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On an inverse problem with applications in cardiac electrophysiology

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Abstract

In this paper, we study the monodomain model of cardiac electrophysiology, which is widely used to describe the propagation of electrical signals in cardiac tissue. The forward problem, described by a reaction–diffusion equation coupled with an ordinary differential equation in a domain containing a perfectly insulating region, is first analysed to establish its well-posedness under standard assumptions on the conductivity and ionic current terms. We then investigate the inverse problem of identifying perfectly insulating regions within the cardiac tissue, which serve as mathematical representations of ischemic areas. These regions are characterised by a complete lack of electrical conductivity, impacting the propagation of electrical signals. We prove that the geometry and location of these insulating regions can be uniquely determined using only partial boundary measurements of the transmembrane potential. Our approach combines tools from elliptic and parabolic PDE theory, Carleman estimates, and the analysis of unique continuation properties.

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These results contribute to the theoretical understanding of diagnostic methods in cardiology.

Keywords: inverse problems, nonlinear boundary value problem, cardiac electrophysiology

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1. Introduction

Mathematical models describing the electrical activity of the heart can provide quantitative tools to describe both normal and abnormal heart function. These models often complement imaging techniques, such as computed tomography and magnetic resonance, for diagnostic and therapeutic purposes. In this context, detecting pathological conditions or reconstructing model features, such as tissue conductivities, from potential measurements requires solving an inverse boundary value problem for a nonlinear system of partial differential equations (*monodomain model*, [11]).

It has been observed that, after myocardial infarction and after the healing process is complete, there is a risk of developing lethal ventricular ischemic tachycardia. This condition is caused by the presence of infarct scars, which have conductivity properties that differ from the surrounding healthy tissue, [11, 19]. There has been extensive work on this topic both mathematically and computationally in the last years, see for example [7, 10, 14, 17, 22, 24]. The determination of these regions and their shape from a recording of the electric activity of the heart is fundamental to performing successful ablation for the prevention of tachycardia. The authors of [3] studied a stationary version of the monodomain model, which led to the investigation of a Neumann problem for a semilinear elliptic equation. They modelled ischemic regions as small conductivity inhomogeneities with lower conductivity compared to the surrounding medium. The presence of the inhomogeneity caused a perturbation in the transmembrane potential, which was described in terms of an asymptotic expansion in a smallness parameter that provided information on the size and shape of the altered region. Based on these findings, a topological gradient method was implemented in [5] to effectively reconstruct the inhomogeneities from boundary measurements of the potential. A similar analysis was then generalised in [1] to the monodomain time-dependent system. In [6], the authors analysed a mathematical model that considered inhomogeneities of arbitrary shape and size in a two-dimensional setting. They focused on the difficult issue of reconstructing the conductivity inclusion from boundary measurements, which is a highly nonlinear severely ill-posed inverse problem. In fact, in this case, uniqueness can only be guaranteed if infinitely many measurements of solutions are available and this is clearly not realistic in the application we have in mind. On the other hand, several studies show that the damaged area can be modelled as an electrical insulator [14, 15, 20]. Mathematically, this leads to modelling the infarcted scar as a perfect insulator, i.e. as *cavities* in a nonlinear system of reaction–diffusion differential equations. In this case, the inverse problem is treatable. In fact, for the stationary monodomain, Beretta *et al* in [4] show that one boundary measurement is enough to recover a collection of well-separated planar cavities. Moreover, in this case, it is possible to implement an efficient reconstruction method of the cavities based on a phase field approach, [2]. In this paper we extend the results obtained in [4] to the three-dimensional monodomain time-dependent model.

In our application, the variable u represents the transmembrane potential that propagates through the heart tissue, hereafter denoted as Ω. The heart muscle has a structure consisting of multiple fibres arranged in superimposed sheets, also known as laminas. This arrangement gives rise to preferred directions in the diffusion of the electrical stimulus, which are captured in our model through the use of a tensor-valued conductivity coefficient K_0. The nonlinear reaction terms appearing in the system account for the presence of ionic currents across the cell membrane, modelling the peculiar nonlinear evolution of the voltage, characterised by the propagation of an initial pulse, a plateau phase, and a slow repolarisation (see [21]). Furthermore, w is the so-called gating variable, which represents the number of open channels per unit area of the cellular membrane and thus regulates the transmembrane currents. Finally, D models the infarcted scar and u_0 the initial activation of the tissue, arising from the propagation of the electrical impulse in the cardiac conduction system.

More precisely, we consider the following boundary value problem

$$\begin{cases} \partial_t u - \operatorname{div}(K_0 \nabla u) + f(u,w) = 0 & \text{in } \Omega_D \times (0,T), \\ K_0 \nabla u \cdot \nu = 0 & \text{on } \partial\Omega_D \times (0,T), \\ \partial_t w + g(u,w) = 0 & \text{in } \Omega_D \times (0,T), \\ u(\cdot,0) = u_0 \qquad w(\cdot,0) = w_0 & \text{in } \Omega_D, \end{cases} \tag{1.1}$$

where $\Omega_D = \Omega \backslash D$, $D \subset \Omega \subset \mathbb{R}^3$, ν is the outward unit normal vector to the boundary $\partial\Omega_D$, K_0 the conductivity tensor. Also, we will analyse the problem considering different types of nonlinearities that are suited to describing cardiac electrophysiology: the *Aliev–Panfilov* model

$$f(u,w) = Au(u-a)(u-1) + uw \qquad g(u,w) = \epsilon(Au(u-1-a) + w), \tag{1.2}$$

the *FitzHugh–Nagumo* model, where

$$f(u,w) = Au(u-a)(u-1) + w \qquad g(u,w) = \epsilon(\gamma w - u), \tag{1.3}$$

and the *Roger–McCulloch* model, with

$$f(u,w) = Au(u-a)(u-1) + uw \qquad g(u,w) = \epsilon(\gamma w - u). \tag{1.4}$$

In each of the above models, A, ϵ and γ are positive constants, while $0 < a < 1$ (see [11] for a general overview).

Our main result concerns the determination of the cavity D from one measurement of the potential u on $\Sigma \times (0,T)$, where Σ is an open subset of $\partial\Omega$. For the forward problem, we prove the existence, and global uniqueness of classical solutions, and derive key uniform bounds via the construction of lower and upper solutions. We then use the properties of solutions to derive the uniqueness of the solution to the inverse problem. To accomplish this we use the structure of the coupled parabolic system and the uniform boundedness of its solutions showing that the transmembrane potential u is the solution of a linear parabolic integro-differential equation. As a byproduct of the results obtained in [12] and [23] a three cylinder inequality is obtained for this class of equations. This guarantees the unique continuation property needed to prove the uniqueness of the solution to the inverse problem.

The plan of the paper is the following: in section 2 we discuss the well-posedness of the forward problem. In section 3 we present the preliminary results needed to prove the main uniqueness result (theorem 3.1).

2. Analysis of the direct problem

We consider the initial-boundary value problem

$$\begin{cases} \partial_t u - \operatorname{div}(K_0 \nabla u) + f(u,w) = 0 & \text{in } \Omega_D \times (0,T), \\ K_0 \nabla u \cdot \nu = 0 & \text{on } \partial\Omega_D \times (0,T), \\ \partial_t w + g(u,w) = 0 & \text{in } \Omega_D \times (0,T), \\ u(\cdot,0) = u_0 \qquad w(\cdot,0) = w_0 & \text{in } \Omega_D, \end{cases} \tag{2.1}$$

where $\Omega_D = \Omega \backslash D$, $D \subset \Omega$, ν is the outward unit normal vector to the boundary $\partial\Omega_D$, K_0 is the conductivity tensor and the nonlinearities f and g are of the kind mentioned in the introduction i.e. (1.2), (1.3), or (1.4).

In this section, we discuss the well-posedness of problem (2.1) in the case of the aforementioned nonlinearities f and g. First, let us introduce some preliminary notation, definitions, and our main assumptions.

Let B'_{r_0} be the open ball of radius r_0 in $\mathbb{R}^2$ centred at the origin and denote by $Q_{r_0,2M_0} = B'_{r_0} \times [-2M_0, 2M_0] \subset \mathbb{R}^3$.

Definition 2.1. ($C^{k+\alpha}$ regularity) Let E be a domain in $\mathbb{R}^3$. Given $k \in \mathbb{N}$ and $0 < \alpha \leqslant 1$, we say that ∂E is of *class* $C^{k+\alpha}$ *with constants* r_0, $M_0 > 0$, if, for any $P \in \partial E$, there exists a rigid transformation of coordinates under which we have $P = 0$ and

$$E \cap B_{r_0}(0) = \{(x', x_3) \in Q_{r_0,2M_0} \quad | \quad x_3 > \varphi(x')\},$$

where φ is a $C^{k+\alpha}$ function on B'_{r_0} satisfying

$$\varphi(0) = 0,$$

$$\nabla\varphi(0) = 0, \quad \text{when } k \geqslant 1,$$

$$\|\varphi\|_{C^{k+\alpha}\left(B'_{r_0}(0)\right)} \leqslant M_0 r_0.$$

When $k = 0$, $\alpha = 1$, we also say that E is of *Lipschitz class with constants* r_0, M_0.

