IDENTIFICATION OF SPACE-TIME DISTRIBUTED PARAMETERS IN THE GIERER–MEINHARDT REACTION-DIFFUSION SYSTEM

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Abstract. We consider parameter identification for the classic Gierer–Meinhardt reaction-diffusion system. The original Gierer–Meinhardt model [A. Gierer and H. Meinhardt, Kybernetik, 12 (1972), pp. 30–39] was formulated with constant parameters and has been used as a prototype system for investigating pattern formation in developmental biology. In our paper the parameters are extended in time and space and used as distributed control variables. The methodology employs PDE-constrained optimization in the context of image-driven spatiotemporal pattern formation. We prove the existence of optimal solutions, derive an optimality system, and determine optimal solutions. The results of numerical experiments in two dimensions are presented using the finite element method, which illustrates the convergence of a variable-step gradient algorithm for finding the optimal parameters of the system. A practical target function is constructed for the optimal control algorithm corresponding to the actual image of a marine angelfish.

Key words. optimal control theory, parameter identification, reaction-diffusion equations, image-driven optimization, variable-step gradient algorithm, finite element method, Gierer–Meinhardt, pattern formation

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1. Introduction. Many processes in the applied sciences are adequately modeled by partial differential equations (PDEs) [19]. However, it is not always possible to measure, or calculate, the model parameters with the necessary accuracy, particularly in living organisms. In these cases, mathematical techniques for estimating model parameters become important. Parameter estimation is an important technique for identifying redundant parameters (and hence the key parameters) in complex systems with many parameters. It is also of interest to know for which parameters the model is most sensitive. This might be useful in practical problems because it could help us prioritize which parameters should be the focus of experimental investigation [23].

The need to identify parameters in evolution equations arises in many disciplines, including biology, physics, engineering, and chemistry. Much research has been devoted to the development of computational methods for estimating parameters in such equations (see, for example, [1, 2, 3, 4, 5, 10, 11, 14, 18, 31, 36, 45, 46, 53, 63] and the references therein). The typical procedure involves integrating the evolution equation to obtain a simulation result that is compared to an observed data set, and then applying least squares techniques to minimize a cost functional with respect to parameters in an admissible set [6, 21, 30, 34, 38, 39, 40, 50].

There are relatively few works that focus on parameter identification for reaction-diffusion (RD) equations [23, 25, 27, 28, 35], which is a fertile and growing area of research with many applications, for example, population dynamics [16, 39], synaptic...
transmission at a neuromuscular junction [13], color negative film development [20],
chemotaxis [17], epidemiology [37], and brain tumor growth [32].

Traditional studies of RD equations have focused on models with homogeneous
parameters, i.e., parameters that are constant in time and space. In reality, pa-
rameters often operate in heterogeneous environments. A number of authors have
considered RD models with spatially varying parameters [8, 41, 47, 48], or temporally
varying parameters [56, 61, 64], but to our knowledge none allow the parameters to
vary freely in time and space. By relaxing this assumption, and allowing the parameters
to vary in time and space, we apply an image-driven methodology for parameter
identification in RD equations with broad applicability. Another novel aspect of our
work is that the image used as data for the optimal control procedure is taken directly
from nature.

For concreteness, we illustrate our method by considering the identification prob-
lem for the two-component system of RD equations introduced by Gierer and Mein-
hardt [26] for pattern formation. The Gierer–Meinhardt system is one of the most
famous models in biological pattern formation. The original formulation has fixed
parameter values. We consider the more general situation where two key parameters,
\( \mu \) and \( \alpha \), depend on space \( x \) and time \( t \). In nondimensional form [47] the RD system
has the form

\[
\begin{align*}
\frac{\partial u}{\partial t} &= D_u \Delta u + \frac{ru^2}{v} - \mu(x,t)u + r, \\
\frac{\partial v}{\partial t} &= D_v \Delta v + ru^2 - \alpha(x,t)v,
\end{align*}
\]

with nonnegative parameters \( r, D_u, \) and \( D_v \) and nonnegative morphogen concentra-
tions \( u(x,t) \) and \( v(x,t) \). \( \Delta \) denotes the standard Laplacian operator in two space
dimensions.

The Gierer–Meinhardt model with constant coefficients is of the activator-inhibitor
type and was originally used to model the regenerative properties of hydra. The model
derivation is given in [26]. The parameters \( \mu \) and \( \alpha \) model the removal rates from
the system of the activator \( u(x,t) \) and inhibitor \( v(x,t) \), respectively. We generalize
the investigations in [47, 48] to consider the case that these removal rates vary in
both space and time. We comment that the mechanisms leading to patterning in
developmental biology are not well understood, and so all Turing models for this area
are essentially hypothetical (since the appearance of Turing’s seminal work [62] on
diffusion-induced instability in 1952, not a single work has conclusively demonstrated
the Turing mechanism in biological systems [47]). Thus like many other researchers,
we used this system as a prototype system for pattern formation, and so the precise
meaning of the parameters is not important.

When the parameters in the Gierer–Meinhardt model are appropriately chosen,
the mechanism of diffusion-induced instability, or Turing mechanism [62], leads to
morphogen concentrations with characteristic regular spacing of peaks and troughs (a
pattern) [26]. The identification problem for the case of constant parameters \( \mu, \alpha \) was
treated in [23]. The model that we use with heterogeneous parameters generalizes the
research of Page, Maini, and Monk [47, 48], who investigated the Gierer–Meinhardt
model with a spatially varying parameter \( \mu(x) \). Their investigations demonstrated
that the Gierer–Meinhardt model could produce spatial pattern formation outside
the classical Turing space parameter regime for patterning. Our paper builds on this
work by investigating the potential for patterning in the Gierer–Meinhardt model with
two space-time varying parameters \( \mu(x,t) \) and \( \alpha(x,t) \). Typical numerical solutions
of the Gierer–Meinhardt system (1.1) for spatially homogeneous and inhomogeneous parameters are shown in Figure 1.1.

The main purpose of our work is not modeling of biological problems, but rather to outline a general procedure for parameter identification in nonlinear RD equations that uses an image-driven PDE-constrained optimization technique. This is a general procedure that can be applied to a variety of problems, and the success or usefulness of the procedure depends on how well the problem models the situation from which the image data is taken. The Gierer–Meinhardt model that we used to illustrate the methodology is a hypothetical model for patterning in developmental biology, and so we needed a lot of flexibility in the control parameters in order for the controlled solutions to match the data. Nevertheless, the procedure still yielded useful information.

The remainder of this paper is structured as follows. In section 2, the well-posedness of the direct problem is discussed, while in section 3, a cost functional is defined that allows us to set up the inverse problem. In section 4, we establish the existence of optimal solutions, derive an optimality system, and determine optimal solutions. In section 5, we give second-order optimality conditions. In section 6, the numerical methods are discussed, including the statement of the discrete optimality system and the construction of a discrete target function. In section 7, the results of numerical experiments are presented that illustrate the convergence of a variable-step gradient algorithm for finding optimal parameters. Finally, in section 8, we make some conclusions.

