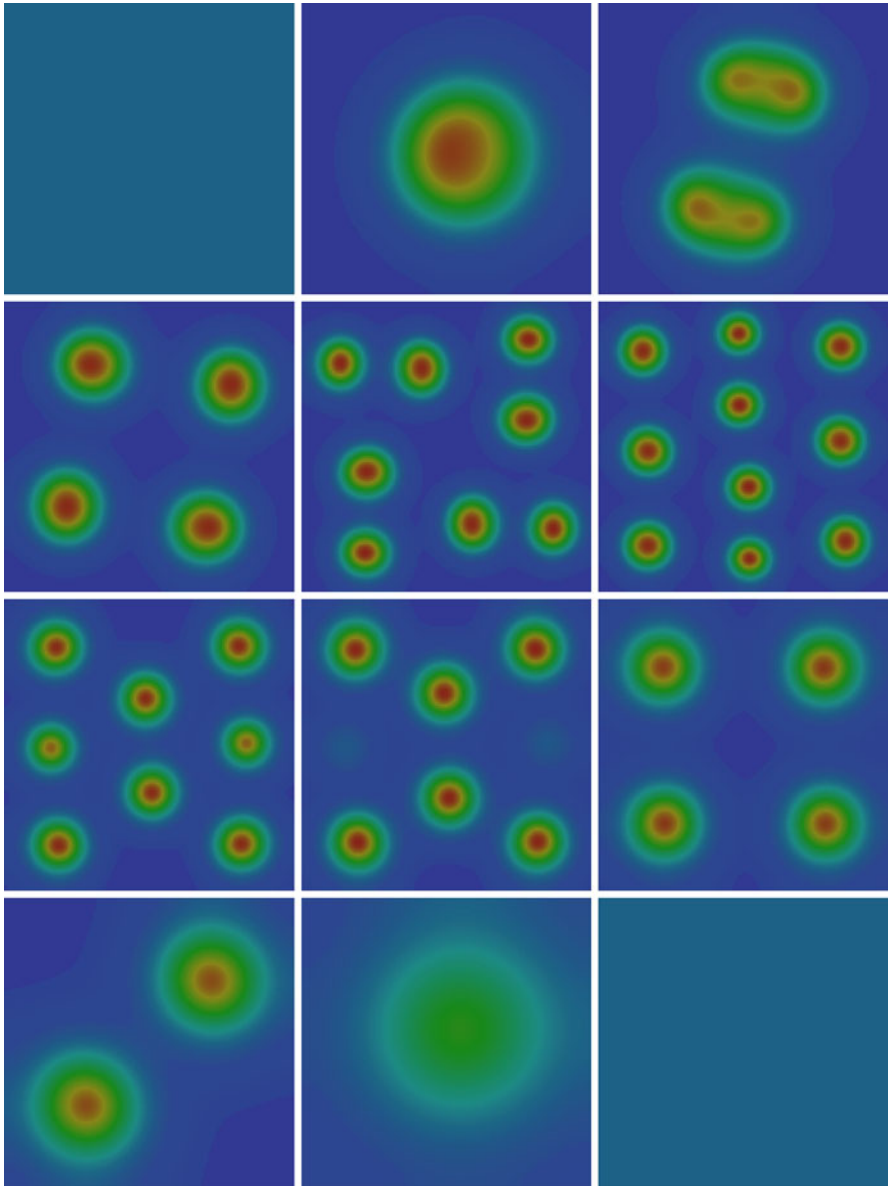
Under suitable assumptions, we have extended existence results from problems posed on fixed domains to problems posed on an evolving domain. We have illustrated