Assumption 2.1. $\Omega \subset \mathbb{R}^3$ is a bounded connected domain, and $\partial\Omega \in C^{2+\alpha}$, $0 < \alpha < 1$.

Assumption 2.2. $K_0(x)$ is a symmetric matrix satisfying the boundedness and ellipticity conditions

$$\lambda^{-1}\|\boldsymbol{\xi}\|^2 \leqslant \xi^T K_0(x)\xi \leqslant \lambda\|\boldsymbol{\xi}\|^2, \forall \xi \in \mathbb{R}^3, \forall x \in \overline{\Omega}, \tag{2.2}$$

where $\lambda > 1$.

Assumption 2.3. K_0 is $C^{1+\alpha}(\overline{\Omega})$.

Assumption 2.4. $D \subset \Omega$, $\partial D \in C^{2+\alpha}$, D is homeomorphic to the sphere and

$$\operatorname{dist}(D, \partial\Omega) \geqslant d_0 > 0. \tag{2.3}$$

Assumption 2.5. $u_0 \in C^{2+\alpha}(\overline{\Omega})$, $w_0 \in C^{\alpha}(\overline{\Omega})$, and $K_0 \nabla u_0 \cdot \nu = 0$ on $\partial\Omega$.

Assumption 2.6. Let us define

$$\mathcal{S} := [0, 1+a] \times \left[0, \frac{A(1+a)^2}{4}\right]$$

for the Aliev–Panfilov and Rogers–McCulloch models, where the nonlinear functions are described in (1.2) and (1.4), while for the FitzHugh–Nagumo model, described by (1.3), we define

$$\mathcal{S} := [-m, m] \times [-m/\gamma, m/\gamma]$$

with m such that

$$\begin{cases} m \geqslant K_+, \quad \text{if} \quad a \leqslant (\gamma A)^{-1}; \\ m \in (0, K_-] \cup [K_+, +\infty) \quad \text{if} \quad a > (\gamma A)^{-1} \end{cases}$$

and $K_\pm = \frac{1}{2}\left[(a+1) \pm \sqrt{(a+1)^2 + 4((\gamma A)^{-1} - a)}\right.$.

In each case, we assume

$$(u_0(x), w_0(x)) \in \mathcal{S} \quad \text{for every } x \in \Omega.$$

We now state the main results regarding the well-posedness of problem (2.1). The proofs of the subsequent results are based on a fixed point argument that leads to a local in-time existence and uniqueness result for classical solutions. Then the properties of the nonlinearities allow the construction of constant upper and lower solutions implying uniform boundness of solutions and global existence in time. This approach is an adaptation of that given in [18] (chapter 8, sections 9 and 11). Hence, we will give here a sketch of the proofs, highlighting the differences with respect to the treatment in [18].

In the following we use the notations:

$$Q_T := \Omega_D \times (0, T); \qquad S_T := \partial\Omega_D \times (0, T). \tag{2.4}$$

We assume for the moment that the nonlinear terms in (2.1) satisfy a global Lipschitz condition with respect to (u, w), that is

$$\begin{aligned} |f(u,w) - f(u',w')| &\leqslant M_1 (|u-u'| + |w-w'|), \\ |g(u,w) - g(u',w')| &\leqslant M_2 (|u-u'| + |w-w'|), \end{aligned} \tag{2.5}$$

for some positive M_1, M_2 and for any $(u,w), (u',w') \in \mathbb{R}^2$.

Theorem 2.1. *Let assumptions 2.1–2.5 hold and assume also the global Lipschitz conditions (2.5) hold. Then, problem (2.1) admits a unique classical solution (u, w), namely $u \in C^{2+\alpha,1+\alpha/2}(\overline{Q_T})$, $w \in C^{\alpha,1+\alpha/2}(\overline{Q_T})$.*

Proof. Let us define the new variables $v := \mathrm{e}^{-\kappa t}u$, $w := \mathrm{e}^{-\kappa t}w$, where $\kappa > 0$ is a constant to be chosen. Then, problem (2.1) becomes

$$\begin{cases} \partial_t v - \operatorname{div}(K_0 \nabla v) + \kappa v = f^*(t, v, w) & \text{in } Q_T, \\ K_0 \nabla v \cdot \nu = 0 & \text{on } S_T, \\ \partial_t w + \kappa w = g^*(t, v, w) & \text{in } Q_T, \\ v(\cdot, 0) = u_0, \quad w(\cdot, 0) = w_0 & \text{in } \Omega_D, \end{cases} \tag{2.6}$$

where

$$f^*(t,v,w) = -\mathrm{e}^{-\kappa t}f(\mathrm{e}^{\kappa t}v,\mathrm{e}^{\kappa t}w) \qquad g^*(t,v,w) = -\mathrm{e}^{-\kappa t}g(\mathrm{e}^{\kappa t}v,\mathrm{e}^{\kappa t}w)\,. \quad (2.7)$$

Note that the same global Lipschitz condition (2.5) holds for f^* and g^* with constants independent of t; hence, in the following we will drop the explicit dependence on t of f^* and g^*. We will reformulate the problem (2.6) as a fixed point equation in the Banach space of the pairs (v,w), v, $w \in C(\overline{Q_T})$, equipped with the sup norm. Let us first define the map

$$\mathcal{A} : \mathcal{D}(\mathcal{A}) \to C(Q_T)\,; \qquad \mathcal{A}v := \partial_t v - \mathrm{div}(K_0\nabla v) + \kappa v\,, \quad (2.8)$$

where

$$\mathcal{D}(\mathcal{A}) := \left\{ v \in C^{2+\alpha,1+\alpha/2}\left(\overline{Q_T}\right),\, K_0\nabla v\cdot\nu\big|_{S_T} = 0, v(\cdot,0) = u_0 \right\}. \quad (2.9)$$

We further observe that the problem for w in (2.6) is equivalent to the integral equation

$$w(x,t) = \mathrm{e}^{-\kappa t}w_0(x) + \int_0^t \mathrm{e}^{-\kappa(t-\tau)}g^*(\tau, v(x,\tau), w(x,\tau))\,\mathrm{d}\tau\,. \quad (2.10)$$

Hence, by denoting with $G(t,v,w)$ the right hand side of (2.10), we can write (2.6) in the operator form

$$\begin{cases} \mathcal{A}v = f^*(t,v,w)\,, \\ w = G(t,v,w)\,. \end{cases} \quad (2.11)$$

Now, in order to get the fixed point equation we discuss the invertibility of the map $\mathcal{A}$ following [18]. To this aim, by exploiting the regularity of K_0, we write (2.8) in non-divergence form.

Then by known results in the theory of linear parabolic equations, see for example theorem 5.1.20 in [16], we can ensure the existence of a unique solution $v \in \mathcal{D}(\mathcal{A})$ such that $\mathcal{A}v = h$ provided $h \in C^{\alpha,\alpha/2}(\overline{Q_T})$.

Then the inverse map $\mathcal{A}^{-1}$ is well defined on the subspace $X = C^{\alpha,\alpha/2}(\overline{Q_T})$; furthermore, it is easily verified that f^* and G map $X \times X$ into X. Hence we finally get

$$\begin{cases} v = \mathcal{A}^{-1}f^*(t,v,w)\,, \\ w = G(t,v,w) \end{cases} \quad (2.12)$$

with $(v,w) \in X \times X$.

By denoting with $|\cdot|_0$ the sup norm in $C(\overline{Q_T})$, we can now follow the same pattern as in the proof of lemma 9.1 in [18] chapter 8, section 9, using assumption 2.2 and maximum principle arguments to get the estimate

$$|\mathcal{A}v - \mathcal{A}v'|_0 \geqslant \kappa|v - v'|_0 \qquad v, v', \in \mathcal{D}(\mathcal{A})\,. \quad (2.13)$$

The only delicate point is that in [18] it is assumed a Neumann (or Dirichlet) boundary condition on S_T, which is different from the condition in (2.9). Nevertheless, it can be shown that the proof still works because, by assumption 2.2, we have that $K_0\nu\cdot\nu > 0$.

