

WELL-POSEDNESS RESULTS FOR GENERAL REACTION–DIFFUSION TRANSPORT OF OXYGEN IN ENCAPSULATED CELLS

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Abstract

We provide well-posedness results for nonlinear parabolic partial differential equations (PDEs) given by reaction–diffusion equations describing the concentration of oxygen in encapsulated cells. The cells are described in terms of a core and a shell, which introduces a discontinuous diffusion coefficient as the material properties of the core and shell differ. In addition, the cells are subject to general nonlinear consumption of oxygen. As no monotonicity condition is imposed on the consumption, monotone operator theory cannot be used. Moreover, the discontinuity in the diffusion coefficient bars us from applying classical results on strong solutions. However, by directly applying a Galerkin method, we obtain uniqueness and existence of the strong form solution. These results provide the basis to study the dynamics of cells in critical states.

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1. Introduction

King *et al.* [5, 6] proposed models that describe reaction–diffusion of oxygen through a protective shell encapsulating a core of donor cells to determine conditions so that hypoxia of the donor cells can be avoided. This geometry introduces a discontinuous diffusion coefficient as the material properties of the core and shell differ. The results of King *et al.* are restricted to numerical computation of stationary solutions assuming spherical geometries. Their results were made rigorous in [2]. In [1], the corresponding parabolic partial differential equation (PDE) is studied for general core–shell geometries. It is shown that the PDE is well posed and that stationary solutions are stable. These last results crucially depend on the monotonicity of the oxygen consumption and are derived from Michaelis–Menten kinetics. However, during critical cell states such as partial death of donor cells, these monotonicity conditions will not be satisfied. In this paper, we consider the PDE for general

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consumption, that is, consumption is bounded, nonnegative and zero for negative concentrations.

In the classical theory on existence and uniqueness for nonlinear reaction–diffusion equations, it is typically assumed that the reaction term has asymptotics similar to an odd degree polynomial [8, 9]. This means that the reaction term is unbounded. Consequently, the regularity of the constructed solution will depend on the degree of the leading asymptotics of the reaction term. However, in our setting, the reaction term is bounded which leads to a degenerate setting with respect to classical theory.

We construct the solutions using the Galerkin method (see [8, 9]). Although the nonlinearity in our setting does not exactly satisfy the classical results in [8, 9], a Galerkin set-up still works. Additionally, we are dealing with a so-called diffraction problem [7] meaning that the diffusion coefficient is discontinuous. However, it turns out that the bounds on the term with the Laplacian guarantee that the bounds for the Galerkin approximation are not in danger. Finally, as with diffraction problems, the loss of regularity resulting from the discontinuity will not be visible when considering the well-posedness of weak solutions, but only when we consider the well-posedness of strong solutions.

This paper is organised as follows. In Section 2, we present the statement of the problem and in Section 3, we provide preliminaries. In Section 4, we first establish the global existence and uniqueness of the weak solutions in Section 4.1, followed by the main results on global existence and uniqueness of the strong solutions in Section 4.2. Finally, in Section 5, we provide conclusions and some remarks for future work.

2. Statement of the problem

We start with a description of the core–shell geometry. For an integer $N \geq 2$, let $\Omega \subset \mathbb{R}^N$ with $\bar{\Omega}$ compact, $S := \partial\Omega$ be the boundary of Ω , $\nu: S \rightarrow \mathbb{R}^N$ be the outward unit vector and $T > 0$ be a constant. Let $\Gamma (\subset \Omega)$ be an $(N - 1)$ -dimensional surface that divides Ω into two open domains Ω_1 and Ω_2 , that is, $\Gamma = \bar{\Omega}_1 \cap \bar{\Omega}_2$, $\Omega = \Omega_1 \cup \Omega_2 \cup \Gamma$. We suppose $\partial\Omega_1 = \Gamma$ and $\partial\Omega_2 = S \cup \Gamma$ (see Figure 1). We take S, Γ of class C^2 .