2. Well-posedness of the direct problem. Before stating the well-posedness result for the Gierer–Meinhardt model, we need to establish the formal setting and restate the RD system with appropriate initial and boundary conditions. Let \( \Omega \) be a bounded and open subset of \( \mathbb{R}^d, \ d \leq 2, \) with a Lipschitz continuous boundary, and let \( Q := \Omega \times (0, T) \) be the space-time cylinder. The direct problem is formulated as follows: Find the morphogen concentrations \( u(x, t) \) and \( v(x, t) \) such that
where the reaction kinetics are defined as

\begin{align}
(2.2a) \quad f(u,v) &:= \frac{ru^2}{v} - \mu(x,t)u + r, \\
(2.2b) \quad g(u,v) &:= ru^2 - \alpha(x,t)v,
\end{align}

the fixed parameters $r$, $D_u$, and $D_v$ are positive, and $u(x,t)$ and $v(x,t)$ are the morphogen concentrations defined for $(x,t) \in Q$. $D_u$ and $D_v$ are the diffusion coefficients of $u$ and $v$, respectively, $\Delta = \sum_{i=1}^{d} \partial^2 / \partial x_i^2$ denotes the standard Laplacian operator in $d \leq 2$ space dimensions, and $\nu$ denotes the outward normal to $\partial \Omega$, the boundary of $\Omega$. We assume that $\mu(x,t)$ and $\alpha(x,t)$ are bounded, Lipschitz continuous functions on $Q$, which we denote by $\mu, \alpha \in \text{Lip}(Q)$, belonging to the set of admissible parameters

\begin{equation}
U_{ad} := \left\{ (\mu, \alpha) \in \text{Lip}(Q)^2; 0 \leq \mu(x,t) \leq \mu_1, 0 \leq \alpha(x,t) \leq \alpha_1 \quad \forall (x,t) \in Q \right\},
\end{equation}

for some finite real numbers $\mu_1, \alpha_1$. We assume zero flux of the morphogen concentrations across the boundary and that the initial concentrations are continuous and positive, with

\begin{equation}
(2.4) \quad u_0(x) \geq u_0^{\min} > 0, \quad v_0(x) \geq v_0^{\min} > 0 \quad \forall x \in \overline{\Omega}.
\end{equation}

**Theorem 2.1.** Let $(\mu, \alpha) \in U_{ad}$ and $u_0, v_0 \in C(\overline{\Omega})$ satisfying (2.4). Then there exists a unique global positive classical solution of the Gierer–Meinhardt RD system \((2.1a)–(2.1d)\).

**Proof.** The existence of a unique global classical solution of the system \((2.1a)–(2.1d)\) follows from [54]. To prove the nonnegativity of solutions, observe that the reaction kinetics \((2.2a)–(2.2b)\) satisfy

\[ f(0, v), g(u, 0) > 0 \quad \forall u, v > 0, \]

and the initial data \((u_0(x), v_0(x))\) are in \((0, \infty)^2\) for all $x \in \Omega$. Thus by a maximum principle [57, Corollary 14.8], the solution \((u(x,t), v(x,t))\) lie in \([0, \infty)^2\) for all $x \in \Omega$ and for all $t > 0$ for which the solution of \((2.1a)–(2.1d)\) exists. In other words, \([0, \infty)^2\) is positively invariant for the system.

For the positivity of the solutions satisfying \((2.1a)–(2.1d)\) let $\underline{u} = u(x,t)$, $\underline{v} = v(x,t)$ be solutions of the simplified system

\begin{align}
(2.5a) \quad \frac{\partial \underline{u}}{\partial t} - D_u \Delta \underline{u} + \mu(x,t)\underline{u} &= r, \\
(2.5b) \quad \frac{\partial \underline{v}}{\partial t} - D_v \Delta \underline{v} + \alpha(x,t)\underline{v} &= ru^2,
\end{align}

and for all $t > 0$ for which the solution of \((2.1a)–(2.1d)\) exists. In other words, \([0, \infty)^2\) is positively invariant for the system.
with homogeneous Neumann boundary conditions and initial conditions
\[ u(x, 0) = u_0(x), \quad v(x, 0) = v_0(x) \quad \forall x \in \Omega. \]

Applying the comparison principle (see, e.g., [54, 51]) to (2.5a) we deduce \( u > 0 \), and similarly from (2.5b), we infer that \( v > 0 \). Subtracting (2.5a)–(2.5b) from (2.1a)–(2.1b), we obtain
\[
\frac{\partial(u - w)}{\partial t} - Du \Delta (u - w) + \mu(x,t)(u - w) = r \frac{u^2}{v},
\]
\[
\frac{\partial(v - w)}{\partial t} - Dv \Delta (v - w) + \alpha(x,t)(v - w) = r(u^2 - w^2).
\]

Using the comparison theorem once again and the nonnegativity of \( v \) in the first equation above, we obtain that \( u > w \) on \( \Omega \times (0, T) \). From the second equation using the same theorem, we conclude that the solution to the Gierer–Meinhardt system (2.1a)–(2.1d) has a positive lower bound
\[
(2.6) \quad u(x, t) > w(x, t) > 0, \quad v(x, t) > w(x, t) > 0 \quad \text{in} \quad \Omega \times (0, T). \quad \square
\]

**Lemma 2.2.** The solution \((u, v)\) of system (2.1a)–(2.1d) can be estimated, with respect to \( \mu, \alpha \), uniformly from below by
\[
u(x, t) \geq V(t) := r \int_0^t e^{\alpha_1(s-t)} U^2(s) ds + v_0^{\min} e^{-\alpha_1 t},
\]
in \( \Omega \times [0, T] \), where \( U(0) = u_0^{\min} \), \( V(0) = v_0^{\min} \).

The proof of this lemma is given in Appendix C. We note that the proof of Lemma 2.2 yields the lower bound \( v(x, t) \geq v_0^{\min} e^{-\alpha_1 T} \) on \( \Omega \).

**3. Setup of the inverse problem.** For the inverse problem, we are given possibly perturbed measurements \((\overline{u}, \overline{v})\) corresponding to the state variables \((u, v)\) and seek parameters \( \mu, \alpha \) such that \((u, v)\) best approximates \((\overline{u}, \overline{v})\).