By (2.12) and (2.13), we now have

$$|\mathcal{A}^{-1}f^*(t,v,w)-\mathcal{A}^{-1}f^*(t,v',w')|_0 \leqslant \frac{1}{\kappa}|f^*(t,v,w)-f^*(t,v',w')|_0 \\ \leqslant \frac{M_1}{\kappa}\left(|v-v'|_0+|w-w'|_0\right). \tag{2.14}$$

Finally, by the definition of G (see (2.10)) and by (2.5) it follows readily

$$|G(t,v,w)-G(t,v',w')|_0 \leqslant \frac{M_2}{\kappa}\left(|v-v'|_0+|w-w'|_0\right). \tag{2.15}$$

By choosing $\kappa > M_1+M_2$ the map defined by the right-hand side of (2.12) is a contraction in $X\times X$ with respect to the sup norm. Let us now consider the Picard approximations $(v^{(k)},w^{(k)})$ such that

$$\begin{cases} v^{(k)} = \mathcal{A}^{-1}f^*\left(t,v^{(k-1)},w^{(k-1)}\right), \\ w^{(k)} = G\left(t,v^{(k-1)},w^{(k-1)}\right), \end{cases} \tag{2.16}$$

$(v^{(0)},w^{(0)})\in X\times X$ arbitrary. Since $(\mathcal{A}^{-1}f^*,G)$ is a contraction in the sup norm, by standard arguments $\{v^{(k)},w^{(k)}\}$ is a Cauchy sequence with respect to the sup norm. By the arguments from (2.8) to (2.12), for $k=1,2\ldots$ the pair $(v^{(k)},w^{(k)})$ is the unique solution in $C^{2+\alpha,1+\alpha/2}((\overline{Q_T})\times C^{\alpha,1+\alpha/2}(\overline{Q_T})$ of the linear problem

$$\begin{cases} \mathcal{A}v^{(k)} = f^*\left(t,v^{(k-1)},w^{(k-1)}\right), \\ w^{(k)} = G\left(t,v^{(k-1)},w^{(k-1)}\right). \end{cases} \tag{2.17}$$

Then, by classical regularity estimates (see e.g. [16], section 5.1.2 theorem 5.1.17) and by (2.5) we have for every $m>k\geqslant 1$

$$\|v^{(m)}-v^{(k)}\|_{C^{\alpha,\alpha/2}(\overline{Q_T})} \leqslant C|f^*(t,v^{(m-1)},w^{(m-1)})-f^*(t,v^{(k-1)},w^{(k-1)}|_0 \\ \leqslant C^*(|v^{(m-1)}-v^{(k-1)}|_0+|w^{(m-1)}-w^{(k-1)}|_0).$$

Since $\{v^{(k)},w^{(k)}\}$ is a Cauchy sequence in the $|\cdot|_0$ norm it follows that $\{v^{(k)}\}$ is also a Cauchy sequence in the $\|\cdot\|_{C^{\alpha,\alpha/2}(\overline{Q_T})}$ norm. A similar conclusion holds for the sequence $\{w^{(k)}\}$ by elementary (but tedious) estimates of $\|w^{(m)}-w^{(k)}\|_{C^{\alpha,\alpha/2}(\overline{Q_T})}$ starting from (2.10). Then, the sequence $\{v^{(k)},w^{(k)}\}$ converges to a unique solution (v,w) of (2.12) in $X\times X$. Clearly, (v,w) is also the unique solution of (2.11) i.e. (2.6) which implies that (u,w) is the unique solution of (2.1) and the claim follows. □

We now need to replace the global Lipschitz condition on the nonlinear terms with a local one in order to include the cases of the nonlinearities (1.2), (1.3) and (1.4).

Preliminarily, we introduce further definitions and results from [18], Chapter 8, section 9.

Definition 2.2. Two pairs of functions $(\overline{u},\overline{w})$, $(\underline{u},\underline{w})$, each one in $C^{2+\alpha,1+\alpha/2}(\overline{Q_T})\times C^{\alpha,1+\alpha/2}(\overline{Q_T})$, are called generalised coupled upper and lower solutions of (2.1) if $\overline{u}\geqslant\underline{u}$,

$\overline{w} \geqslant \underline{w}$ and if they satisfy

$$\begin{cases} \partial_t \overline{u} - \operatorname{div}(K_0 \nabla \overline{u}) + f(\overline{u}, z) \geqslant 0 & \text{in } Q_T, \quad \forall z \in [\underline{w}, \overline{w}], \\ K_0 \nabla \overline{u} \cdot \nu \geqslant 0 & \text{on } S_T, \\ \partial_t \overline{w} + g(v, \overline{w}) \geqslant 0 & \text{in } Q_T, \quad \forall v \in [\underline{u}, \overline{u}], \\ \overline{u}(\cdot, 0) \geqslant u_0 \qquad \overline{w}(\cdot, 0) \geqslant w_0 & \text{in } \Omega_D, \end{cases} \tag{2.18}$$

$$\begin{cases} \partial_t \underline{u} - \operatorname{div}(K_0 \nabla \underline{u}) + f(\underline{u}, z) \leqslant 0 & \text{in } Q_T, \quad \forall z \in [\underline{w}, \overline{w}], \\ K_0 \nabla \underline{u} \cdot \nu \leqslant 0 & \text{on } S_T, \\ \partial_t \underline{w} + g(v, \underline{w}) \leqslant 0 & \text{in } Q_T, \quad \forall v \in [\underline{u}, \overline{u}], \\ \underline{u}(\cdot, 0) \leqslant u_0 \qquad \underline{w}(\cdot, 0) \leqslant w_0 & \text{in } \Omega_D, \end{cases} \tag{2.19}$$

where, as in [18], we denote by

$$[\underline{w}, \overline{w}] = \left\{ z \in C\left(\overline{Q_T}\right) \,:\, \underline{w} \leqslant z \leqslant \overline{w} \right\} \quad \text{and} \quad [\underline{u}, \overline{u}] = \left\{ v \in C\left(\overline{Q_T}\right) \,:\, \underline{u} \leqslant v \leqslant \overline{u} \right\}.$$

We now suppose that for every $R > 0$ there are constants $M_1 = M_1(R)$, $M_2 = M_2(R)$ such that

$$\begin{aligned} |f(u,w) - f(u',w')| &\leqslant M_1 \left(|u - u'| + |w - w'| \right), \\ |g(u,w) - g(u',w')| &\leqslant M_2 \left(|u - u'| + |w - w'| \right), \end{aligned} \tag{2.20}$$

whenever $|u| + |w| \leqslant R$, $|u'| + |w'| \leqslant R$.

Then we can prove (see [18], chapter 8, theorem 9.3)

Theorem 2.2. *Let assumptions 2.1–2.5 hold and let* $(\overline{u}, \overline{w})$*,* $(\underline{u}, \underline{w})$ *be generalised coupled upper and lower solutions to (2.1), where f, g satisfy (2.20). Then the problem (2.1) has a unique solution (u, w) with* $\underline{u} \leqslant u \leqslant \overline{u}$*,* $\underline{w} \leqslant w \leqslant \overline{w}$*.*

Proof. Let us define

$$\mathcal{S} := \left\{ (v,z) \in C^{2+\alpha, 1+\alpha/2}\left(\overline{Q_T}\right) \times C^{\alpha, 1+\alpha/2}\left(\overline{Q_T}\right) \,:\, \underline{u} \leqslant v \leqslant \overline{u}, \quad \underline{w} \leqslant z \leqslant \overline{w} \right\} \tag{2.21}$$

For any pair $(v,z) \in \mathcal{S}$ let (u^*, w^*) be the solution of the *linear* problem

$$\begin{cases} \partial_t u^* - \operatorname{div}(K_0 \nabla u^*) + M_1 u^* = M_1 v - f(v,z) & \text{in } Q_T, \\ K_0 \nabla u^* \cdot \nu = 0 & \text{on } S_T, \\ \partial_t w^* + M_2 w^* = M_2 z - g(v,z) & \text{in } Q_T, \\ u^*(\cdot, 0) = u_0 \qquad w^*(\cdot, 0) = w_0 & \text{in } \Omega_D, \end{cases} \tag{2.22}$$

where M_1, M_2 are the Lipschitz constants in (2.20) and we assume R larger than any $|v|_0 + |z|_0$ for $(v,z) \in \mathcal{S}$. Let us point out that this value of R only depends on $(\overline{u}, \overline{w})$ and $(\underline{u}, \underline{w})$. Let $U := \overline{u} - u^*$; by (2.18) and (2.22) we get

$$\partial_t U - \operatorname{div}(K_0 \nabla U) + M_1 U \geqslant -f(\overline{u}, z) + M_1 (\overline{u} - v) + f(v,z). \tag{2.23}$$

Now, by the Lipschitz condition and recalling that $v \leqslant \overline{u}$, we get

$$f(v,z) - f(\overline{u}, z) \geqslant -M_1 (\overline{u} - v).$$

Hence,

$$\partial_t U - \mathrm{div}\,(K_0 \nabla U) + M_1 U \geqslant 0, \tag{2.24}$$

together with the boundary condition $K_0 \nabla U \cdot \nu \geqslant 0$ and the initial condition $U(x,0) \geqslant 0$.