The governing equations of our problem are given by

$$\frac{du}{dt} - b\Delta u = f(u) \quad \text{in } \Omega_i \times (0, T), \quad i = 1, 2, \quad (2.1)$$

$$u = 0 \quad \text{on } S \times (0, T), \quad (2.2)$$

$$[u]_\Gamma = 0 \quad \text{on } \Gamma \times (0, T), \quad (2.3)$$

$$[b\nabla u \cdot \nu]_\Gamma = 0 \quad \text{on } \Gamma \times (0, T), \quad (2.4)$$

$$u = u_0 \quad \text{in } \Omega, \text{ at } t = 0, \quad (2.5)$$

where $b: \bar{\Omega}_1 \cup \Omega_2 \rightarrow \mathbb{R}$ is given by

$$b(x) := \begin{cases} b_1 & \text{if } x \in \bar{\Omega}_1, \\ b_2 & \text{if } x \in \Omega_2, \end{cases}$$

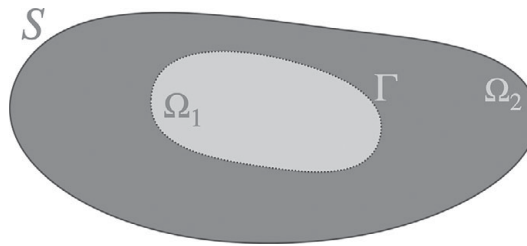


FIGURE 1. Core–shell geometry of an encapsulated cell.

with constants $b_1, b_2 > 0$. Here, the discontinuous diffusion term, $b\Delta u$, is called the *diffraction Laplacian*, $u_0: \Omega \rightarrow \mathbb{R}$ is a given initial value and $[\cdot]_\Gamma: \Gamma \times (0, T) \rightarrow \mathbb{R}$ denotes the difference of limiting values on Γ , which is defined by

$$[u]_\Gamma(x, t) := u_2(x, t) - u_1(x, t) = \lim_{\substack{y \rightarrow x \\ y \in \Omega_2}} u_2(y, t) - \lim_{\substack{y \rightarrow x \\ y \in \Omega_1}} u_1(y, t),$$

where u_1 and u_2 are the restrictions of u to Ω_1 and Ω_2 , respectively. Finally, we consider a linear operator $f: L^2(\Omega) \rightarrow L^2(\Omega)$ that is assumed to be Lipschitz and satisfies the conditions:

$$\begin{aligned} (u, f(u)) &\leq K \quad \text{for all } u \in L^2(\Omega), \\ \|f\|_{L^2(\Omega)} &\leq K, \end{aligned} \quad (2.6)$$

with $K > 0$. Here, (\cdot, \cdot) denotes the inner product on $L^2(\Omega)$ and $\|f\|_{L^2(\Omega)}$ is the operator norm given by

$$\|f\|_{L^2(\Omega)} := \sup_{u \in L^2(\Omega), u \neq 0} \frac{\|f(u)\|_{L^2(\Omega)}}{\|u\|_{L^2(\Omega)}}.$$

Equations (2.1)–(2.5) are for the transformed concentration. The concentration can be retrieved by $v = c_0 - u$ with $v = c_0$ on $S \times (0, T)$ (see [1, Appendix A]). We assume that the consumption $g(v) := f(c_0 - v)$ is bounded, nonnegative and zero for negative concentrations. Then, (2.6) is satisfied.

3. Preliminaries

3.1. Notation. We define $V := H_0^1(\Omega)$, $H := L^2(\Omega)$ and V^* , H^* as their dual spaces, respectively. The inner product on V is defined by $(u, v)_V = (u, v)_H + (\nabla u, \nabla v)_H$. We denote by (\cdot, \cdot) the inner product on H , and by $\langle \cdot, \cdot \rangle$ the pairing between V^* and V . Then, $V \subset\subset H = H^* \subset V^*$, where we write $V \subset\subset H$ to emphasise the compactness of the embedding of V in H . Let $X = V, H$ or V^* . The $L^p(0, T; X)$ -norm ($p = 2, \infty$) is

$$\|u\|_{L^p(0, T; X)} := \begin{cases} \left(\int_0^T \|u(t)\|_X^2 dt \right)^{1/2} & \text{if } p = 2, \\ \text{ess sup}_{t \in [0, T]} \|u\|_X & \text{if } p = \infty. \end{cases}$$

We define $b_{\max} := \max\{b_1, b_2\}$ and $b_{\min} := \min\{b_1, b_2\}$. We denote u_n converging weakly to u in X by $u_n \rightharpoonup u$ in X . We reserve $c > 0$ to denote generic positive constants that do not depend on the relevant parameters and variables.