For given \( T > 0, u_0, v_0 \in C(\Omega) \), and \( \overline{u}, \overline{v} \in L^2(Q) \) not necessarily a solution of (2.1a)–(2.1d), the least squares approach leads to the minimization of the cost functional
\[
\tilde{J}(\mu, \alpha) = \frac{1}{2} \int_0^T \int_\Omega \left( \beta_1 |u_{\mu, \alpha} - \overline{u}|^2 + \beta_2 |v_{\mu, \alpha} - \overline{v}|^2 \right) dx \, dt
\]
\[
+ \frac{1}{2} \int_\Omega \left( \gamma_1 |u_{\mu, \alpha}(x, T) - \overline{u}(x, T)|^2 + \gamma_2 |v_{\mu, \alpha}(x, T) - \overline{v}(x, T)|^2 \right) dx,
\]
where \((u_{\mu, \alpha}, v_{\mu, \alpha})\) is the solution of (2.1a)–(2.1d) that corresponds to \((\mu, \alpha)\). Inverse problems related to PDEs are usually ill-posed (see, e.g., [60, 33]), and thus the least squares approach is not numerically sufficient. To circumvent this problem we use Tikhonov regularization [15], which yields the following minimization problem:

**P** Find \((\mu^*, \alpha^*) \in U_{ad} \) such that
\[
\mathcal{J}(\mu^*, \alpha^*) = \inf_{\mu, \alpha \in U_{ad}} \mathcal{J}(\mu, \alpha),
\]
where
\[
J(\mu, \alpha) = \tilde{J}(\mu, \alpha) + \frac{1}{2} \int_0^T \int_{\Omega} \left( \delta_1 \mu^2 + \delta_2 \alpha^2 \right) \, dx \, dt.
\]

The terms weighted by \( \beta_i \) measure the discrepancy between the solution and measurements over the space-time cylinder \( Q \), while the weights \( \gamma_i \) assign varying emphasis on the match at the final time \( T \). The terms weighted by \( \delta_i \) effectively bound the size of the key parameters \( \mu \) and \( \alpha \) and allow for possibly noisy data.

4. The minimization problem.

4.1. Existence of an optimal solution. We establish the existence of an optimal solution of the minimization problem \((P)\). As before, we assume \( \Omega \) is an open bounded domain with Lipschitz continuous boundary \( \partial \Omega \). We denote \( u^* = u_{\mu^*, \alpha^*} \) and \( v^* = v_{\mu^*, \alpha^*} \).

Proposition 4.1. Given \( u_0, v_0 \in C(\overline{\Omega}) \) and \( \pi, \pi \in L^2(Q) \), there exists a solution \((\mu^*, \alpha^*) \in U_{ad}\) of the minimization problem \((P)\) such that \((u^*, v^*) \in C([0, T]; L^2(\Omega)^2) \cap L^2(0, T; H^1(\Omega)^2)\).

Proof. The argument is standard [6], so we give only a sketch of the proof. By energy-type estimates on minimizing sequences to \((P)\), using the uniform lower bound from Lemma 2.2, the set
\[\{(\mu, \alpha), (u, v) \in U_{ad} \times L^2(Q)^2 : (2.1a)-(2.1d) \text{ holds}\}\]
is closed in \(C(\overline{Q})^2 \times C([0, T]; L^2(\Omega)^2) \cap L^2(0, T; H^1(\Omega)^2)\). The weak lower semicontinuity of the function \((\mu, \alpha), (u, v) \mapsto J(\mu, \alpha)\) on \(L^2(Q)^2 \times L^2(Q)^2\) implies the existence of a global minimizer. \(\Box\)

4.2. First-order necessary conditions. We derive first-order necessary conditions associated with the optimal control problem \((P)\), which the optimal solution must satisfy if the Gâteaux derivative of the functional exists [59, 52].

Lemma 4.2. Let \( u_0, v_0 \in C(\overline{\Omega})\). If \((\mu^*, \alpha^*)\) is an optimal solution and the functional \( J(\mu^*, \alpha^*) \) is Gâteaux differentiable, then a necessary condition for \((\mu^*, \alpha^*)\) to be a minimizer of \( J(\mu^*, \alpha^*) \) is
\[
\frac{dJ(\mu^*, \alpha^*)}{d(\mu, \alpha)} \cdot (\mu - \mu^*, \alpha - \alpha^*) \geq 0 \quad \forall (\mu, \alpha) \in U_{ad}.
\]

It is clear that for \((\mu, \alpha) \in U_{ad}\), the solution \((u, v)\) is classical and hence weak. It is convenient to work in the topology of \(L^2(0, T; H^1(\Omega))\), which facilitates the use of well-known results. We recall that the solution of \((2.1a)-(2.1b)\) defines a mapping \( u = u_{\mu, \alpha}, v = v_{\mu, \alpha} \) from \( U_{ad} \) to \( L^2(0, T; H^1(\Omega))\), which is Gâteaux differentiable, and thus Lemma 4.2 can be applied.

Lemma 4.3. Let \( u_0, v_0 \in C(\overline{\Omega})\). The map \((\mu, \alpha) \mapsto (u_{\mu, \alpha}, v_{\mu, \alpha})\) from \( U_{ad} \) to \( L^2(0, T; H^1(\Omega)^2)\), defined as the solution of \((2.1a)-(2.1b)\), has a Gâteaux derivative in every direction \((\hat{\mu}, \hat{\alpha})\) in the tangential cone \( \text{Tan} U_{ad}(\mu, \alpha) \) of \( U_{ad} \) at \((\mu, \alpha)\). Furthermore, \((\hat{u}, \hat{v}) = \left( \frac{du}{d(\mu, \alpha)}, \frac{dv}{d(\mu, \alpha)} \right) \) \(\cdot\) \((\hat{\mu}, \hat{\alpha})\) is the solution of the problem
\[
\begin{align*}
\hat{u}_t - D_u \Delta \hat{u} &= \frac{2 \mu \hat{u}v - u^2 \hat{v}}{v^2} - \hat{\mu}u - \hat{\mu} \hat{u}, \\
\hat{v}_t - D_v \Delta \hat{u} &= 2 ru \hat{u} - \hat{\alpha}v - \hat{\alpha} \hat{v}, \\
\hat{u}(0) &= 0, \quad \hat{v}(0) = 0.
\end{align*}
\]
Then we have

\[\int_0^T \int_\Omega (F\hat{u} + G\hat{v}) dx \, dt = -\int_\Omega (p\hat{u} + q\hat{v}) \bigg|_0^T \, dx - \int_0^T \int_\Omega (\hat{\mu}u p + \hat{\alpha}v q) \, dx \, dt,\]

where \((p, q)\) is the solution of the adjoint problem

\[-p_t - D_u \Delta p - \left(2\frac{ru}{v} - \mu\right) p - 2ruq = F,\]
\[-q_t - D_v \Delta q + \frac{ru^2}{v}p + \alpha q = G,\]
\[\frac{\partial p}{\partial v}(x, t) = \frac{\partial q}{\partial v}(x, t) = 0, \quad x \in \partial \Omega,\]
\[p(x, T) = p_T(x), \quad q(x, T) = q_T(x), \quad x \in \Omega.\]

**Proof.** The left-hand side of (4.2) can be evaluated by (4.3) and (4.1) via integration by parts, which is justified by the regularity properties of the quantities involved. \(\Box\)

Next, we show that the optimal coefficients \(\mu^*, \alpha^*\) in Lemma 4.2 are characterized by the solution of a particular adjoint system.