Thus, by the maximum principle for parabolic operators (see [18, lemma 2.1]) $U \geqslant 0$ in $\overline{Q_T}$, which yields $u^* \leqslant \overline{u}$. An analogous argument with the lower solution gives $u^* \geqslant \underline{u}$.

Similarly, by defining $W = \overline{w} - w^*$ we readily find that

$$\partial_t W + M_2 W \geqslant 0, \tag{2.25}$$

together with the initial condition $W(x,0) \geqslant 0$, so that we still have $W \geqslant 0$ and $w^* \leqslant \overline{w}$. Finally, we get $w^* \geqslant \underline{w}$ by considering the lower solution.

Now, by suitably modifying the functions f, g outside $[-R,R]^2$, we can still assume that they are globally Lipschitz; then, for any $(u^{(0)}, w^{(0)}) \in \mathcal{S}$, consider the sequence defined by

$$\begin{cases} \partial_t u^{(k)} - \mathrm{div}\left(K_0 \nabla u^{(k)}\right) + M_1 u^{(k)} = M_1 u^{(k-1)} - f\left(u^{(k-1)}, w^{(k-1)}\right) & \text{in } Q_T \\ K_0 \nabla u^{(k)} \cdot \nu = 0 & \text{on } S_T, \\ \partial_t w^{(k)} + M_2 w^{(k)} = M_2 w^{(k-1)} - g\left(u^{(k-1)}, w^{(k-1)}\right) & \text{in } Q_T, \\ u^{(k)}(\cdot,0) = u_0 \qquad w^{(k)}(\cdot,0) = w_0 & \text{in } \Omega_D, \end{cases} \tag{2.26}$$

with $k = 1, 2, \ldots$. By the previous bounds, every pair $(u^{(k)}, w^{(k)})$ belongs to $\mathcal{S}$. Hence, we can still apply the arguments of theorem 2.1 with the global Lipschitz condition to conclude that the sequence $(u^{(k)}, w^{(k)})$ converges uniformly to a unique solution (u,w) of the problem 2.1 and that $\underline{u} \leqslant u \leqslant \overline{u}$, $\underline{w} \leqslant w \leqslant \overline{w}$.

□

In order to apply theorem 2.2 to our models we need to find suitable upper and lower solutions for f and g as in (1.2), (1.3), (1.4). Actually, it is convenient to look for *constant* upper and lower solutions:

Lemma 2.3. *For each one of the nonlinear terms (1.2)–(1.4), if assumption 2.6 holds, there exist constant upper and lower solutions.*

Precisely, in the Aliev–Panfilov and Rogers–McCulloch models one can take $\underline{u} = 0$, $\underline{w} = 0$, while

$$\overline{u} = 1 + a, \qquad \overline{w} \geqslant A(1+a)^2/4 \tag{2.27}$$

in the Aliev -Panfilov model and

$$\overline{u} \in (0,a) \cup (1,+\infty), \qquad \overline{w} \geqslant \overline{u}/\gamma, \tag{2.28}$$

in the Rogers-McCulloch model.

Finally, in the Fitzhugh–Nagumo model one can take $\overline{u} = m = -\underline{u}$, $\overline{w} = m/\gamma = -\underline{w}$, with

$$\begin{cases} m \geqslant K_+, & \text{if} \quad a \leqslant (\gamma A)^{-1}; \\ m \in (0, K_-] \cup [K_+, +\infty) & \text{if} \quad a > (\gamma A)^{-1} \end{cases} \tag{2.29}$$

and $K_\pm = \frac{1}{2}\left[(a+1) \pm \sqrt{(a+1)^2 + 4((\gamma A)^{-1} - a)}\right.$.

Proof. We have to check definition 2.2 for the three nonlinearities.

If $f(u,w) = Au(u-a)(u-1)+uw$, $g(u,w) = \epsilon(Au(u-1-a)+w)$, we have $f(0,w) = 0$, $g(u,0) = \epsilon Au(u-1-a) \leqslant 0$ for any $u \in [0,1+a]$; moreover $f(1+a,w) = (1+a)(Aa+w) \geqslant 0$. Finally, $g(u,\overline{w}) \geqslant 0$ if $\overline{w} \geqslant Au(1+a-u)$ and by an elementary calculation we get

$$\max_{0\leqslant u\leqslant 1+a} Au(1+a-u) = A\frac{(1+a)^2}{4}. \tag{2.30}$$

Hence, in the Aliev–Panfilov model theorem 2.2 applies if the values (u_0,w_0) of the initial data lie in the rectangle $\mathrm{S} = [0,1+a] \times \left[0, \frac{A(1+a)^2}{4}\right]$.

Let us now consider the Rogers-McCulloch model, where f is unchanged and $g(u,w) = \epsilon(\gamma w - u)$. Clearly, we still have $f(0,w) = 0$ for every w and $g(u,0) = -\epsilon u \leqslant 0$ for any $u \geqslant 0$. Now, since

$$f(\overline{u},w) = A\overline{u}\left((\overline{u}-a)(\overline{u}-1)+w\right),$$

we see that the condition $f(\overline{u},w) \geqslant 0$ for any $w \geqslant 0$ holds provided that $(\overline{u}-a)(\overline{u}-1) \geqslant 0$, i.e. $\overline{u} \in (0,a) \cup (1+\infty)$. Finally, by choosing $\overline{w} \geqslant \overline{u}/\gamma$ we get

$$g(u,\overline{w}) = \epsilon(\gamma\overline{w}-u) \geqslant 0 \qquad \forall\, u \in [0,\overline{u}]\,.$$

Thus, in this model we can take $S = [0,\overline{u}] \times [0,\overline{w}]$, with the above $\overline{u}$, $\overline{w}$.

We are left to consider the Fitzhugh–Nagumo model where

$$f(u,w) = Au(u-a)(u-1)+w, \qquad g(u,w) = \epsilon(\gamma w - u)\,. \tag{2.31}$$

As can be readily checked, in this case we can choose $S = [-m,m] \times [-m/\gamma, m/\gamma]$, provided that m satisfies

$$-A(m+a)(m+1)+\frac{1}{\gamma} \leqslant 0 \leqslant A(m-a)(m-1)-\frac{1}{\gamma}\,.$$

Hence, by elementary calculations we deduce the conditions (2.29) on m.

□

Remark 2.4. It is worthwhile to remark that non-negative constant lower and upper solutions also exist in the Fitzhugh–Nagumo model if the product γA is large enough.

In fact, we first observe that by taking $\underline{u} > 0$ and $\underline{w} = 0$, we get $g(u,0) = -\epsilon u < 0$; moreover, the inequality

$$f(\underline{u},w) = A\underline{u}(\underline{u}-a)(\underline{u}-1)+w \leqslant 0$$

could be satisfied if $a < \underline{u} < 1$ and $w > 0$ is small enough. Actually, by defining $m_a = -\min_{a<u<1} u(u-a)(u-1) > 0$ and by choosing $\underline{u}$ at the minimum point, the above bound is satisfied if $\overline{w} \leqslant Am_a$.

Finally, the upper solutions must satisfy

$$g(u,\overline{w}) = \epsilon(\gamma\overline{w}-u) \geqslant \epsilon(\gamma\overline{w}-\overline{u}) \geqslant 0$$

and

$$f(\overline{u},w) = A\overline{u}(\overline{u}-a)(\overline{u}-1)+w \geqslant 0.$$

These two conditions lead to $\overline{u} \leqslant \gamma\overline{w} \leqslant \gamma A m_a$ and to $\overline{u} > 1$ respectively. The last inequalities are compatible only if $\gamma A > 1/m_a$.

Collecting the results obtained so far, we can state

Theorem 2.5. *Let assumptions 2.1–2.6 hold with (f, g), be defined as in (1.2), (1.3), (1.4) respectively. Then, problem (2.1) admits a unique classical solution (u, w), namely $u \in C^{2+\alpha,1+\alpha/2}(\overline{Q_T})$, $w \in C^{\alpha,1+\alpha/2}(\overline{Q_T})$. Moreover, $(u, v) \in \mathcal{S}$ for every T, where $\mathcal{S}$ is given in assumption 2.6.*

3. Analysis of the inverse problem: uniqueness

Consider the initial-boundary value problem

$$\begin{cases} \partial_t u - \operatorname{div}(K_0 \nabla u) + f(u,w) = 0 & \text{in } \Omega_D, \\ K_0 \nabla u \cdot \nu = 0 & \text{on } \partial\Omega_D, \\ \partial_t w + g(u,w) = 0 & \text{in } \Omega_D \times (0,T), \\ u(\cdot,0) = u_0 \qquad w(\cdot,0) = w_0 & \text{in } \Omega_D. \end{cases} \tag{3.1}$$

In this section, we will investigate the uniqueness of the inverse problem i.e.