3.2. Diffraction Laplacian. We introduce the bilinear form $a : V \times V \rightarrow \mathbb{R}$ given by

$$a(u, v) = \int_{\Omega} b \nabla u \cdot \nabla v \, dx.$$

This induces a linear operator $A : V \rightarrow V^*$ given by $\langle Au, v \rangle = a(u, v)$ for $v \in V$.

Note that $a(\cdot, \cdot)$ is bounded ($|a(u, v)| \leq c \|u\|_V \|v\|_V$) and coercive ($c \|u\|_V^2 \leq a(u, u)$). Consequently, by the Lax–Milgram theorem, A is bijective. Also, observe that A^{-1} is bounded since for $Au = f \in V^*$, we can write $\|u\|_V^2 \leq ca(u, u) = c \langle f, u \rangle \leq c \|f\|_{V^*} \|u\|_V$, which gives $\|u\|_V \leq c \|f\|_{V^*}$. Define $S : H \rightarrow H$ by $S = r \circ A^{-1} \circ \iota$, with $A^{-1} : V^* \rightarrow V$, ι the inclusion map $\iota : H \rightarrow V^*$ and r the restriction map $r : V \rightarrow H$. Since A is bijective and A^{-1} bounded, S is compact. Abusing notation, we write $A = S^{-1}$ and consider $A : H \rightarrow H$. Observe that A is symmetric. From spectral theory for unbounded operators, A can be represented by $Au = \sum_{j=1}^{\infty} \lambda_j(u, w_j) w_j$, where λ_j and w_j are the real eigenvalues and eigenfunctions of A , respectively. From the smoothness on the boundaries, the domain of A is given by $D(A) = \{u \in V : u|_{\Omega_i} \in H^2(\Omega_i), u \text{ satisfies (2.4)}\}$. The inner product on $D(A)$ is given by $(u, v)_{D(A)} = (Au, Av)$.

3.3. Projections. We define the projection P_n which maps $u \in H$ into the first n eigenfunctions of A : $P_n u := \sum_{j=1}^n (u, w_j) w_j$. The projection orthogonal to P_n is defined by $Q_n := \text{id} - P_n$.

3.4. Classical results. We review the classical results from [9]. Most of these results have been reduced to fit the application. A page number is included so that the full statement can be recovered.

LEMMA 3.1 [9, page 199]. *If $X = H, V$ or V^* , then*

$$\|P_n u\|_X \leq \|u\|_X, \quad P_n u \rightarrow u \text{ in } X \quad (n \rightarrow \infty).$$

LEMMA 3.2 [9, page 218]. *Let \mathcal{O} be a bounded open set in \mathbb{R}^m and let g_j be a sequence of functions in $L^2(\mathcal{O})$ with $\|g_j\|_{L^p(\mathcal{O})} \leq C$. If $g \in L^2(\mathcal{O})$ and $g_j \rightarrow g$ pointwise almost everywhere, then $g_j \rightarrow g$ in $L^2(\mathcal{O})$.*

THEOREM 3.3 [9, page 191]. *Suppose that*

$$u \in L^2(0, T; V) \quad \text{and} \quad \frac{du}{dt} \in L^2(0, T; V^*).$$

Then $u \in C^0([0, T], H)$, with the caveat that u may have to be adjusted on a set of measure zero.

4. Well-posedness results

We will start with the well-posedness of the weak solutions which we then straightforwardly extend to the well-posedness of the strong solution.

4.1. Weak solutions. We consider

$$\frac{du}{dt} + Au = f(u), \quad (4.1)$$

as an equality in $L^2(0, T; V^*)$.