**Theorem 4.5.** Let \((\mu^*, \alpha^*)\) be an optimal solution to problem \((P)\), \(\overline{\mu}, \overline{\alpha} \in C(\overline{\Omega})\), and let \((p, q)\) be the solution of the particular adjoint problem

\[-p_t - D_u \Delta p - \left(2\frac{ru^*}{v^*} - \mu\right) p - 2ru^*q = \beta_1(u^* - \overline{\mu}),\]
\[-q_t - D_v \Delta q + \frac{ru^2}{v^*}p + \alpha q = \beta_2(v^* - \overline{\alpha}),\]
\[\frac{\partial p}{\partial v}(x, t) = 0, \quad \frac{\partial p}{\partial v}(x, t) = 0, \quad x \in \partial \Omega,\]
\[p(x, T) = \gamma_1(u^*(x, T) - \overline{\mu}(x, T)),\]
\[q(x, T) = \gamma_2(v^*(x, T) - \overline{\alpha}(x, T)), \quad x \in \Omega.\]

Then we have

\[\mu^* = \max \left\{0, \min \left\{\frac{1}{\delta_1}u^* p, \mu_1\right\}\right\}, \quad \alpha^* = \max \left\{0, \min \left\{\frac{1}{\delta_2}v^* q, \alpha_1\right\}\right\}.\]
Proof. We compute the Gâteaux derivative of the cost functional $J(\mu^*, \alpha^*)$ in the direction of $(\hat{\mu}, \hat{\alpha}) \in \mathcal{T} \mathcal{U}_{ad}(\mu^*, \alpha^*)$. We have

$$
\frac{dJ(\mu^*, \alpha^*)}{d(\mu, \alpha)} \cdot (\hat{\mu}, \hat{\alpha}) = \int_Q \beta_1(u^* - \bar{u}) \left( \frac{dv^*, \alpha^*}{d(\mu, \alpha)} \cdot (\hat{\mu}, \hat{\alpha}) \right) dx dt \\
+ \beta_2(v^* - \bar{v}) \left( \frac{dv^*, \alpha^*}{d(\mu, \alpha)} \cdot (\hat{\mu}, \hat{\alpha}) \right) dx dt \\
+ \gamma_1 \int_{\Omega} (u^*(T, x) - \bar{u}(T, x)) \left( \frac{dv^*, \alpha^*}{d(\mu, \alpha)} \cdot (\hat{\mu}, \hat{\alpha}) \right) (T, x) dx \\
+ \gamma_2 \int_{\Omega} (v^*(T, x) - \bar{v}(T, x)) \left( \frac{dv^*, \alpha^*}{d(\mu, \alpha)} \cdot (\hat{\mu}, \hat{\alpha}) \right) (T, x) dx \\
+ \int_Q (\delta_1 \mu^* \hat{\mu} + \delta_2 \alpha^* \hat{\alpha}) dx dt \\
= \int_Q (-\hat{\mu} u^* p - \hat{\alpha} v^* q + \delta_1 \mu^* \hat{\mu} + \delta_2 \alpha^* \hat{\alpha}) dx dt,
$$

where $(du^*, \alpha^* / d(\mu, \alpha), dv^*, \alpha^* / d(\mu, \alpha))$ is the solution of the sensitivity system (4.1). Now from the definition of optimality in problem (P), as $(\mu^*, \alpha^*)$ is an optimal solution and the Gâteaux derivative of the functional exists, then from Lemma 4.4,

$$
\int_Q (\delta_1 \mu^* - u^* p)(\mu - \mu^*) + (\delta_2 \alpha^* - v^* q)(\alpha - \alpha^*) dx dt \geq 0 \quad \forall (\mu, \alpha) \in \mathcal{U}_{ad},
$$

which completes the proof. \[\square\]

5. Second-order optimality conditions. To ensure that a solution $(\mu^*, \alpha^*)$ satisfying the first-order optimality conditions (4.4)–(4.5) solves (P), we state without proof second-order sufficient optimality conditions (see, e.g., [11, 42]). First, we require the following differentiability results.

**Lemma 5.1.** The map $(\mu, \alpha) \mapsto (u_{\mu, \alpha}, v_{\mu, \alpha})$ defined in Lemma 4.3 is of class $C^2$. Moreover, for every $(\hat{\mu}_1, \hat{\alpha}_1), (\hat{\mu}_2, \hat{\alpha}_2) \in \mathcal{T} \mathcal{U}_{ad}(\mu, \alpha),$

$$(\hat{u}_{12}, \hat{v}_{12}) = \left( \frac{d^2 u}{d(\mu, \alpha)^2}, \frac{d^2 v}{d(\mu, \alpha)^2} \right) (\hat{\mu}_1, \hat{\alpha}_1)(\hat{\mu}_2, \hat{\alpha}_2)$$

is the solution of

$$
\begin{align*}
\hat{u}_{12} - D_u \Delta \hat{u}_{12} &= r \left( \frac{(\hat{u}_{12} + \hat{\mu}_1 \hat{u}_2 + \hat{\alpha}_1 \hat{v}_2) v - \hat{u}_1 \hat{v}_2}{v^2} - \frac{(2u\hat{u}_2 \hat{v}_1 + u^2 \hat{v}_2) v - 2u^2 \hat{v}_1 v \hat{v}_2}{v^4} \right) \\
&\quad - \hat{\mu}_1 \hat{u}_2 - \hat{\alpha}_1 \hat{v}_2 - \hat{u}_{12}, \\
\hat{v}_{12} - D_v \Delta \hat{v}_{12} &= 2r \left( \hat{u}_{12} + \hat{\mu}_2 \hat{u}_1 - \hat{\alpha}_2 \hat{v}_1 - \hat{\alpha}_2 \hat{v}_1 - \alpha \hat{v}_{12}, \right)
\end{align*}
$$

where $(\hat{u}_i, \hat{v}_i) = \left( \frac{d u}{d(\mu, \alpha)}, \frac{d v}{d(\mu, \alpha)} \right) (\hat{\mu}_i, \hat{\alpha}_i), i = 1, 2,$ is the solution of problem (4.1).
The cost functional (3.1) \( J : \mathcal{U}_{ad} \rightarrow \mathbb{R} \) is of class \( C^2 \) and

\[
\frac{d^2 J(\mu, \alpha)}{d(\mu, \alpha)^2}(\hat{\mu}_1, \hat{\alpha}_1)(\hat{\mu}_2, \hat{\alpha}_2) = \int_Q (\beta_1 \hat{u}_1 \hat{u}_2 + \beta_2 \hat{v}_1 \hat{v}_2) \, dx \, dt + \int_{\Omega} (\gamma_1 \hat{u}_1(T)\hat{u}_2(T) + \gamma_2 \hat{v}_1(T)\hat{v}_2(T)) \, dx + \int_Q p \left( r \frac{u^2}{v^2} \hat{u}_1^2 - 2r \frac{u}{v} \hat{u}_1 \hat{v}_2 - \mu_1 \hat{u}_1 - \mu_2 \hat{u}_1 + 2r \left( \frac{2u \hat{u}_2 \hat{v}_1 + u^2 \hat{v}_1^2}{v^4} \right) \right) \, dx \, dt + \int_Q q (2r \hat{u}_1 \hat{u}_2 - \hat{\alpha}_1 \hat{v}_2 - \hat{\alpha}_2 \hat{v}_2) \, dx \, dt + \int_Q (\delta_1 \hat{\mu}_1 \hat{\mu}_2 + \delta_2 \hat{\alpha}_1 \hat{\alpha}_2) \, dx \, dt,
\]

where \((p, q)\) is the adjoint state satisfying (4.4).