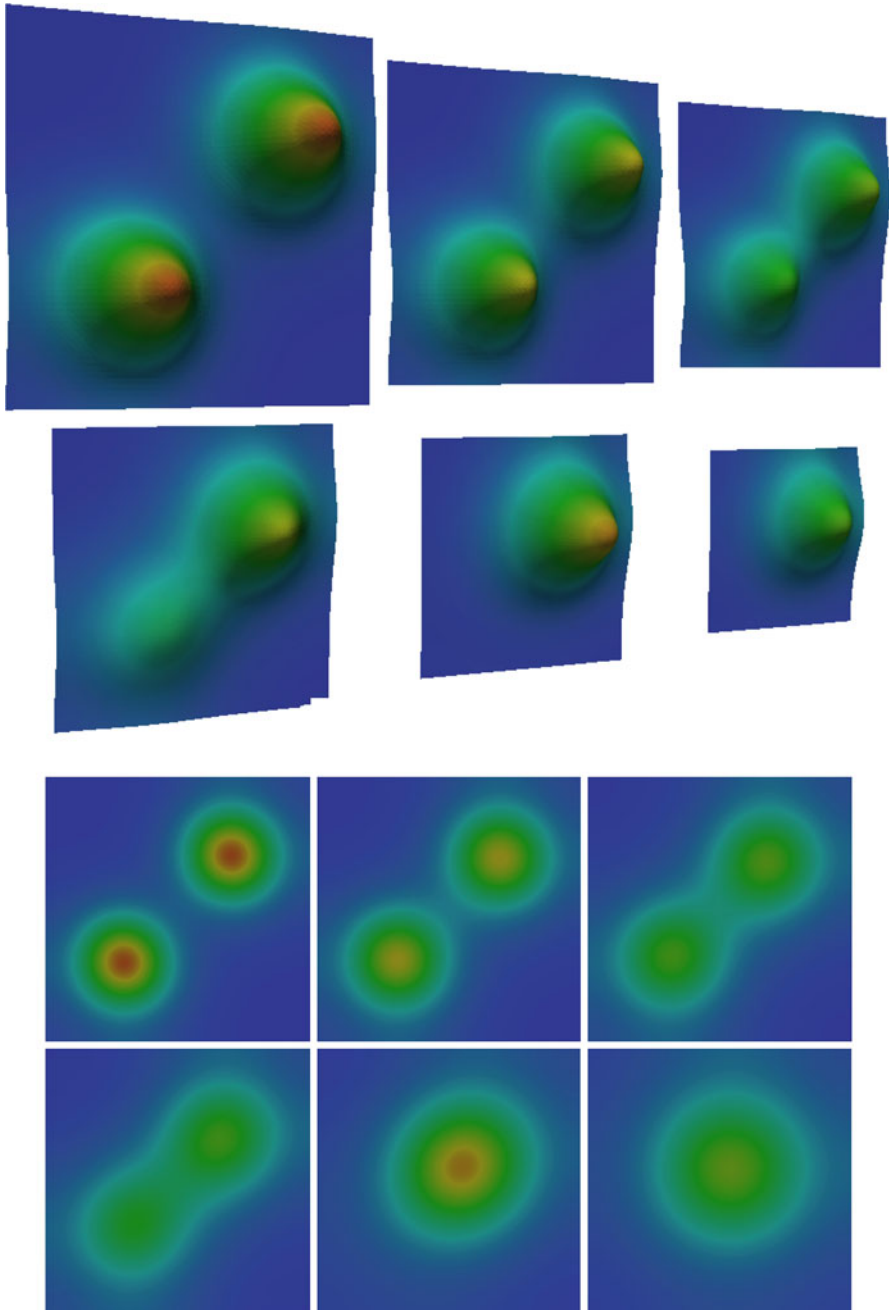
**Fig. 1** Snapshots of the discrete solution  $U_2$  corresponding to system (6.8) at times 0, 50, 160, 220, 380, 500, 700, 740, 820, 900, 980 and 1,000 reading from *left to right* and then *top to bottom*. For parameter and numerical values see Sect. 6.3. The solution exhibits a mode doubling sequence of 1, 2, 4, 8 and finally 10 as the domain grows. As the domain contracts the spots are annihilated in a sequence of 8, 6, 4, 2 and the final transition to a single spot occurs via merging, with the final domain exhibiting no patterns

the applicability of the existence results of [Morgan \(1989\)](#) to problems on evolving domains. We have shown that global existence of solutions to many commonly encountered RDS's on fixed domains implies global existence of solutions to the same RDS's on a class of evolving domains. The results are significant in the theory of pattern formation especially in fields such as developmental biology where problems posed on



**Fig. 2** Snapshots of the discrete solution  $W_2$  corresponding to system (6.9) at times 0, 50, 160, 220, 380, 500, 700, 740, 820, 900, 980 and 1,000 reading from *left to right* and then *top to bottom*. For parameter and numerical values see Sect. 6.3. The mode transition follows exactly that of Fig. 1, corroborating the results in Sect. 2.2

evolving domains are commonly encountered. Our results hold with no assumptions on the sign of the growth rate, which may prove useful in other fields where monotonic domain growth is not valid from a modelling perspective. The applicability of



**Fig. 3** Snapshots of the discrete solution corresponding to system (6.8) (*top*) and system (6.9) (*bottom*) at times 930, 940, 950, 955, 965, 975. The spot merging phenomena observed in the transition from two spots to one spot is displayed

our results is demonstrated by considering different forms of domain evolution (linear, logistic and exponential).