THEOREM 4.1 (Well-posedness of weak solutions). *For any $T > 0$, (4.1) with $u(0) = u_0 \in H$ has a unique weak solution u such that $u, du/dt \in L^2(0, T; V^*)$ and $u \in C^0([0, T]; H)$ with the caveat that it may have to be adjusted on a set of measure zero. Furthermore, $u_0 \mapsto u(t)$ is in $C^0(H; H)$.*

PROOF. We consider the solutions expressed by the first n eigenfunctions of A :

$$u_n(t) = \sum_{j=1}^n u_{nj}(t)w_j,$$

satisfying

$$\left(\frac{du_n}{dt}, w_i\right) + (Au_n, w_i) = (f(u_n), w_i), \quad 1 \leq i \leq n,$$

with $(u_n(0), w_i) = (u_0, w_i)$. Define $H_n := P_n H \subset H$. We need to solve the initial value problem

$$\frac{dv}{dt} + Av = P_n f(v), \quad v(0) = P_n u(0), \quad (4.2)$$

on the finite-dimensional space H_n . The mapping $v \mapsto -Av + P_n f(v)$ is Lipschitz continuous from H_n to H_n . By standard existence–uniqueness results for ordinary differential equations (ODEs), (4.2) has a unique solution on some finite interval $[0, T]$ with T dependent on n and u_0 . We will see that the solution exists for all $T > 0$.

Consider the inner product of (4.2) with u_n :

$$\left(\frac{du_n}{dt}, u_n\right) + (Au_n, u_n) = (P_n f(u_n), u_n).$$

Observe that $(P_n f(u_n), u_n) = (f(u_n), P_n u_n) = (f(u_n), u_n)$. From the assumption that $(u, f(u)) \leq K$ and the coercivity of $a(\cdot, \cdot)$,

$$\frac{1}{2} \frac{d\|u_n\|_H^2}{dt} + b_{\min} \|u_n\|_V^2 \leq K.$$

Integrating both sides over t between 0 and T gives

$$\frac{1}{2} \|u_n(T)\|_H^2 + b_{\min} \int_0^T \|u_n\|_V^2 dt \leq KT + \frac{1}{2} \|u(0)\|_H^2.$$

We define $\gamma := KT + \frac{1}{2} \|u(0)\|_H^2$. Then, we obtain the bounds:

$$\sup_{t \in [0, T]} \|u_n(t)\|_H^2 \leq 2\gamma, \quad (4.3)$$

$$\int_0^T \|u_n\|_V^2 dt \leq \frac{\gamma}{b_{\min}}. \tag{4.4}$$

Observe that γ is linear in T . Hence, (4.3) with local existence of solutions for (4.2) gives existence of solutions for any $T > 0$. From (4.3) and (4.4), u_n is uniformly bounded in $L^\infty(0, T; H)$ and $L^2(0, T; V)$.

Since $\|f\|_H \leq K$, we see that $f(u_n)$ is uniformly bounded in $L^2(0, T; H)$ and Au_n is uniformly bounded in $L^2(0, T; V^*)$. Hence, from (4.2), du_n/dt is uniformly bounded in $L^2(0, T; V^*)$. By Alogoğlu’s compactness theorem, we can extract a weakly convergent subsequence u_n , with $u_n \rightharpoonup u$ in $L^2(0, T; V)$ and $f(u_n) \rightharpoonup \chi$ in $L^2(0, T; H)$. The strong convergence $u_n \rightarrow u$ in $L^2(0, T; H)$ is obtained by using Lemma 3.2.

Now we want to show that $P_n f(u_n) \rightharpoonup \chi$ in $L^2(0, T; H)$. We have

$$\int_{\Omega_T} (P_n f(u_n) - \chi)\phi \, dx \, dt = \int_{\Omega_T} (f(u_n) - \chi)\phi \, dx \, dt - \int_{\Omega_T} Q_n f(u_n)\phi \, dx \, dt \tag{4.5}$$

for all $\phi \in L^2(0, T; H)$. Recall that $f(u_n) \rightharpoonup \chi$ in $L^2(0, T; H)$. So we just need to consider the Q_n term in (4.5). Observe that $\|Q_n f(u_n)\|_H = \|f(u_n)\|_H \leq K$. We can consider $\phi = \sum_{j=1}^m \alpha_j(t)\phi_j$, where $\alpha_j \in L^2(0, T)$ and $\phi_j \in C_c^\infty(\Omega)$ since ϕ is dense in $L^2(0, T; H)$. From Lemma 3.1, $Q_n \phi_j \rightarrow 0$ in H and we have shown that $P_n f(u_n) \rightharpoonup \chi$ in $L^2(0, T; H)$. By combining the results, we arrive at the equality

$$\frac{du}{dt} + Au = \chi,$$

which holds in the dual space $L^2((0, T); V^*)$.