The sufficient second-order optimality conditions are given by the following result (see, e.g., [11, 27, 42]).

**Theorem 5.2.** Assume that \((\mu^*, \alpha^*) \in \mathcal{U}_{ad}\) are admissible parameters of problem (P), \((u^*, v^*)\) are the associated states, \((\mu^*, \alpha^*, u^*, v^*)\) satisfy (4.4)–(4.5), and there exists \(\kappa > 0\) such that

\[
\frac{d^2 J(\mu^*, \alpha^*)}{d(\mu, \alpha)^2}(\hat{\mu}_1, \hat{\alpha}_1)^2 \geq \kappa \| (\hat{\mu}_1, \hat{\alpha}_1) \|^2_{L^2(Q)} \quad \forall (\hat{\mu}_1, \hat{\alpha}_1) \in \text{Tan} \mathcal{U}_{ad}(\mu^*, \alpha^*).
\]

Then there exist \(\varepsilon > 0\) and \(\delta > 0\) such that for all admissible parameters \((\mu, \alpha)\) of problem (P), the following inequality holds:

\[
J(\mu^*, \alpha^*) + \frac{\delta}{2} \left( \| \mu^* - \mu \|^2_{L^2(Q)} + \| \alpha^* - \alpha \|^2_{L^2(Q)} \right) \leq J(\mu, \alpha) \quad \text{if} \quad \| \mu^* - \mu \|^2_{L^2(Q)} + \| \alpha^* - \alpha \|^2_{L^2(Q)} \leq \varepsilon.
\]

If the second-order sufficient optimality condition is satisfied, then the stability of a locally optimal solution holds and the convergence of a gradient-type algorithm is guaranteed (see, e.g., [12, 29]).


6.1. Discrete optimality system. Initially we partition the domain \(\Omega\) into a large number of approximately equilateral triangles \(\tau\) using an unstructured mesh generator. We used the automatic mesh generator MESH2D (available from http://www.mathworks.com/matlabcentral/fileexchange/), which utilizes a convenient mesh quality indicator for ensuring a good quality mesh (see (7.1) in [49]). The spatial discretization of the state equations and adjoint equations was undertaken using a “lumped mass” [58] Galerkin finite element method with piecewise linear continuous basis functions (e.g., [7, 9, 22, 24]). We introduce \(S^h\), the standard Galerkin finite element space

\[
S^h := \{ \chi \in C(\overline{\Omega}) : \chi|_\tau \text{ is linear } \forall \tau \in \Omega \} \subset H^1(\Omega).
\]

The time discretization of RD equations for pattern formation requires careful treatment. This is because several popular first-order accurate time-stepping schemes, as well as schemes that produce weak decay of high frequency spatial errors, may yield qualitatively misleading and incorrect results [55]. To approximate the Gierer–Meinhardt system (2.1a)–(2.1b) we employed the following second-order, three-level,
implicit-explicit (IMEX) scheme (2-SBDF; see Ruuth [55]):

\[
\begin{align*}
\frac{3u^{n+1} - 4u^n + u^{n-1}}{2\Delta t} - D_u \Delta u^{n+1} &= 2f(u^n, v^n) - f(u^{n-1}, v^{n-1}), \\
\frac{3v^{n+1} - 4v^n + v^{n-1}}{2\Delta t} - D_v \Delta v^{n+1} &= 2g(u^n, v^n) - g(u^{n-1}, v^{n-1}),
\end{align*}
\]

where \( u^n \approx u(n\Delta t), \; v^n \approx v(n\Delta t) \), and \( \Delta t \) is the step size. The backward differentiation formula 2-SBDF is recommended by Ruuth as a good choice for most RD systems for pattern formation. To approximate the RD system at the first time step, we used a well-known first-order semi-implicit backward differentiation IMEX scheme, namely 1-SBDF [55].

The derivation of a discrete optimality system led to similar time-stepping schemes for the linear adjoint equations (see Appendix B for details). Application of the finite element method for the spatial discretization, coupled with the time-stepping schemes, led to a sparse linear system of algebraic equations. Because of the block structure of the linear system, we solved for \( u \) and \( v \) independently at each time step using the GMRES iterative solver in MATLAB.

Corresponding to the continuous cost functional (3.1), the discrete cost functional is given by

\[
J^N = \frac{\Delta t}{2} \sum_{n=1}^{N} \left( \beta_1 \| u^n_h - \bar{u}^n_h \|_{L^2(\Omega)}^2 + \beta_2 \| v^n_h - \bar{v}^n_h \|_{L^2(\Omega)}^2 \right) \\
+ \frac{1}{2} \left( \gamma_1 \| u^n_h - \bar{u}^n_h \|_{L^2(\Omega)}^2 + \gamma_2 \| v^n_h - \bar{v}^n_h \|_{L^2(\Omega)}^2 \right) \\
+ \frac{\Delta t}{2} \sum_{n=1}^{N} \left( \delta_1 \| \mu^n_h \|_{L^2(\Omega)}^2 + \delta_2 \| \alpha^n_h \|_{L^2(\Omega)}^2 \right)
\]

for discrete parameters \( \mu^n_h, \alpha^n_h \in \text{Lip}(\Omega), \; 0 \leq \mu^n_h(x) \leq \mu_1, \; 0 \leq \alpha^n_h(x) \leq \alpha_1 \), discrete target functions \( \bar{u}^n_h, \bar{v}^n_h \in S^h \), and discrete states \( u^n_h, v^n_h \in S^h \). Letting \( \pi^h \) be the Lagrange interpolation operator such that \( \pi^h : C(\Omega) \mapsto S^h \), the initial states were taken as \( u^0_h = \pi^h u_0(x), \; v^0_h = \pi^h v_0(x) \).