In order to validate our theoretical findings, we presented results on a periodically evolving domain. Our results illustrate the well-known period-doubling phenomenon during domain growth but more interesting and surprising is the development of spot annihilation and spot merging phenomena during contraction. This raises new questions about bifurcation analysis on growing and contracting domains.

One of our primary goals is the numerical analysis of finite element approximations of RDS's on evolving domains. The classical existence results obtained will be an important tool in future work. Numerical experiments have been carried out and they illustrate the need for further numerical analysis especially in the case of contracting domains. Extension of our work onto domains with more complex evolution is another area for future research.

**Acknowledgments** The authors would like to thank the anonymous reviewers whose positive comments have improved parts of the article. The research of C.Venkataraman is partially supported by an EPSRC doctoral training grant and a University of Sussex graduate teaching assistantship. C. Venkataraman and O. Lakkis would like to thank the Hausdorff Center for Mathematics (Lipschitz lectures) and the Hausdorff Research Institute for Mathematics, in Bonn, for the support, training and hospitality provided for part of this research. A. Madzvamuse would like to acknowledge support from the EPSRC grant: *Mathematical modelling of spatial patterning on evolving surfaces* (EP/H020349/1) and the LMS grant (R4P2), both of which were in support of the visit by Professor T. Sekimura as well as support from the Royal Society grant, 2009/R1.

## Appendix A: A priori estimates for systems with time dependent reaction kinetics

In this section we prove Theorem 3.7 remains applicable for solutions of Problem (2.8). For conciseness we focus on assertion (3.14). We adapt the proof of Morgan (1989, Th. 3.2) to our purposes. In Appendix B, we use the a priori estimates obtained in this section to prove the global existence of classical solutions to Problem (2.8). We state the main result of this section in the following Lemma.

**Lemma A.1** (An a priori estimate for solutions of Problem (2.8)) *Suppose Assumptions 2.3, 3.4 and 4.1 hold and let (3.8)–(3.10) and (3.13) hold. Then, assertion (3.14) is valid with  $\tilde{u}$  a solution of Problem (2.8).*

*Proof* Let  $\tilde{f}$  be as defined in (4.2). From the proof of Lemma 4.1, (4.7) holds. We split the remainder of the proof into steps.

*Step 1:* We first show the following inequality for  $H$ :

$$\begin{aligned}
 H(\tilde{u}(\xi, t)) &\leq \int_{\tau}^t \sum_{i=1}^m D_i \Delta_{\xi} h_i(\tilde{u}_i(\xi, r)) + (k_5 C_1^2 + k_{12}) H(\tilde{u}(\xi, r)) dr \\
 &\quad + H(\tilde{u}(\xi, \tau)) + k_6 C_1^2(t - \tau) \quad \text{for } \xi \in \Omega_0 \text{ and } t < T_{\max}.
 \end{aligned}
 \tag{A.1}$$

From (2.8) we have for  $(\xi, t) \in \Omega_0 \times (0, T_{\max})$ ,

$$\nabla H(\tilde{u}(\xi, t)) \cdot \partial_t \tilde{u}(\xi, t) = \nabla H(\tilde{u}(\xi, t)) \cdot \left( D \Delta \tilde{u}(\xi, t) + \tilde{f}(\tilde{u}(\xi, t), t) \right). \tag{A.2}$$

Using (3.8), (4.7) and (A.2) we obtain the following generalisation of Morgan (1989, (3.1)),

$$\begin{aligned} \nabla H(\tilde{u}(\xi, t)) \cdot \partial_t \tilde{u}(\xi, t) &\leq \sum_{i=1}^m D_i \Delta_{\xi} h_i(\tilde{u}_i(\xi, t)) \\ &\quad + \left( k_5 C_1^2 + k_{12} \right) H(\tilde{u}(\xi, t)) + k_6 C_1^2, \end{aligned} \tag{A.3}$$

where we have used the convexity of  $H$  (3.9). Integrating (A.3) in time gives (A.1).