Next, we show that $\chi = f(u)$. Since $u_n \rightarrow u$ in $L^2(0, T; H)$, there exists a subsequence u_{n_j} such that $u_{n_j}(x, t) \rightarrow u(x, t)$ for almost every $(x, t) \in [0, T] \times \Omega$. Note that $f(u_{n_j})(x, t) \rightarrow f(u)(x, t)$ for almost every $(x, t) \in [0, T] \times \Omega$ and $f(u_{n_j})$ is uniformly bounded in $L^2(0, T; H)$. Therefore, by Lemma 3.2, $f(u_{n_j}) \rightharpoonup f(u)$ in $L^2(0, T; H)$. This implies that the function χ , which is the weak limit of the sequence $f(u_{n_j})$, must be equal to $f(u)$ because there can only be one weak limit in the given function space. Now we have $u \in L^2(0, T; V)$ and $du/dt \in L^2(0, T; V^*)$. By Theorem 3.3, $u \in C^0([0, T]; H)$.

To show that $u_n(0) = u(0)$, let $\phi \in C^1([0, T]; V)$ with $\phi(T) = 0$. Consider the limiting equation of the approximation

$$\left\langle \frac{du}{dt}, v \right\rangle + a(u, v) = \langle f(u), v \rangle \quad (v \in V).$$

Integrating from 0 to T and using integration by parts,

$$\int_0^T -\langle u, \phi' \rangle + a(u, \phi) \, dt = \int_0^T \langle f(u(t)), \phi \rangle \, dt + (u(0), \phi(0)). \tag{4.6}$$

However, from the Galerkin approximation,

$$\int_0^T -\langle u_n, \phi' \rangle + a(u_n, \phi) \, dt = \int_0^T \langle P_n f(u_n(t)), \phi \rangle \, dt + (u_n(0), \phi(0)). \tag{4.7}$$

Recall that $u_n(0) = P_n u_0 \rightarrow u_0$. Taking the limit in (4.7) and comparing it with (4.6) yields $(u_0 - u(0), \phi(0)) = 0$, which implies $u_0 = u(0)$ as $\phi(0)$ is arbitrary.

To show the uniqueness and continuous dependence of the solutions, take $u_0, v_0 \in H$ and consider the corresponding solutions u, v . We define $w := u - v$. Then, w satisfies

$$\frac{dw}{dt} + Aw = f(u) - f(v), \quad w(0) = u_0 - v_0.$$

We take the inner product with w to obtain

$$\frac{1}{2} \frac{d\|w\|_H^2}{dt} + (Aw, w) = (f(u) - f(v), u - v).$$

Because $(f(u) - f(v), u - v) \leq c\|u - v\|_H^2$ and $(Aw, w) \geq b_{\min}\|w\|_V$,

$$\frac{1}{2} \frac{d\|w\|_H^2}{dt} \leq c\|w\|_H^2.$$

By integrating over t , we get $\|u(t) - v(t)\|_H \leq \|u_0 - v_0\|_H e^{ct}$, which implies the uniqueness and continuous dependence on initial conditions. \square

4.2. Strong solutions. In this section, we consider more regular solutions (we refer to such solutions as strong solutions) by regarding (4.1) as an equality that holds in $L^2(0, T; H)$.