Problem 3.1. Assume it is possible to measure the solution to (3.1), $u_{|\Sigma\times(0,T)}$ where Σ is an open connected portion of $\partial\Omega$. Is it possible to uniquely determine D?

The answer is positive under the further assumption that the initial datum u_0 is non trivial and its support lies so close to the boundary of Ω that it never intersects the cavity D. More precisely we assume that

Assumption 3.1. $u_0 \not\equiv 0$ and

$$\operatorname{supp}(u_0) \subset \{x \in \Omega : d(x, \partial\Omega) \leqslant d_0/2\}. \tag{3.2}$$

Then the following result holds:

Theorem 3.1. *Let assumptions 2.1–2.6 and assumption 3.1 hold and let (f, g), be defined as in (1.2), (1.3), (1.4). Let (u_1, w_1), $(u_2, w_2) \in C^{2+\alpha,1+\alpha/2}(\overline{Q_T}) \times C^{\alpha,1+\alpha/2}(\overline{Q_T})$ be solutions of (3.1) corresponding to $D = D_1$ and D_2 respectively. If $u_1 = u_2$ on $\Sigma \times (0,T)$ where Σ is an open portion of $\partial\Omega$, then $D_1 = D_2$.*

To prove the theorem we will state and prove some preliminary results.

3.1. Estimates of unique continuation

We will show that solutions of system (3.1) enjoy the unique continuation property by deriving a three cylinder inequality. We denote by B_r the open ball of radius r in $\mathbb{R}^3$ centred at the origin and by Q_r^T the cylinder $Q_r^T = B_r \times (0,T)$ in $\mathbb{R}^4$.

Theorem 3.2. *Let $u \in H^{2,1}\left(Q_R^T\right)$ be such that*

$$|\partial_t u - \operatorname{div}(K_0 \nabla u)| \leqslant \Lambda_0 \left(|u| + |\nabla u| + \int_0^t |u(x,s)|\,\mathrm{d}s \right) \quad \text{in } Q_R^T, \tag{3.3}$$

for some constant Λ_0 *and where* K_0 *satisfies assumptions* 2.2 *and* 2.3, *and*

$$u(x,0) = 0. \tag{3.4}$$

There exists a constant C depending on λ, $\|K_0\|_{C^{1,\alpha}}$ *and* Λ_0 *such that, for*

$$r \leqslant \rho \leqslant R/C$$

and $\delta \in (0,T)$, *we have*

$$\|u\|_{L^2(Q_\rho^{T-\delta})} \leqslant \left(\frac{CTR}{\delta\rho}\right)^{\beta} \|u\|^{\theta}_{L^2(Q_r^T)} \|u\|^{1-\theta}_{L^2(Q_R^T)} \tag{3.5}$$

where

$$\theta = \frac{\log \frac{R}{C\rho}}{C\log\frac{R}{r}} \text{ and } \beta = C\left(\frac{R^2}{T} + \frac{T}{\delta}\right)^{C}. \tag{3.6}$$

Proof. The proof can be obtained by following the proofs in [12] (that contains the Carleman estimate needed for this result) and [23] (that contains the proof of how three cylinder inequality follows from Carleman estimate). The main difference in the present case is the integral term in the right-hand side of (3.3). Let us sketch the procedure to perform the proof in our case, without repeating all the technical details that can be already found in the cited references. We point out that those results hold in any dimension.

The main tool we use in the proof is a Carleman estimate with a singular weight. This estimate is proved in [12] and [23] (in both cases, the matrix K_0 also depends on t). In [12], only Lipschitz continuity of the matrix K_0 is required, while in [23], a bit more regularity is needed. This discrepancy between the assumptions in [12] and [23] is due to the use of different proof techniques and, incidentally, this discrepancy is due to the dependence on t. However, in any case, it has no impact on the proof of the three-cylinder inequality.

Due to the local nature of the Carleman estimate (derived from [12]) that we are about to write, we can assume that

$$K_0(0) = I_3, \tag{3.7}$$

where I_3 is the identity matrix on $\mathbb{R}^3$.

We denote by

$$Pv = \partial_t v - \operatorname{div}(K_0 \nabla v), \tag{3.8}$$

$$\gamma(s) = s\exp\left(\int_0^s \frac{\mathrm{e}^{-\mu z}-1}{z}\,\mathrm{d}z\right),$$

where μ is a positive real constant that depends only on λ and we denote by

$$\rho(x) = \gamma(|x|).$$

For simplicity, we assume $T=1$ in the following.

We observe that

$$\rho(x) \sim |x|, \quad \text{as } x \to 0. \tag{3.9}$$

Relation (3.9) together with the fact that γ is an increasing function are the only relevant facts to deduce theorem 3.2 from the Carleman estimate (from [23]):

$$\tau \int_{\mathbb{R}^4} \rho^{1-2\tau} |\nabla_x v|^2 \, \mathrm{d}x\,\mathrm{d}t + \tau^3 \int_{\mathbb{R}^4} \rho^{-1-2\tau} |v|^2 \, \mathrm{d}x\,\mathrm{d}t \leqslant C \int_{\mathbb{R}^4} \rho^{2-2\tau} |Pv|^2 \, \mathrm{d}x\,\mathrm{d}t \tag{3.10}$$

for every $v \in C_0^\infty((B_R \setminus \{0\}) \times (-1,1))$ and for every $\tau \geqslant \tau_0$, where C, R, and τ_0 depend on λ.

In the following, for brevity, we will omit both the integration domain and the volume element $\mathrm{d}x\,\mathrm{d}t$.

By virtue of (3.4), we can extend u to zero for $t \leqslant 0$. This extension, which we will continue to denote by u, belongs to $H^{2,1}(B_R \times (-1,1))$. By density, we can apply the estimate (3.10) to

$$v(x,t) = \zeta(x,t)\, u(x,t),$$

where $\zeta(x,t) = \widetilde{\xi}(x)\eta(t)$ and $\widetilde{\xi}$, η are two cutoff functions that we now define.

Let $r \leqslant \frac{R}{2}$ and let $\widetilde{\xi}(s)$ be a $C_0^\infty(0,R)$ function such that $0 \leqslant \widetilde{\xi} \leqslant 1$, $\widetilde{\xi}(s) = 1$ on $\left[\frac{r}{2}, \frac{R}{2}\right]$, and also:

$$\widetilde{\xi}(s) = 0, \quad \text{for } s \in \left(0, \frac{r}{4}\right] \cup \left[\frac{3R}{4}, R\right),$$

$$\left|\widetilde{\xi}'(s)\right| \leqslant cr^{-1}, \quad \left|\widetilde{\xi}''(s)\right| \leqslant cr^{-2}, \quad \text{for } s \in \left[\frac{r}{4}, \frac{r}{2}\right],$$

$$\left|\widetilde{\xi}'(s)\right| \leqslant cR^{-1}, \quad \left|\widetilde{\xi}''(s)\right| \leqslant cR^{-2}, \quad \text{for } s \in \left[\frac{R}{2}, \frac{3R}{2}\right],$$

where c is a constant.

Regarding η, for the moment we limit ourselves to stating that $\eta \in C_0^\infty(-1,1)$, $0 \leqslant \eta \leqslant 1$, η is even, and for $\delta \in \left(0, \frac{1}{2}\right)$, $\eta(s) = 1$ for $|t| \leqslant 1 - 2\delta$, $\eta(s) = 0$ for $1 - \delta \leqslant t < 1$. Additionally, η is decreasing in the interval $[1-2\delta, 1-\delta]$. At this point, we believe it is useful to emphasise that: (a) in reality, the behaviour of η for $t \leqslant 0$ is irrelevant, as $u = 0$ for $t \leqslant 0$, (b) the fact that η is decreasing in the interval $[1-2\delta, 1-\delta]$ is the only relevant aspect to connect to the proof of theorem 15 in [23], (c) the explicit expression of η on the interval $[1-2\delta, 1-\delta]$ requires a careful choice that, however, concerns exclusively the proof of theorem 15 in [23]. Note in this regard that the weight function ρ in the Carleman estimate (3.10) depends only on x and not on t. This implies that the control over the strips $B_R \times [1-2\delta, 1-\delta]$ in the proof of theorem 15 in [23] is not entirely standard and therefore requires a specific form of η to effectively exploit the estimate (3.10) (especially the presence, which is very useful for our purposes, of the coefficient τ^3 in the second term on the left side of the estimate (3.10)).