We now formulate the fully discrete optimal control problem as

\[
(P^{h, \Delta t}) \text{ Given a time step of } \Delta t = T/N, \text{ a maximum triangle size } h, \; \; u_0, v_0 \in H^1(\Omega) \cap L^\infty(\Omega), \text{ and } \bar{u}^n_h, \bar{v}^n_h \in S^h; \text{ find } (u^n_h, v^n_h, \mu^n_h, \alpha^n_h) \in S^h \times S^h \times S^h \times S^h \text{ such that (6.1) is satisfied for } n = 1, 2, \ldots, N \text{ and the cost functional (6.2) is minimized.}
\]

The construction of the discrete target functions \( \bar{u}^n_h, \bar{v}^n_h \) is described below (section 6.2). Let \( p^n_h, q^n_h \in S^h \) denote the fully discrete approximations to the adjoint variables \( p, q \); then corresponding to (4.5) the following theorem holds, which characterizes the relationship between discrete adjoint variables and discrete parameter values.

**Theorem 6.1.** If \( \{u^n_h, v^n_h\}_{n=0}^{N} \) and \( \{\mu^n_h, \alpha^n_h\}_{n=0}^{N} \) are optimal for problem \((P^{h, \Delta t})\), then there exist \( \{p^n_h, q^n_h\}_{n=0}^{N} \) satisfying the discrete adjoint equations such that for \( n = 1, \ldots, N - 2 \),

\[3^\text{In order to prove stable finite element schemes (details omitted) we used regularized versions of these equations. However, in practice we saw little difference between the regularized and nonregularized solutions. See Appendix A for further details.} \]
\[
\alpha_h^{(n)} = \max \left\{ 0, \min \left\{ \frac{u_h^{(n)}}{\delta_2} \left( 2q_h^{(n)} - q_h^{(n+1)} \right), \alpha_1 \right\} \right\},
\]
\[
\mu_h^{(n)} = \max \left\{ 0, \min \left\{ \frac{u_h^{(n)}}{\delta_1} \left( 2p_h^{(n)} - p_h^{(n+1)} \right), \mu_1 \right\} \right\},
\]
for \( n = N - 1, \)
\[
\alpha_h^{(N-1)} = \max \left\{ 0, \min \left\{ \frac{2v_h^{(N-1)}}{\delta_2} q_h^{(N-1)}, \alpha_1 \right\} \right\},
\]
\[
\mu_h^{(N-1)} = \max \left\{ 0, \min \left\{ \frac{2u_h^{(N-1)}}{\delta_1} p_h^{(N-1)}, \mu_1 \right\} \right\},
\]
and for \( n = N, \) \( \alpha_h^{(N)} = \mu_h^{(N)} = 0. \)

Proof. The proof is standard and is similar to the proof of the corresponding continuous result.

6.2. Construction of targets. For the specific target functions \((\overline{u}, \overline{v})\), in our numerical simulations we chose the skin patterns of the Emperor angelfish \((Pomacanthus imperator)\), which is widespread in the central and western Pacific Ocean. This angelfish was chosen because of the complex series of stripes and spots on its skin. Our starting point prior to preprocessing of the image was a high resolution JPEG image \((1050 \times 750 \text{ (3.5 in by 2.5 in at 300 ppi)})\).

The preprocessing steps are illustrated in Figure 6.1. The original image is shown in Figure 6.1(a). The image is then cropped, which excludes the portion of the tail with no pattern and the background details (Figure 6.1(b)). The cropped image is also fitted into a square \([0, 2] \times [0, 2]\), which defines the domain \(\Omega\). The image in Figure 6.1(b) is then converted to a grayscale image with 256 shades of gray (Figure 6.1(c)). This image is then interpolated (2D bicubic) onto the finite element mesh, with a large number of equilateral triangles (Figure 6.1(d)).

As we have no knowledge of the actual maximum and minimum values of the angelfish image, we set the target functions \(\overline{u}\) and \(\overline{v}\) equal to the image scaled between \(\pm 10\%\) of the equilibrium solutions (i.e., solutions corresponding to \(f = g = 0\)) of \(u\) and \(v\), respectively. The equilibrium solutions \((u_s, v_s)\) are calculated via
\[
\begin{align*}
u_s &= \alpha(0) + r \mu(0), \quad v_s = \frac{ru_s^2}{\alpha(0)},
\end{align*}
\]
where \(\alpha(0)\) and \(\mu(0)\) are the initial guesses for \(\alpha\) and \(\mu\) in the discrete optimal control procedure (see section 6.3). Finally, we also reverse the grayscale of the target functions for better visibility of the fine structure of the pattern.

6.3. Discrete optimal control procedure. With the above numerical methods we force the solution of the RD system to match the stationary target function at the final time \(T\). This necessitates appropriate choices of the weights in the discrete cost functional \((6.2)\). By making the weights \(\gamma_i\) large in relation to the weights \(\beta_i\), we place more emphasis on the solutions matching the target functions at the final time \(T\). This makes sense because the angelfish image corresponds to the end of the developmental period, and we have no information regarding the earlier developmental stages.
To approximate the inverse problem we apply a variable-step gradient algorithm [12, 25, 29] yielding a sequence of discrete approximations

$$\{(\mu(k), \alpha(k)), (u(k), v(k))\}_{k \in \mathbb{N}}$$

to the optimal parameters $$(\mu^*, \alpha^*)$$ and corresponding solutions $$(u^*, v^*)$$. The sensitivities of the system (2.1a)–(2.1b) and cost functional (3.1) with respect to the parameters $$(\mu, \alpha)$$ are used to compute the Lagrange multipliers, satisfying the adjoint system that marches backward in time. The Lagrange multipliers are then used in a variable-step gradient algorithm (Algorithm 1) to minimize the cost functional. The implementation is straightforward, although computationally intensive. The bulk of the computational costs are found in the backward-in-time solution of the adjoint system and the forward-in-time solution of the state system. We begin by making an initial guess for the parameters $$(\mu(0), \alpha(0))$$ and the step length $$\lambda$$. Then for each iteration $$k$$ of the gradient method, we solve the nonlinear RD system for $$u(k), v(k)$$ and store the cost $$J(\mu(k), \alpha(k))$$. We also compute the adjoint variables $$(p(k), q(k))$$, determine $$\frac{dJ(\mu(k), \alpha(k))}{d(\mu(k), \alpha(k))}$$, the total derivative of $$J$$ with respect to the vector $$(u(k), v(k))$$, and take a step along this direction using the appropriate step length, provided the cost functional decreases. If the cost functional fails to decrease, then the step is rejected and the step length decreased. If the step length is accepted, then the parameters $$(\mu(k+1), \alpha(k+1))$$ are updated using a standard gradient update

$$\begin{align*}
(\mu(k+1), \alpha(k+1)) &= (\mu(k), \alpha(k)) - \lambda(k) \frac{dJ(\mu(k), \alpha(k))}{d(\mu(k), \alpha(k))}.
\end{align*}$$

Fig. 6.1. Preprocessing of a JPEG image of the Emperor angelfish ($P$. imperator). (a) Original image. (b) Image cropped and fitted into a square. (c) Conversion to grayscale. (d) Image interpolated onto a finite element mesh. Copyright Robert Fenner, WetWebMedia.com.
In the following algorithm we omit the subscript \( h \) for notational convenience in the discrete variables: \( u^n_h, v^n_h, p^n_h, q^n_h, \mu^n_h, \alpha^n_h \).