THEOREM 4.2 (Well-posedness of strong solutions). *Equation (4.1) with $u(0) = u_0 \in V$ has a unique solution u for any $T > 0$ with $u \in L^2(0, T; D(A))$ and $du/dt \in L^2(0, T; H)$, and $u \in C^0([0, T]; V)$ with the caveat that it may have to be adjusted on a set of measure zero. Furthermore, $u_0 \mapsto u(t)$ in $C^0(V; V)$.*

PROOF. We follow a similar method as in the proof of Theorem 4.1. We consider the inner product of (4.2) with Au_n , which gives

$$\left(\frac{du_n}{dt}, Au_n \right) + \|Au_n\|_H^2 = (P_n f(u_n), Au_n). \quad (4.8)$$

Now, let us assume that $b_1 > b_2$. By integrating the first term on the left-hand side of (4.8) over $t \in [0, T]$, and using the fact that $(du_n/dt, Au_n) = a(u_n, du_n/dt)$,

$$\frac{b_2}{2} \|u_n(T)\|_V^2 - \frac{b_1}{2} \|u_n(0)\|_V^2 \leq \int_0^T \left(\frac{du_n}{dt}, Au_n \right) dt. \quad (4.9)$$

However, by applying the Cauchy–Schwarz inequality and Young’s inequality to the right-hand side of (4.8) and combining with (4.9),

$$\frac{b_2}{2} \|u_n(T)\|_V^2 - \frac{b_1}{2} \|u_n(0)\|_V^2 + \|u_n\|_{L^2(0, T; D(A))}^2 \leq \frac{1}{2} \|P_n f(u_n)\|_{L^2(0, T; H)}^2 + \frac{1}{2} \|u_n\|_{L^2(0, T; D(A))}^2,$$

which implies

$$b_2 \|u_n(T)\|_V^2 - b_1 \|u_n(0)\|_V^2 \leq \|P_n f(u_n)\|_{L^2(0, T; H)}^2 \leq \|f(u_n)\|_{L^2(0, T; H)}^2.$$

By a similar argument as in the proof of Theorem 4.1, we can show that $u_n \rightarrow u$ in $L^2(0, T; D(A))$ and $P_n f(u_n) \rightarrow f(u)$ in $L^2(0, T; H)$.

We have $u \in L^2(0, T; D(A))$ and $du/dt \in L^2(0, T; H)$, so if we take $v = (\nabla u)_i$, then $v \in L^2(0, T; V)$ and $dv/dt \in L^2(0, T; V^*)$, which allows us to apply Theorem 3.3 to deduce that $v \in C^0([0, T]; H)$. Consequently, $u \in C^0([0, T]; V)$.

Next, we adapt the continuous uniqueness proof of Theorem 4.1 for V . Take $u_0, v_0 \in V$ and consider the corresponding solutions u, v . Define $w := u - v$. Then, w satisfies

$$\frac{dw}{dt} + Aw = f(u) - f(v), \quad w(0) = u_0 - v_0.$$

By taking the inner product with Aw and using the fact that f is Lipschitz continuous,

$$\left(\frac{dw}{dt}, Aw\right) + \|Aw\|_H^2 \leq (f(u) - f(v), Aw) \leq \frac{1}{2}c^2\|w\|_V^2 + \frac{1}{2}\|Aw\|_H^2.$$

We move the second term on the right-hand side to the left-hand side, and drop the $\|Aw\|_H^2$ term. By integration over $[0, t]$ and applying similar steps as in (4.9) to the left-hand side,

$$\|w(t)\|_V^2 \leq \frac{c^2}{b_2} \int_0^t \|w(s)\|_V^2 ds + \frac{b_1}{b_2} \|w(0)\|_V^2.$$

From Gronwall’s inequality, $\|u(t) - v(t)\|_V^2 \leq (b_1/b_2)\|u(0) - v(0)\|_V^2 \exp(c^2t/b_2)$, which implies uniqueness and continuous dependence on initial conditions. In the case of $b_2 > b_1$, the result can be obtained by interchanging b_2 and b_1 . □

REMARK 4.3. Let us consider the classical approach to the Laplacian problem with smooth diffusion and regularise the jump in diffusivity by passing to a limit where the transition region between b_1 and b_2 shrinks to a lower-dimensional surface.