We have

$$P(\zeta u) = \zeta P u + H, \tag{3.11}$$

where

$$H = uP\zeta - 2K_0 \nabla_x \zeta \cdot \nabla_x u.$$

From (3.2), we immediately have

$$|P(\zeta u)|^2 \leqslant 4\Lambda_0^2\zeta^2\left(|u(x,t)|^2+|\nabla_x u(x,t)|^2+\left(\int_0^t |u(x,s)|\,\mathrm{d}s\right)^2\right)+2H^2.$$

From the latter and the estimate (3.10), we obtain

$$\begin{aligned}
&\tau\int\rho^{1-2\tau}|\nabla_x(\zeta u)|^2+\tau^3\int\rho^{-1-2\tau}|\zeta u|^2\\
&\quad\leqslant C\int\rho^{2-2\tau}|P(\zeta u)|^2\leqslant 2C\int\rho^{2-2\tau}H^2\\
&\qquad+4\Lambda_0^2\int\rho^{2-2\tau}\zeta^2\left(|u(x,t)|^2+|\nabla_x u(x,t)|^2+\left(\int_0^t|u(x,s)|\,\mathrm{d}s\right)^2\right)
\end{aligned}\tag{3.12}$$

for every $\tau \geqslant \tau_0$.

At this point, we refer back to the situation already addressed in theorem 15 of [23]. Since the terms

$$\int\rho^{2-2\tau}H^2 \quad\text{and}\quad \int\rho^{2-2\tau}\zeta^2\left(|u(x,t)|^2+|\nabla_x u(x,t)|^2\right)$$

already appear in [23] (more precisely, taking into account the different notations used in [23], in inequality (120)), the only new term to handle is

$$\int\rho^{2-2\tau}\zeta^2\left(\int_0^t|u(x,s)|\,\mathrm{d}s\right)^2. \tag{3.13}$$

For greater clarity, we reintroduce the integration domain and the volume element. Applying the Cauchy–Schwarz inequality to the inner integral and then using the fact that η is non-increasing in $[0,1)$, we have

$$\begin{aligned}
&\int_{\mathbb{R}^4}\rho^{2-2\tau}\zeta^2\left(\int_0^t|u(x,s)|\,\mathrm{d}s\right)^2\mathrm{d}x\,\mathrm{d}t\\
&\quad\leqslant\int_{\mathbb{R}^3}\mathrm{d}x\,\rho^{2-2\tau}\widetilde{\xi}^2(x)\int_0^1\mathrm{d}t\left\{\eta^2(t)\,t\int_0^t|u(x,s)|^2\,\mathrm{d}s\right\}\\
&\quad\leqslant\int_{\mathbb{R}^3}\mathrm{d}x\,\rho^{2-2\tau}\widetilde{\xi}^2(x)\int_0^1\mathrm{d}t\left\{t\int_0^t\eta^2(s)|u(x,s)|^2\,\mathrm{d}s\right\}.
\end{aligned}\tag{3.14}$$

Now, by simply switching the order of integration, we obtain

$$\begin{aligned}
\int_0^1\mathrm{d}t\left\{t\int_0^t\eta^2(s)|u(x,s)|^2\,\mathrm{d}s\right\}&=\int_0^1\left(\int_s^1 t\,\mathrm{d}t\right)\eta^2(s)|u(x,s)|^2\,\mathrm{d}s\\
&\leqslant\frac{1}{2}\int_0^1\eta^2(t)|u(x,t)|^2\,\mathrm{d}t.
\end{aligned}\tag{3.15}$$

Now, we use (3.15) in (3.14) and obtain

$$\int_{\mathbb{R}^4}\rho^{2-2\tau}\zeta^2\left(\int_0^t|u(x,s)|\,\mathrm{d}s\right)^2\mathrm{d}x\,\mathrm{d}t\leqslant\int_{\mathbb{R}^4}\rho^{2-2\tau}\zeta^2u^2\,\mathrm{d}x\,\mathrm{d}t.$$

From the latter and (3.12), we have

$$
\begin{aligned}
&\tau \int \rho^{1-2\tau} \left|\nabla_x(\zeta u)\right|^2 + \tau^3 \int \rho^{-1-2\tau} \left|\zeta u\right|^2 \\
&\qquad \leqslant 2C \int \rho^{2-2\tau} H^2 + 5\Lambda_0^2 \int \rho^{2-2\tau}\zeta^2\left(|u|^2 + |\nabla_x u|^2\right),
\end{aligned}
\tag{3.16}
$$

for every $\tau \geqslant \tau_0$.

With (3.16), we are led back to the situation in theorem 15 of [23], and by choosing

$$
\eta(t) = \exp\left(-\frac{1-2\delta-t}{\delta^4(1-\delta-t)^3}\right), \quad \text{for } 1-2\delta \leqslant t \leqslant 1-\delta \tag{3.17}
$$

we obtain (3.5).

□

3.2. An auxiliary lemma

Lemma 3.3. *Let $\Omega^* \subset \mathbb{R}^3$ be a bounded measurable set such that $\mathcal{H}^2(\partial\Omega^*) < +\infty$ (where $\mathcal{H}^2$ is the two-dimensional Hausdorff measure) and let $u \in C^{2+\alpha,1+\alpha/2}(\overline{\Omega}^* \times [0,t^*])$ be a solution of*

$$
\begin{cases}
\partial_t u - \operatorname{div}(K_0\nabla u) + \tilde{a}u + k_1\displaystyle\int_0^t \mathrm{e}^{-c_1(t-s)} g_1(u)\,\mathrm{d}s = 0 & \text{in } \Omega^* \times (0,t^*), \\
K_0\nabla u \cdot \nu = 0 & \text{on } \partial\Omega^* \times (0,t^*), \\
u(\cdot,0) = 0 & \text{in } \Omega^*,
\end{cases}
\tag{3.18}
$$

with

$$
|\tilde{a}(x,t)|, |k_1(x,t)| \leqslant C_0 \text{ for all } (x,t) \in \overline{\Omega}^* \times [0,t^*] \text{ and for some positive } C_0.
$$

Furthermore, let c_1 be a positive constant, $g_1 \in C^1(\mathbb{R})$, $g_1(0) = 0$ and for every $u \in \mathbb{R}$

$$
|g_1'(u)| \leqslant C_1, \text{ for some positive } C_1.
$$

Then $u = 0$ in $\overline{\Omega}^* \times [0,t^*]$.

Proof. We proceed similarly as in [9]. Let us multiply the equation

$$
\partial_t u - \operatorname{div}(K_0\nabla u) + \tilde{a}u + k_1\int_0^t \mathrm{e}^{-c_1(t-s)} g_1(u)\,\mathrm{d}s = 0
$$

by $\mathrm{e}^{-4C_0 t}u$ and let us integrate over $\Omega^* \times (0,t)$ for any $t \in (0,t^*]$. We then get

$$
\begin{aligned}
\iint_{\Omega^*\times(0,t)} \Big\{ &\partial_s u \mathrm{e}^{-4C_0 s}u - \operatorname{div}(K_0\nabla u)\mathrm{e}^{-4C_0 s}u + \tilde{a}u^2\mathrm{e}^{-4C_0 s} \\
&+ k_1 u \mathrm{e}^{-4C_0 s}\int_0^s \mathrm{e}^{-c_1(s-\tau)} g_1(u)\,\mathrm{d}\tau \Big\}\,\mathrm{d}x\mathrm{d}s = 0.
\end{aligned}
$$

Since the solution u to (3.18) is in $C^{2+\alpha,1+\alpha/2}(\overline{\Omega}^* \times [0,t^*])$ we can apply Green's formula on sets of finite perimeter (cf for example [13, theorem 5.16]) to derive the following identity

$$\iint_{\Omega^*\times(0,t)} \operatorname{div}(K_0\nabla u)\,\mathrm{e}^{-4C_0 s} u\,\mathrm{d}x\mathrm{d}s = -\iint_{\Omega^*\times(0,t)} K_0\nabla u\cdot\nabla u \mathrm{e}^{-4C_0 s}\,\mathrm{d}x\mathrm{d}s \tag{3.19}$$

where we have used the boundary condition. Note that

$$\begin{aligned}
&\iint_{\Omega^*\times(0,t)} \partial_s u \mathrm{e}^{-4C_0 s} u\,\mathrm{d}x\mathrm{d}s \\
&\quad = \frac{1}{2}\iint_{\Omega^*\times(0,t)} \frac{\partial}{\partial s}\left(\mathrm{e}^{-4C_0 s}u^2\right)\mathrm{d}x\mathrm{d}s + 2C_0\iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}u^2\,\mathrm{d}x\mathrm{d}s \\
&\quad = \frac{1}{2}\int_{\Omega^*} \mathrm{e}^{-4C_0 t}u^2(x,t)\,\mathrm{d}x + 2C_0\iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}u^2\,\mathrm{d}x\mathrm{d}s
\end{aligned}$$

where we have used the condition $u(x,0) = 0$. Hence, we can write

$$\begin{aligned}
\frac{1}{2}\int_{\Omega^*} \mathrm{e}^{-4C_0 t}u^2(x,t)\,\mathrm{d}x &+ \iint_{\Omega^*\times(0,t)} K_0\nabla u\cdot\nabla u\mathrm{e}^{-4C_0 s}\,\mathrm{d}x\mathrm{d}s \\
&+ \iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}\left(\tilde{a}u^2 + 2C_0u^2\right)\mathrm{d}x\mathrm{d}s \\
&+ \iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}k_1 u\mathcal{K}[u](s)\,\mathrm{d}x\mathrm{d}s = 0
\end{aligned}$$

where we have set

$$\mathcal{K}[u](s) = \int_0^s \mathrm{e}^{-c_1(s-\tau)}g_1(u)\,\mathrm{d}\tau.$$