**Algorithm 1.** Variable-step gradient algorithm.

*initialization*

\[
\begin{align*}
\text{RelError} & \leftarrow 10; \\
\lambda & \leftarrow 1, \text{ and tol}; \\
\text{solve (6.1) for } (u^n(0), v^n(0)) \text{ with } (u_0, v_0) & \text{ for } n = 1, \ldots, N; \\
\text{evaluate } J^N(0) & \text{ using (6.2)}; \\
\lambda & \leftarrow 2\lambda/3; \\
\end{align*}
\]

*end initialization*

*main loop*

While RelError > tol do

\[
\begin{align*}
\lambda & \leftarrow 3\lambda/2; \\
\text{solve (B.1)–(B.4) for } (p^n(k), q^n(k)) \text{ with } (p_N(k), q_N(k)) & \text{ for } n = N - 1, \ldots, 0; \\
\text{update } (\alpha^n(k), \mu^n(k)) & \text{ using (6.3)} \text{ for } n = 1, \ldots, N; \\
\text{evaluate } J^N(k) & \text{ using (6.2)}; \\
\end{align*}
\]

While \( J^N(k) \geq J^N(k - 1) \) do

\[
\begin{align*}
\lambda & \leftarrow \lambda/2; \\
\text{update } (\alpha^n(k), \mu^n(k)) & \text{ using (6.3)} \text{ for } n = 1, \ldots, N; \\
\text{solve (6.1) for } (u^n(k), v^n(k)) \text{ with } (u_0, v_0) & \text{ for } n = 1, \ldots, N; \\
\text{evaluate } J^N(k) & \text{ using (6.2)}; \\
\end{align*}
\]

end while

\[
\text{RelError} \leftarrow |J^N(k) - J^N(k - 1)| / |J^N(k)|
\]

end while

*end main loop*

**7. Numerical experiments.** To illustrate the success of our image-driven, PDE-constrained optimization procedure, we present numerical results in two space dimensions. We used a nonuniform triangulation of the angelfish domain \( \Omega \) with 17,904 nodes and 35,280 triangles, and numerically solved the optimal control problem up to time \( T = 10 \) with uniform time steps \( \Delta t = 1 \times 10^{-8} \) (1-SBDF) and \( \Delta t = 0.01 \) (2-SBDF). In all experiments we chose \( \beta_1 = \beta_2 = 0 \) to place more emphasis on solutions matching the target at the final time \( T \) (see comments in section 6.3).

*First experiment.** To obtain a good match between \( \pi \) and \( u \), we chose \( \gamma_2 = 1, \gamma_1 = 0 \) in the discrete cost functional (6.2) (see comments in section 6.3). Figure 7.1 shows a snapshot at \( T = 10 \) of the optimal solution \( u \), the target function \( \bar{u} \), and the optimal parameters \( \alpha \) and \( \mu \) (see the caption for parameter values). The controlled solution \( u \) clearly matches the target \( \pi \) very well. In order to verify the convergence of the discrete optimal control procedure, we also plotted the discrete cost functional with iteration count (Figure 7.2). The cost approaches zero, indicating a good match between the optimally controlled solution and the corresponding target.
Fig. 7.1. (a) Controlled solution $u$, (b) stationary target function $\bar{u}$, (c) optimal parameter $\alpha$, and (d) optimal parameter $\mu$, at time $T = 10$. Parameter values: $D_u = D_v = 0.01$, $\gamma = 10$, $\beta_1 = 0$, $\beta_2 = 0$, $\gamma_1 = 1$, $\gamma_2 = 0$, $\delta_1 = 1 \times 10^{-6}$, $\delta_2 = 1 \times 10^{-6}$. Initial data: $\mu = 3$, $\alpha = 30$, $u_0$ and $v_0$ small random perturbations ($\pm 10\%$) of the steady state solutions. Time steps: $1 \times 10^{-8}$ (1-SBDF), 0.01 (2-SBDF). Mesh: 17,904 nodes and 35,280 triangles.

Fig. 7.2. Change in cost functional with iteration count.

Second experiment. We were unable to obtain a good match between $v$ and $\bar{v}$ with the choice $\gamma_2 = 1, \gamma_1 = 0$, because the discrete optimal control algorithm did not converge, regardless of the starting values of the parameters chosen.
We comment that as we effectively have only a single target function (but scaled differently for $\pi$ and $\overline{\pi}$—see section 6.2), it makes no sense to try to simultaneously match $u$ to $\overline{u}$ and $v$ to $\overline{v}$ with the choices $\gamma_1, \gamma_2$ both nonzero (additional experiments revealed that the discrete optimal control algorithm did not converge in these cases). We were also interested in knowing how the parameters change over the time interval $[0, T]$. The results of animations demonstrated that both key parameters remained approximately constant throughout this time interval except for a rapid change in $\mu$ near $t = T$ (see Figures 7.1(c) and 7.1(d)).

8. Conclusions. In this paper we considered parameter estimation for a well-known reaction-diffusion (RD) system for patterning with a PDE-constrained image-driven optimization procedure using optimal control theory. Unlike previous studies, the parameters are allowed to vary in both time and space. With this added freedom it is possible to widen the class of models that give rise to pattern formation, and move away from the Turing model with its vastly restricted parameter space for patterning [44]. This is demonstrated by our numerical results (Figure 7.1) using equal diffusion coefficients, as a necessary condition for the generation of diffusion-induced instability (“Turing patterns”) is unequal diffusion coefficients [62]. The novelty of our work is also due to the manner in which we constructed a practical target function for the optimal control algorithm, corresponding to the actual image of a marine angelfish. For concreteness we focused on the classic Gierer–Meinhardt RD system for pattern formation, with two key distributed parameters $\alpha$ and $\mu$.

The mathematical formulation, analysis, and numerical solution of the optimal control problem were presented. After undertaking the mathematical analysis of the optimal control problem, numerical solutions were obtained with the aid of a “lumped mass,” Galerkin finite element method with piecewise linear continuous basis functions. The time-stepping procedure was based on a second-order, three-level, implicit-explicit (IMEX) scheme, which is particularly well suited to the effective approximation of RD systems for pattern formation. The numerical results in Figure 7.1 illustrate the success of a variable-step gradient algorithm to identify the space-time distributed parameters needed to drive the solution of the Gierer–Meinhardt system close to the skin pattern of a marine angelfish.