*Step 2:* We use (A.1) to construct an appropriate barrier function with a view to applying the maximum principle, corresponding to Morgan (1989, (3.2)–(3.4)). Introducing an arbitrary  $T^* < T_{\max}$ , we define

$$w(\xi, t) := \int_{\tau}^t \sum_{i=1}^m \frac{D_i}{D^*} h_i(\tilde{u}_i(\xi, r)) \, dr \text{ for } \xi \in \Omega_0 \text{ and } 0 \leq \tau < t \leq T^*, \tag{A.4}$$

where  $D^* := \max_i(D_i)$ . Observe that from (3.8) and (A.4), we have for  $0 \leq \tau < t \leq T^*$

$$\begin{aligned} \left\| \int_{\tau}^t H(\tilde{u}(\cdot, s)) \, ds \right\|_{L_{\infty}(\Omega_0)} &= \left\| \int_{\tau}^t \sum_{i=1}^m h_i(\tilde{u}_i(\cdot, s)) \, ds \right\|_{L_{\infty}(\Omega_0)} \\ &\leq \max_i \left( \frac{D^*}{D_i} \right) \|w(\cdot, s)\|_{L_{\infty}(\Omega_0)}. \end{aligned} \tag{A.5}$$

From (A.1) and (A.4) we obtain

$$\begin{cases} \partial_t w(\xi, t) \leq D^* \Delta w(\xi, t) + L \\ \quad + M w(\xi, t) + k_6 C_1^2 (t - \tau), & \xi \in \Omega_0, 0 \leq \tau < t \leq T^* \\ [\mathbf{v} \cdot \nabla w](\xi, t) = 0, & \xi \in \partial \Omega_0, t \in (\tau, T^*] \\ w(\xi, \tau) = 0, & \xi \in \Omega_0, \end{cases} \tag{A.6}$$

where

$$L := \|H(\tilde{u}(\cdot, \tau))\|_{L^\infty(\Omega_0)} \text{ and } M := \frac{(k_{12} + C_1^2 k_5) D^*}{\min_i (D_i)}. \tag{A.7}$$

Note we have used (2.8) to obtain the boundary conditions. For the purposes of applying the maximum principle we define a barrier function

$$\hat{w}(\xi, t) := w(\xi, t) - \frac{L + K_6 C_1^2 T^*}{M} \text{ for } \xi \in \Omega_0 \text{ and } 0 \leq \tau < t \leq T^*. \tag{A.8}$$

From (A.6) and (A.4) we have

$$\begin{cases} \partial_t \hat{w}(\xi, t) \leq D^* \Delta \hat{w}(\xi, t) + M \hat{w}(\xi, t) & \xi \in \Omega_0, 0 \leq \tau < t \leq T^* \\ [\mathbf{v} \cdot \nabla \hat{w}](\xi, t) = 0, & \xi \in \partial\Omega_0, t \in (\tau, T^*] \\ \hat{w}(\xi, \tau) \leq 0, & \xi \in \Omega_0. \end{cases} \tag{A.9}$$

*Step 3:* We use the maximum principle to complete the proof. Applying the strong maximum principle for parabolic problems (Sperb 1981, Th. 2.9, Rem. (a), p. 21) to (A.9) and noting the positivity of  $w$ , we have

$$-\frac{L + K_6 C_1^2 T^*}{M} \leq \hat{w}(\xi, t) \leq 0 \text{ for all } \xi \in \Omega_0 \text{ and for } t \in (\tau, T^*]. \tag{A.10}$$

From (A.8) and (A.10) we have

$$0 \leq \hat{w}(\xi, t) \leq \frac{L + K_6 C_1^2 T^*}{M} \text{ for all } \xi \in \Omega_0 \text{ and for } t \in (\tau, T^*]. \tag{A.11}$$

We conclude from (A.11) that

$$\|w(\cdot, t)\|_{L^\infty(\Omega_0)} \leq \frac{L + K_6 C_1^2 T^*}{M} \text{ for } t \in (\tau, T^*]. \tag{A.12}$$

Since  $T^*$  was arbitrary, combining (A.5) and (A.12) completes the proof of the Lemma. □

For completeness, we sketch the proof of assertion (3.15) with  $\tilde{u}$  a solution of Problem (2.8). In (A.3) we denote  $K_7 := k_5 C_1^2 + k_{12}$  and  $K_8 := k_6 C_1^2$ , where  $K_7, K_8$  correspond to the terms on the right hand side of Morgan 1989, (3.1). Assertion (3.15) follows from the proofs of Morgan 1989, Th. 3.3 and 3.4.