By the condition $|\tilde{a}| \leqslant C_0$ we have that

$$\tilde{a}u^2 + 2C_0u^2 \geqslant C_0u^2.$$

Hence, we can write

$$\begin{aligned}
&\frac{1}{2}\mathrm{e}^{-4C_0 t}\|u(t)\|^2_{L^2(\Omega^*)} + \lambda^{-1}\iint_{\Omega^*\times(0,t)} |\nabla u|^2\mathrm{e}^{-4C_0 s}\,\mathrm{d}x\mathrm{d}s + C_0\iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}u^2\,\mathrm{d}x\mathrm{d}s \\
&\leqslant -\iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}k_1 u\mathcal{K}[u](s)\,\mathrm{d}x\mathrm{d}s
\end{aligned} \tag{3.20}$$

where we have also used assumption 2.2. Finally, let us bound

$$\left|\iint_{\Omega^*\times(0,t)} \mathrm{e}^{-4C_0 s}k_1 u\mathcal{K}[u](s)\,\mathrm{d}x\mathrm{d}s\right| \leqslant C_0\int_0^t \mathrm{e}^{-4C_0 s}\int_{\Omega^*} |u(x,s)||\mathcal{K}[u](s)|\mathrm{d}x\mathrm{d}s. \tag{3.21}$$

Observe now that

$$\begin{aligned}\int_{\Omega^*}|u(x,s)||\mathcal{K}[u](s)|\mathrm{d}x &\leqslant \left(\int_{\Omega^*}|u(x,s)|^2\mathrm{d}x\right)^{1/2}\left(\int_{\Omega^*}|\mathcal{K}[u](s)|^2\mathrm{d}x\right)^{1/2}\\ &= \|u(s)\|_{L^2(\Omega^*)}\left(\int_{\Omega^*}\left(\int_0^s \mathrm{e}^{-c_1(s-\tau)}g_1(u)\,\mathrm{d}\tau\right)^2\mathrm{d}x\right)^{1/2}\\ &\leqslant C_1\|u(s)\|_{L^2(\Omega^*)}\left(\int_{\Omega^*}\left(\int_0^s \mathrm{e}^{-c_1(s-\tau)}|u|\mathrm{d}\tau\right)^2\mathrm{d}x\right)^{1/2}\\ &\leqslant C_1\|u(s)\|_{L^2(\Omega^*)}\int_0^s\|u(\tau)\|_{L^2(\Omega^*)}\mathrm{d}\tau\\ &\leqslant C_1 t^*\|u(s)\|_{L^2(\Omega^*)}\max_{0\leqslant\tau\leqslant s}\|u(\tau)\|_{L^2(\Omega^*)}\end{aligned}$$

where we have used Minkowski inequality, that is

$$\left(\int_{\Omega^*}\left(\int_0^s|u(x,\tau)|\mathrm{d}\tau\right)^2\mathrm{d}x\right)^{1/2}\leqslant\int_0^s\left(\int_{\Omega^*}|u(x,\tau)|^2\mathrm{d}x\right)^{1/2}\mathrm{d}\tau$$

and plugging it in (3.21) and in (3.20) we derive the following estimate

$$\begin{aligned}&\frac{1}{2}\mathrm{e}^{-4C_0t}\|u(t)\|^2_{L^2(\Omega^*)}+\lambda^{-1}\iint_{\Omega^*\times(0,t)}|\nabla u|^2\mathrm{e}^{-4C_0s}\,\mathrm{d}x\mathrm{d}s+C_0\iint_{\Omega^*\times(0,t)}\mathrm{e}^{-4C_0s}u^2\,\mathrm{d}x\mathrm{d}s\\ &\leqslant C_0C_1t^*\int_0^t\|u(s)\|_{L^2(\Omega^*)}\max_{0\leqslant\tau\leqslant s}\|u(\tau)\|_{L^2(\Omega^*)}\mathrm{d}s\leqslant C_0C_1t^*\int_0^t\max_{0\leqslant\tau\leqslant s}\|u(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}s.\end{aligned}$$

By multiplying the above inequality by e^{4C_0t} we get

$$\|u(t)\|^2_{L^2(\Omega^*)}\leqslant\bar{C}\int_0^t\max_{0\leqslant\tau\leqslant s}\|u(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}s,$$

where $\bar{C}=2C_0C_1t^*\mathrm{e}^{4C_0t^*}$, that is

$$\max_{0\leqslant s\leqslant t}\|u(s)\|^2_{L^2(\Omega^*)}\leqslant\bar{C}\int_0^t\max_{0\leqslant\tau\leqslant s}\|u(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}s.$$

Finally, using Gronwall's inequality to the function $h(t):=\max_{0\leqslant s\leqslant t}\|u(s)\|^2_{L^2(\Omega^*)}$ it follows that $h(t)\leqslant 0$ which implies $\max_{0\leqslant s\leqslant t}\|u(s)\|^2_{L^2(\Omega^*)}=0$ which gives that

$$u(x,s)=0,\forall(x,s)\in\overline{\Omega}^*\times(0,t]$$

and since t is an arbitrary value in $(0,t^*]$ the claim follows. □

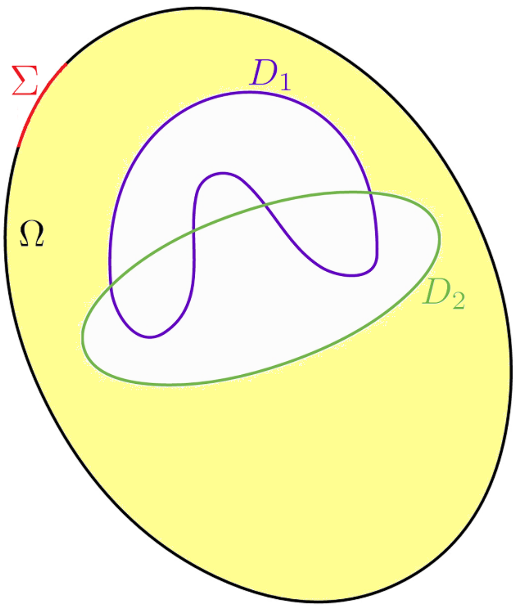

Figure 1. A two-dimensional section of the setting. The connected component G is highlighted in yellow. D_1 and D_2 are the cavities with violet and green-coloured boundaries, respectively.

3.3. *Proof of theorem 3.1*

Proof. Let $u := u_1 - u_2$ and $w = w_1 - w_2$ and let G be the connected component of $\Omega \backslash (D_1 \cup D_2)$ containing Σ (see, for example, figure 1). We can write

$$\begin{cases} \partial_t u - \operatorname{div}(K_0 \nabla u) + a_1 u + a_2 w = 0 & \text{in } G \times (0,T), \\ u = K_0 \nabla u \cdot \nu = 0 & \text{on } \Sigma \times (0,T), \\ \partial_t w + a_3 u + a_4 w = 0 & \text{in } G \times (0,T), \\ u(\cdot,0) = 0 \qquad w(\cdot,0) = 0 & \text{in } G \end{cases} \tag{3.22}$$

where

$$a_1 = \frac{f(u_1,w_1) - f(u_2,w_1)}{u_1 - u_2}, \qquad a_2 = \frac{f(u_2,w_1) - f(u_2,w_2)}{w_1 - w_2}$$
$$a_3 = \frac{g(u_1,w_1) - g(u_2,w_1)}{u_1 - u_2}, \qquad a_4 = \frac{g(u_2,w_1) - g(u_2,w_2)}{w_1 - w_2}.$$