We state a Laplacian problem with diffusion coefficient $b_\varepsilon : \bar{\Omega} \rightarrow \mathbb{R}$ (for all $\varepsilon > 0$), where b_ε is sufficiently smooth. Let u_ε be the solution of the problem

$$\begin{aligned} \frac{du_\varepsilon}{dt} - \nabla \cdot (b_\varepsilon \nabla u_\varepsilon) &= f \quad \text{in } \Omega \times [0, T], \\ u_\varepsilon &= 0 \quad \text{on } \partial\Omega \times [0, T], \\ u_\varepsilon &= u_\varepsilon^0 \quad \text{in } \bar{\Omega} \text{ at } t = 0, \end{aligned}$$

with $f \in L^2(0, T; L^2(\Omega))$. Then, $u_\varepsilon \in L^2(0, T; H^2(\Omega)) \cap L^\infty(0, T; H_0^1(\Omega))$ for all $\varepsilon > 0$ (see [4] for the full statement). We note that the statement can be extended to nonlinear f using the techniques in the proof of Theorem 4.1.

When $b_\varepsilon \rightarrow b$ as $\varepsilon \rightarrow 0$, the regularised solutions u_ε are uniformly bounded in $L^2(0, T; V)$. By the compactness theorem, we can extract a subsequence that converges weakly in $L^2(0, T; V)$. Hence, by passing to the limit $\varepsilon \rightarrow 0$, the weak limit u satisfies the weak formulation of the PDE with the discontinuous diffusion coefficient b . Thus, we can obtain $u \in L^2(0, T; V)$. However, the strong solution in $D(A)$ is not guaranteed due to the potential loss of regularity introduced by the discontinuity in b . This is

because the higher regularity (that is, second-order derivatives) may not be controlled uniformly as $\varepsilon \rightarrow 0$, particularly at the interface where the jump occurs.

Instead, we tackled the discontinuous diffusion problem directly, proving the existence and uniqueness of weak solutions using the Galerkin method and then leveraging elliptic regularity results to demonstrate that these weak solutions are actually strong solutions.

5. Conclusion

In this paper, we established the global existence and uniqueness of strong solutions for reaction–diffusion equations with diffraction Laplacian and nonlinear terms describing general oxygen consumption. These results extend previous work [1] which relied on monotonicity properties of the nonlinear term. This work can be used to make results in [3] rigorous as well as provide the theoretical foundation for future numerical work on the dynamics of critical cell states.

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References

- [1] T. G. de Jong, G. Prokert and A. E. Sterk, ‘Reaction-diffusion transport into core-shell geometry: well-posedness and stability of stationary solutions’, Preprint, 2023, [arXiv:2305.03397](https://arxiv.org/abs/2305.03397).
- [2] T. G. de Jong and A. E. Sterk, ‘Topological shooting of solutions for Fickian diffusion into core-shell geometry’, in: *Nonlinear Dynamics of Discrete and Continuous Systems*, Advanced Structured Materials, 139 (eds. A. K. Abramian, I. V. Andrianov and V. A. Gaiko) (Springer, Cham, 2021), 103–116.
- [3] A. Diez, A. L. Krause, P. K. Maini, E. A. Gaffney and S. Seirin-Lee, ‘Turing pattern formation in reaction-cross-diffusion systems with a bilayer geometry’, *Bull. Math. Biol.* **86**(2) (2024), Article no. 13.
- [4] L. C. Evans, *Partial Differential Equations* (American Mathematical Society, Providence, RI, 1998).
- [5] C. C. King, A. A. Brown, I. Sargin, K. M. Bratlie and S. P. Beckman, ‘Modelling of reaction-diffusion transport into core-shell geometry’, *J. Theoret. Biol.* **260** (2019), 204–208.
- [6] C. C. King, A. A. Brown, I. Sargin, K. M. Bratlie and S. P. Beckman, ‘Corrigendum to: modeling of reaction-diffusion transport into a core-shell geometry’, *J. Theoret. Biol.* **507** (2020), Article no. 110439.
- [7] O. A. Ladyzhenskaya, *The Boundary Value Problems of Mathematical Physics*, Applied Mathematical Series, 49 (Springer, New York, 2013).
- [8] M. Marion, ‘Attractors for reaction-diffusion equations: existence and estimate of their dimension’, *Appl. Anal.* **25**(1–2) (1987), 101–147.
- [9] J. C. Robinson, *Infinite-Dimensional Dynamical Systems: An Introduction to Dissipative Parabolic PDEs and the Theory of Global Attractors*, Cambridge Texts in Applied Mathematics, 28 (Cambridge University Press, Cambridge, 2001).

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