### Appendix B: Global existence results for systems with time dependent reaction kinetics

The main result of this section is Theorem B.4, a special case of Theorem 3.8. It is applicable to solutions of Problem (2.8). Theorem B.4 is enough for our purposes

as seen in the examples in Sect. 5. To prove the Theorem, we will modify the proof of Morgan (1989, Th. 2.2) with stronger control of the parameter  $r$ , that appears in (3.11).

We start with two Lemmas from Morgan (1989, Lem. 4.1, Lem. 4.2, (4.12)) which follow from the results of Ladyzhenskaya et al. (1968)[Th. 9.1, p. 341]. We then use a duality approach to prove global existence of classical solutions to (2.8).

**Lemma B.1** (Global existence) *Let  $\tilde{u}$  be the solution of Problem (2.8). Let the function  $H$  fulfil conditions (3.8)–(3.10) in Sect. 3.6 and let the polynomial growth restriction on  $\tilde{f}$  (4.6) hold. Let  $T_{\max}$  be as defined in (3.1) and suppose that,*

$$\left\{ \begin{array}{l} \text{for } 0 \leq \tau < T < T_{\max} \text{ and for all } p \in (1, \dots, \infty) \\ \text{there exist } M_p, N_p > 0 \text{ and } 0 < \delta_p < 1 \text{ such that} \\ \sum_{i=1}^m \|h_i(\tilde{u}_i)\|_{L_p(\Omega_0 \times (\tau, T))} \leq M_p(T - \tau) + N_p(T - \tau) \|H(\tilde{u})\|_{L_p(\Omega_0 \times (\tau, T))}^{\delta_p}, \end{array} \right. \tag{B.1}$$

then  $T_{\max} = \infty$ .

**Definition B.2** (Dual problem) A key ingredient of the proof of Theorem B.4 is the dual solution  $\psi$ . Where for  $i = 1, \dots, m$ ,  $\psi$  is the solution of the scalar equation

$$\left\{ \begin{array}{ll} \partial_t \psi(\xi, t) = -D_i \Delta \psi(\xi, t) - \theta(\xi, t) & \text{for } \xi \in \Omega_0 \text{ and } 0 \leq t < T < T_{\max} \\ [\mathbf{v} \cdot \nabla \psi](\xi, t) = 0, & \xi \in \partial\Omega_0, t \in [0, T) \\ \psi(\xi, T) = 0, & \xi \in \Omega_0, \end{array} \right. \tag{B.2}$$

where  $\theta \geq 0$  is such that, for all  $p \in (1, \dots, \infty)$ ,  $\|\theta\|_{L_p(\Omega_0 \times [0, T])} = 1$ .

**Lemma B.3** (Control of the solution to the dual problem (B.2)) *Let  $\psi$  be as defined in B.2. For  $i = 1, \dots, m$  and for  $p \in (1, \dots, \infty)$ , there exists  $C_{p,T} > 0$  such that,*

$$\|\psi\|_{L_p(\Omega_0; L_\infty[0, T])} \leq C_{p,T} \tag{B.3}$$

We now state the main result of this section. Namely, the applicability of a special case of Theorem 3.8 to solutions of Problem (2.8).

**Theorem B.4** (Sufficient conditions for global existence of solutions to Problem (2.8)) *Let Assumptions 2.3, 3.4 and 4.1 hold. Let  $H$ ,  $\tilde{f}$  and  $r$  satisfy the conditions in Sect. 3.6 with  $r \leq 1$  (cf. (3.11)), i.e., Problem (3.4) admits a global classical solution by Theorem 3.8. Then, Problem (2.8) admits a global classical solution, i.e.,  $T_{\max} = \infty$  (cf. (3.1)).*

*Proof* We proceed by contradiction. Assume  $T_{\max} < \infty$ . Let  $\tilde{u}$  and  $\tilde{f}$  (cf. 4.2) be the solution and zero order term of Problem (2.8) respectively. From the proof of Lemma 4.3 the polynomial growth restriction (4.6) is satisfied by  $\tilde{f}$  and  $H$ . Since  $T_{\max} < \infty$ , Lemma B.1 implies that (B.1) does not hold. Let  $j \in [1, \dots, m]$  denote the smallest  $k$  for which  $\sum_{i=1}^k \|h_i(\tilde{u}_i)\|_{L_p(\Omega_0 \times (\tau, T))}$  does not satisfy (B.1). From the proof of Lemma 4.3, the intermediate sum condition (4.5) is satisfied for with  $\tilde{r} = 1$  (cf. (4.5)). From Lemma A.1, we have the a priori estimate (3.14).