The numerical results suggest that pattern selection in the Gierer–Meinhardt system depends more on changes in $\mu$ than on changes in $\alpha$. First, we were unable to match $v$ and $\overline{v}$ with the choices $\gamma_1 = 0$ and $\gamma_2 = 1$ in the discrete cost functional (6.2). The parameter $\alpha$ occurs in the second equation (2.1b) for $v$, and with a weak dependence of pattern selection on $\alpha$ we have effectively only one control in the system (i.e., $\mu$ in (2.1a)). It would appear that the coupling between (2.1a) and (2.1b) is not sufficiently strong for us to match $\overline{v}$ and $\overline{v}$ via control of $\mu$ in the first equation. The question of whether one can control the whole system with only one control is not simple and requires additional investigation. Second, when matching $u$ and $\overline{u}$ with the choices $\gamma_1 = 0$ and $\gamma_2 = 1$, the parameter $\alpha$ remained constant throughout the space-time cylinder $Q$. These results are consistent with the results obtained in [23], where parameter identification for the Gierer–Meinhardt system for the constant parameter case was investigated. It was found that the parameter $\mu$ is the key parameter in determining pattern selection; however, the pattern was relatively insensitive to changes in the parameter $\alpha$.

It is important to note that the Gierer–Meinhardt model is not based on real kinetics and is used in our paper for the purpose of illustrating the methodology for parameter identification in nonlinear RD equations; thus no biological implications
of our results should be made. However, by allowing the parameters to depend on space and time, the numerical results support the hypothesis that the optimal control procedure forced the solution \( u \) of the Gierer–Meinhardt RD system to match an arbitrary skin pattern from nature in a pointwise sense. This is an intriguing observation and requires further study.

**Appendix A. Regularized system.** To construct stable finite element approximations (details omitted), we used the following regularized version of (2.1a)–(2.1b):

\[
\frac{\partial u_{\varepsilon}}{\partial t} = D_u \Delta u_{\varepsilon} + \frac{ru_{\varepsilon}^2}{v_{\varepsilon} + \varepsilon u_{\varepsilon}^2 + \varepsilon} - \mu(x, t)u_{\varepsilon} + r,
\]

\[
\frac{\partial v_{\varepsilon}}{\partial t} = D_v \Delta v_{\varepsilon} + \frac{ru_{\varepsilon}^2}{1 + \varepsilon u_{\varepsilon}^2} - \alpha(x, t)v_{\varepsilon},
\]

with \( \varepsilon = 10^{-6} \). We confirmed that there is little difference in solutions with \( \varepsilon = 0 \). The global existence and uniqueness of the classical solutions of this regularized system follows in a straightforward manner from the theoretical framework of Morgan [43].

**Appendix B. Time-stepping scheme for the adjoint equations.** We omit the subscript \( h \) in the discrete adjoint variables \( p^n, q^n \) for notational convenience. The adjoint variables \( p^n, q^n \) satisfy, for the first time step,

\[
\frac{2p^0 - 4p^1 + p^2}{2\Delta t} - D_u \Delta p^0 = \left( \frac{r}{(|v^1| + \varepsilon|u^1|^2 + \varepsilon)^2} - \mu^1 \right) \cdot (2p^1 - p^2) + 2r \frac{u^1}{1 + \varepsilon|u^1|^2} \cdot (2q^1 - q^2) + \beta_1 (u^1 - \overline{u}),
\]

\[
\frac{2q^0 - 4q^1 + q^2}{2\Delta t} - D_v \Delta q^0 = r \frac{|u^1|^2 \text{sign}(v^1)}{(|v^1| + \varepsilon|u^1|^2 + \varepsilon)^2} \cdot (-2p^1 + p^2) + \alpha^1 (-2q^1 + q^2) + \beta_2 (v^1 - \overline{v}),
\]

for \( n = 2, \ldots, N - 2 \) we have

\[
\frac{3p^{n-1} - 4p^n + p^{n+1}}{2\Delta t} - D_u \Delta p^{n-1} = \left( \frac{r}{(|v^n| + \varepsilon|u^n|^2 + \varepsilon)^2} - \mu^n \right) \cdot (2p^n - p^{n+1}) + 2r \frac{u^n}{1 + \varepsilon|u^n|^2} \cdot (2q^n - q^{n+1}) + \beta_1 (u^n - \overline{u}^n),
\]

\[
\frac{3q^{n-1} - 4q^n + q^{n+1}}{2\Delta t} - D_v \Delta q^{n-1} = r \frac{|u^n|^2 \text{sign}(v^n)}{(|v^n| + \varepsilon|u^n|^2 + \varepsilon)^2} \cdot (-2p^n + p^{n+1}) + \alpha^n (-2q^n + q^{n+1}) + \beta_2 (v^n - \overline{v}^n),
\]
for \( n = N - 1 \),

\[
\frac{3p^{N-2} - 4p^{N-1}}{2\Delta t} - D_u \Delta p^{N-2} = \left( r \frac{2u^{N-1}(|v^{N-1}| + \varepsilon)}{(|v^{N-1}| + \varepsilon|u^{N-1}|^2 + \varepsilon)^2} - \mu^{N-1} \right) \cdot (2p^{N-1} - 2p^{N}) \\
+ 2r \frac{u^{N-1}}{1 + \varepsilon|u^{N-1}|^2} \cdot (2q^{N-1} - q^{N}) + \beta_1(u^{N-1} - \pi^{N-1}),
\]

\[(B.3)\]

and for \( n = N \),

\[
\frac{3p^{N-1} - 2p^{N}}{2\Delta t} - D_u \Delta p^{N-1} = \beta_1(u^{N} - \pi^{N}), \\
\frac{3q^{N-1} - 2q^{N}}{2\Delta t} - D_v \Delta q^{N-1} = \beta_2(v^{N} - \pi^{N}),
\]

supplemented with the final conditions

\[(B.4)\]

\[p^{N} = \gamma_1(u^{N} - \pi^{N}), \quad q^{N} = \gamma_2(v^{N} - \pi^{N}).\]

**Appendix C. Proof of Lemma 2.2.**

**Proof.** Consider the following system of linear first-order ordinary differential equations for \( U(t) \) and \( V(t) \):

\[
U' + \mu_1 U = r, \\
V' + \alpha_1 V = rU^2.
\]

Applying the standard integrating factor approach to these equations yields the lower bound for \( u \) and \( v \) in Lemma 2.2. Because \( \underline{u}, \underline{v} \) satisfy

\[
\frac{\partial}{\partial t} (\underline{u} - U) - D_u \Delta (\underline{u} - U) + \mu(x, t)(\underline{u} - U) = (\mu_1 - \mu(x, t))U \geq 0,
\]

and \( U(t) > 0 \), by a maximum principle [51] we deduce that \( \underline{u} \geq U \) in \( \Omega \times (0, T) \).

Since \( V(t) > 0 \), a similar argument holds for \( \underline{v} \) and \( V \), so we have

\[
\frac{\partial}{\partial t} (\underline{v} - V) - D_v \Delta (\underline{v} - V) + \alpha(x, t)(\underline{v} - V) = (\alpha_1 - \alpha(x, t))V + r(\underline{u}^2 - U^2) \geq 0.
\]

Finally, from (2.6) we obtain the lower bounds on \( u \) and \( v \). \( \square \)

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