We will show (3.14) and (4.5) imply (B.1) is satisfied for  $j$ , obtaining a contradiction. We split the remainder of the proof into steps.

Step 1: We first show the following inequality [corresponding to Morgan (1989, (4.6)–(4.9))]: For  $0 < T < T_{\max}$

$$\begin{aligned}
 & \int_{\Omega_0} \int_0^T \sum_{i=1}^j a_{ji} \frac{D_i}{D_j} h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds \\
 & \leq \int_0^T \int_{\Omega_0} \sum_{i=1}^{j-1} a_{ji} \left(1 - \frac{D_i}{D_j}\right) h_i(\tilde{u}_i(\xi, s)) \partial_s \psi(\xi, s) \\
 & \quad + \psi(\xi, s) \left( (k_1 C_1^2 + k_7) H(\tilde{u}(\xi, s)) + k_8 \right) ds \\
 & \quad + \sum_{i=1}^j a_{ji} \psi(\xi, 0) h_i(\tilde{u}_i^0(\xi)) d\xi \\
 & := I_1 + I_2 + I_3.
 \end{aligned}
 \tag{B.4}$$

From (B.2) we have for  $i \in [1, \dots, m]$

$$\begin{aligned}
 \int_0^T \int_{\Omega_0} h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds &= \int_0^T \int_{\Omega_0} -h_i(\tilde{u}_i(\xi, s)) \\
 & \quad [\partial_s \psi + D_j \Delta \psi](\xi, s) d\xi ds \\
 & \leq \int_0^T \int_{\Omega_0} -h_i(\tilde{u}_i(\xi, s)) \partial_s \psi(\xi, s) \\
 & \quad - \frac{D_j}{D_i} \psi(\xi, s) D_i \Delta_{\xi} h_i(\tilde{u}_i(\xi, s)) d\xi ds,
 \end{aligned}
 \tag{B.5}$$

where we have used integration by parts and the homogenous Neumann boundary conditions. From Problem (2.8) and the convexity of  $H$  (3.9), we have

$$\begin{aligned}
 & - \int_0^T \int_{\Omega_0} \psi(\xi, s) D_i \Delta_{\xi} h_i(\tilde{u}_i(\xi, s)) d\xi ds \\
 & \leq \int_0^T \int_{\Omega_0} \psi(\xi, s) h'_i(\tilde{u}_i(\xi, s)) \left( \tilde{f}_i(\tilde{u}(\xi, s), s) - \partial_s \tilde{u}_i(\xi, s) \right) d\xi ds \\
 & = \int_0^T \int_{\Omega_0} \psi(\xi, s) h'_i(\tilde{u}_i(\xi, s)) \tilde{f}_i(\tilde{u}(\xi, s), s)
 \end{aligned}$$



$$+h_i(\tilde{u}_i(\xi, s)) \partial_s \psi(\xi, s) d\xi ds + \int_{\Omega_0} \psi(\xi, 0) h_i(\tilde{u}_i^0(\xi)) d\xi, \tag{B.6}$$

where we have used integration by parts and the final condition of (B.2). Combining (B.6) and (B.5), we obtain

$$\begin{aligned} \int_0^T \int_{\Omega_0} h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds &\leq \int_{\Omega_0} \int_0^T \left( \frac{D_j}{D_i} - 1 \right) h_i(\tilde{u}_i(\xi, s)) \partial_s \psi(\xi, s) \\ &\quad + \frac{D_j}{D_i} \psi(\xi, s) h'_i(\tilde{u}_i(\xi, s)) \tilde{f}_i(\tilde{\mathbf{u}}(\xi, s), s) ds \\ &\quad + \frac{D_j}{D_i} \psi(\xi, 0) h_i(\tilde{u}_i^0(\xi)) d\xi. \end{aligned} \tag{B.7}$$

Summing (B.7) over  $i \leq j$  and using condition (4.5) with  $\tilde{r} = 1$ , we obtain (B.4). For the case  $j = 1$ , we have introduced the convention  $\sum_{i=1}^0 (\cdot) = 0$ . *Step 2:* We shall use Lemma B.3 and (B.4) to obtain the following inequality (as in Morgan (1989, (4.10)–(4.16))): For all  $p \in (1, \dots, \infty)$  there exists  $K_{p,T} > 0$  and  $0 < \delta_p < 1$  independent of  $\tilde{\mathbf{u}}$  and  $\theta$  such that,

$$\int_0^T \int_{\Omega_0} \sum_{i=1}^j a_{ji} \frac{D_i}{D_j} h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds \leq K_{p,T} \left( 1 + \|H(\tilde{\mathbf{u}})\|_{L_p(\Omega_0 \times [0, T])}^{\delta_p} \right). \tag{B.8}$$

Let  $p, q \in (1, \dots, \infty)$  be such that,  $\frac{1}{p} + \frac{1}{q} = 1$ . Dealing firstly with  $I_1$  (cf. (B.4)), we have by Hölder’s inequality and the regularity estimate (B.3)

$$\begin{aligned} I_1 &\leq \sum_{i=1}^{j-1} a_{ji} \left| 1 - \frac{D_i}{D_j} \right| C_{q,T} T \|h_i(\tilde{u}_i)\|_{L_p(\Omega_0 \times [0, T])} \\ &\leq \sum_{i=1}^{j-1} a_{ji} \left| 1 - \frac{D_i}{D_j} \right| C_{q,T} T \left( M_p + N_p \|H(\tilde{\mathbf{u}})\|_{L_p(\Omega_0 \times [0, T])}^{\delta_q} \right), \end{aligned} \tag{B.9}$$

where we have the assumption that (B.1) is valid for  $i < j$ . Dealing with  $I_2$ , we have by Hölder’s inequality and the regularity estimate (B.3)

$$\begin{aligned}
I_2 &\leq \int_{\Omega_0} \|\psi(\xi, \cdot)\|_{L^\infty[0,T]} \left( \int_0^T ((k_1 C_1^2 + k_7)H(\tilde{\mathbf{u}}(\xi, s)) + k_8 ds) \right) d\xi \\
&\leq C_{q,T} \left( (k_1 C_1^2 + k_7) \left\| \int_0^T H(\tilde{\mathbf{u}}(\cdot, s)) \right\|_{L_q(\Omega_0)} + k_8 T \right) \\
&\leq C_{q,T} \left( g(T) |\Omega_0|^{1/p} + k_8 T \right), \tag{B.10}
\end{aligned}$$

for some  $g \in C[0, \infty)$ . Where we have used the a priori estimate (3.14). Finally dealing with  $I_3$  using Hölder's inequality and estimate (B.3) we have

$$\begin{aligned}
I_3 &\leq \sum_{i=1}^j a_{ji} C_{q,T} \|h_i(\tilde{u}_i^0)\|_{L_p(\Omega_0 \times [0,T])} \\
&\leq \sum_{i=1}^j a_{ji} C_{q,T} C_p, \tag{B.11}
\end{aligned}$$

where we have used the boundedness of  $\tilde{\mathbf{u}}^0$  and condition (3.9). Combining (B.9), (B.10), (B.11) and (B.4) yields (B.8).

*Step 3:* We now show (B.1) holds for  $j$ . Let  $p, q \in (1, \dots, \infty)$ , be such that,  $\frac{1}{p} + \frac{1}{q} = 1$ . We recall, from (3.9) and Definition B.2, that for  $i \in [1, \dots, m]$ ,  $h_i, \theta \geq 0$  and  $\|\theta\|_{L_q(\Omega_0 \times (0,T))} = 1$ . Using duality we obtain

$$\begin{aligned}
&\min_{i \leq j} \left( a_{ji} \frac{D_i}{D_j} \right) \sum_{i=1}^j \|h_i(\tilde{u}_i)\|_{L_p(\Omega_0 \times (0,T))} \\
&= \min_{i \leq j} \left( a_{ji} \frac{D_i}{D_j} \right) \int_0^T \int_{\Omega_0} \sum_{i=1}^j h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds \\
&\leq \int_0^T \int_{\Omega_0} \sum_{i=1}^j a_{ji} \frac{D_i}{D_j} h_i(\tilde{u}_i(\xi, s)) \theta(\xi, s) d\xi ds \\
&\leq K_{p,T} \left( 1 + \|H(\tilde{\mathbf{u}})\|_{L_p(\Omega_0 \times [0,T])}^{\delta_p} \right), \tag{B.12}
\end{aligned}$$

where we have used (B.8).

Thus we have a contradiction and we conclude  $T_{\max} = \infty$  completing the proof.  $\square$

The proof of Theorem 3.8 follows from more technical use of Hölder's inequality in (B.10) and in the case of assertion (3.17) we also require the a priori estimate (3.15). We refer to Morgan (1989, (4.13)–(4.16) and (4.27)–(4.19)) for specific details.

## References

- Acheson D (1990) Elementary fluid dynamics. Oxford University Press, New York
- Baines M (1994) Moving finite elements. Oxford University Press, New York
- Barras I, Crampin E, Maini P (2006) Mode transitions in a model reaction–diffusion system driven by domain growth and noise. *Bull Math Biol* 68(5):981–995
- Bendahmane M, Saad M (2010) Mathematical analysis and pattern formation for a partial immune system modeling the spread of an epidemic disease. *Acta Appl Math* 1–26. doi:10.1007/s10440-010-9569-3
- Comanici A, Golubitsky M (2008) Patterns on growing square domains via mode interactions. *Dyn Syst* 23(2):167–206
- Crampin E, Gaffney E, Maini P (1999) Reaction and diffusion on growing domains: scenarios for robust pattern formation. *Bull Math Biol* 61(6):1093–1120
- Crampin E, Gaffney E, Maini P (2002) Mode-doubling and tripling in reaction–diffusion patterns on growing domains: a piecewise linear model. *J Math Biol* 44(2):107–128
- Garvie M, Trenchea C (2009) Spatiotemporal dynamics of two generic predator–prey models. *J Biol Dyn* 4(6):559–570
- Gierer A, Meinhardt H (1972) A theory of biological pattern formation. *Biol Cybern* 12(1):30–39
- Hollis S, Martin R Jr, Pierre M (1987) Global existence and boundedness in reaction–diffusion systems. *SIAM J Math Anal* 18:744
- Kelkel J, Surulescu C (2009) A weak solution approach to a reaction–diffusion system modeling pattern formation on seashells. *Math Methods Appl Sci* 32:2267–2286
- Kondo S, Asai R (1995) A reaction–diffusion wave on the skin of the marine angelfish *Pomacanthus*. *Nature* 376(6543):765–768
- Labadie M (2008) The stabilizing effect of growth on pattern formation. Preprint
- Ladyzhenskaya O, Solonnikov V, Ural'tseva N (1968) Linear and quasilinear equations of parabolic type. Am Math Soc. Providence
- Lefever R, Prigogine I (1968) Symmetry-breaking instabilities in dissipative systems II. *J Chem Phys* 48:1695–1700
- Madzvamuse A (2000) A numerical approach to the study of spatial pattern formation. PhD thesis, University of Oxford
- Madzvamuse A (2006) Time-stepping schemes for moving grid finite elements applied to reaction–diffusion systems on fixed and growing domains. *J Comput Phys* 214(1):239–263
- Madzvamuse A, Maini P (2007) Velocity-induced numerical solutions of reaction–diffusion systems on continuously growing domains. *J Comput Phys* 225(1):100–119
- Madzvamuse A, Gaffney E, Maini P (2010) Stability analysis of non-autonomous reaction–diffusion systems: the effects of growing domains. *J Math Biol* 61(1):133–164
- Morgan J (1989) Global existence for semilinear parabolic systems. *SIAM J Math Anal* 20:1128
- Morgan J, Hollis S (1995) The existence of periodic solutions to reaction–diffusion systems with periodic data. *SIAM J Math Anal* 26(5):1225–1232
- Murray J (2003) Mathematical biology. Springer-Verlag, New York
- Rothe F (1984) Global solutions of reaction–diffusion systems. Lecture notes in mathematics, vol 1072
- Schmidt A, Siebert K (2005) Design of adaptive finite element software: the finite element toolbox ALBERTA. Springer-Verlag, New York
- Schnakenberg J (1979) Simple chemical reaction systems with limit cycle behaviour. *J Theor Biol* 81(3):389
- Smoller J (1994) Shock waves and reaction–diffusion equations. Springer, New York
- Sperb R (1981) Maximum principles and their applications. Academic Press, New York
- Thomas D (1975) Artificial enzyme membranes, transport, memory, and oscillatory phenomena. In: Analysis and control of immobilized enzyme systems, pp 115–150
- Turing A (1952) The chemical basis of morphogenesis. *Phil R Soc* 237(641):37–72
- Wei J, Winter M (2008) Stationary multiple spots for reaction–diffusion systems. *J Math Biol* 57(1):53–89