Notice that, since f and g are polynomials in cases (1.2)–(1.4), and since solutions (u_1, w_1) and (u_2, w_2) are uniformly bounded by theorem 2.5, we have

$$|a_i| \leqslant C_0 \text{ in } G \times [0,T], \quad i = 1,2,3,4, \tag{3.23}$$

where C_0 depends only on A, a, ϵ and γ. Hence,

$$|\partial_t w| \leqslant C_0 (|u| + |w|), \tag{3.24}$$

and we obtain straightforwardly, for every $(x,t) \in G \times (0,T)$,

$$|w(x,t)| \leqslant \left| \int_0^t \partial_s w(x,s)\,\mathrm{d}s \right| \leqslant C_0 \left(\int_0^t |u(x,s)|\,\mathrm{d}s + \int_0^t |w(x,s)|\,\mathrm{d}s \right),$$

which implies

$$\left(|w(x,t)| - C_0 \int_0^t |w(x,s)|\,\mathrm{d}s \right) \mathrm{e}^{-C_0 t} \leqslant C_0 \mathrm{e}^{-C_0 t} \int_0^t |u(x,s)|\,\mathrm{d}s.$$

Hence

$$\frac{\mathrm{d}}{\mathrm{d}t} \left[\mathrm{e}^{-C_0 t} \int_0^t |w(x,s)|\,\mathrm{d}s \right] \leqslant C_0 \mathrm{e}^{-C_0 t} \int_0^t |u(x,s)|\,\mathrm{d}s$$

and integrating it follows that

$$\mathrm{e}^{-C_0 t} \int_0^t |w(x,s)|\,\mathrm{d}s \leqslant C_0 \int_0^t \left(\mathrm{e}^{-C_0 \eta} \int_0^\eta |u(x,s)|\,\mathrm{d}s \right) \mathrm{d}\eta$$

which finally gives

$$\int_0^t |w(x,s)|\,\mathrm{d}s \leqslant C_0 \int_0^t \left(\mathrm{e}^{C_0 (t-\eta)} \int_0^\eta |u(x,s)|\,\mathrm{d}s \right) \mathrm{d}\eta \leqslant \left(\mathrm{e}^{C_0 T} - 1 \right) \int_0^t |u(x,s)|\,\mathrm{d}s$$

Hence, for every $(x,t) \in G \times (0,T)$,

$$|w(x,t)| \leqslant C_0 \left(\int_0^t |u(x,s)|\,\mathrm{d}s + \int_0^t |w(x,s)|\,\mathrm{d}s \right) \leqslant C_0 \mathrm{e}^{C_0 T} \int_0^t |u(x,s)|\,\mathrm{d}s$$

and inserting this last inequality and (3.23) into the first equation in (3.22) it follows that

$$|\partial_t u - \operatorname{div}(K_0 \nabla u)| \leqslant \Lambda_0 \left(|u| + \int_0^t |u(x,s)|\,\mathrm{d}s \right) \tag{3.25}$$

with $\Lambda_0 = C_0 + C_0^2 e^{C_0 T}$.

In order to apply the three cylinder inequality (3.5) we now follow the approach used in [8]. We consider an interior point $P \in \Sigma$ that up to a rigid motion can be fixed to be the origin and such that the unit outward normal vector points in the direction of $-e_3 = (-1,0,0)$. Furthermore, we assume that $\partial\Omega \cap Q_{r_0,2M_0} \subset \Sigma$. Note that by the regularity of u it follows that $u \in H^{2,1}((Q_{r_0,2M_0} \cap \Omega) \times (0,T))$. We start extending $u = 0$ for $t \leqslant 0$. Next, we consider the function

$$\bar{u} = \begin{cases} u \text{ in } (Q_{r_0,2M_0} \cap \Omega) \times (-\infty, T) \\ 0 \text{ in } Q_{r_0,2M_0} \setminus (Q_{r_0,2M_0} \cap \Omega) \times (-\infty, T). \end{cases}$$

Then since the Cauchy data of u are zero on $\partial\Omega \cap Q_{r_0,2M_0}$ it follows straightforwardly that $\bar{u} \in H^{2,1}(Q_{r_0,2M_0} \times (-\infty,T))$ and satisfies (3.25). We now pick up the ball $B_r(-re_3)$ with $r \in (0, \mu_0 r_0)$ and $\mu_0 = \min(M_0, \frac{1}{M_0})$ in such a way that $B_r(-re_3) \subset Q_{r_0,2M_0} \setminus (Q_{r_0,2M_0} \cap \Omega)$ and is tangent to Σ at the origin. As a consequence, $\bar{u} = 0$ in $B_r(-re_3)$. Applying the three cylinder inequality to $\bar{u}$ and reminding that $u \in C^{2+\alpha,1+\alpha/2}$ we finally have that $u = 0$ in $(B_{2r}(-re_3) \cap \Omega) \times (0,T]$ and iterating (3.5) we obtain that $u = 0$ in $G \times [0, T-\delta]$ for $\delta \in (0,T)$. Let us now

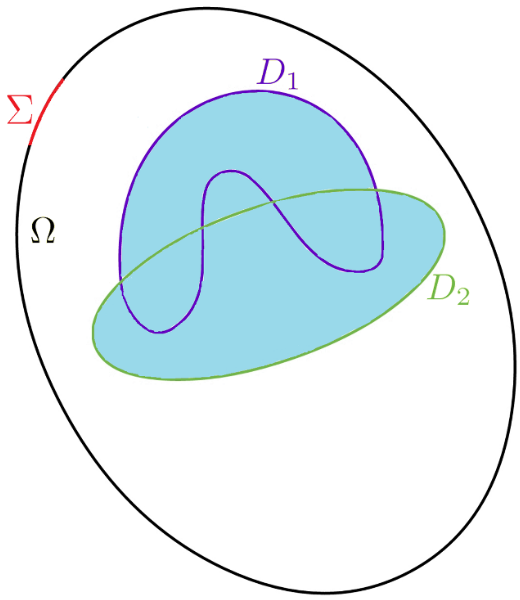

Figure 2. A two-dimensional section of the set $\tilde{G}$ (highlighted in light blue).

argue by contradiction. Assume that $D_1 \neq D_2$. Let $\tilde{G} = \Omega \setminus G$ (see, for example, figure 2) and observe that: $\tilde{G} \supseteq D_1 \cup D_2$ and

$$\partial\tilde{G} = (\partial D_1 \cup \partial D_2) \cap \partial G. \tag{3.26}$$

Let $\tilde{D}$ be a connected component of $\tilde{G} \setminus D_2$ (note that $\tilde{D} = D_1$ if $D_1 \cap D_2 = \emptyset$), see, for example, figure 3. Then we have

$$\partial\tilde{D} \subseteq \partial\left(\tilde{G} \setminus D_2\right) \subseteq \partial\tilde{G} \cup \partial D_2. \tag{3.27}$$

We further note that, unless $D_1 \subset D_2$, we may assume that $\tilde{D}$ contains a subset (of D_1) with nonempty interior. Otherwise, we just exchange the roles of D_1 and D_2. Let us now define $\Gamma_1 \equiv \partial\tilde{D} \cap \partial D_1 \cap \partial\tilde{G}$ and let $\partial\tilde{D} = \Gamma_1 \cup \Gamma_2$. Observe that (3.26) implies that $\Gamma_1 \subset \partial D_1 \cap \partial G$ and from (3.27) $\Gamma_2 \equiv \partial\tilde{D} \setminus \Gamma_1 \subset \partial D_2$ including possibly the case where $\Gamma_2 = \emptyset$.

Notice that u_2 and w_2 solve the system

$$\begin{cases} \partial_t u_2 - \operatorname{div}(K_0 \nabla u_2) + \tilde{a} u_2 + k_1 w_2 = 0 & \text{in } \tilde{D} \times (0,T), \\ K_0 \nabla u_2 \cdot \nu = 0 & \text{on } \partial\tilde{D} \times (0,T), \\ \partial_t w_2 + c_1 w_2 = g_1(u_2) & \text{in } \tilde{D} \times (0,T), \\ u_2(\cdot,0) = 0 \quad w_2(\cdot,0) = 0 & \text{in } \tilde{D} \end{cases} \tag{3.28}$$

where $\tilde{a} = A(u_2 - a)(u_2 - 1)$, $c_1 = \epsilon\gamma$ in the Fitzhugh–Nagumo and Rogers–McCulloch models, $c_1 = \epsilon$ in the Aliev–Panfilov model, $k_1 = 1$ in Fitzhugh–Nagumo model and $k_1 = u_2$ in the Aliev–Panfilov and Rogers–McCulloch models, $g_1(u) = \epsilon u$ in the Fitzhugh–Nagumo and Rogers–McCulloch models and $g_1(u) = \epsilon A u(u - 1 - a)$ in the Aliev–Panfilov model. Then

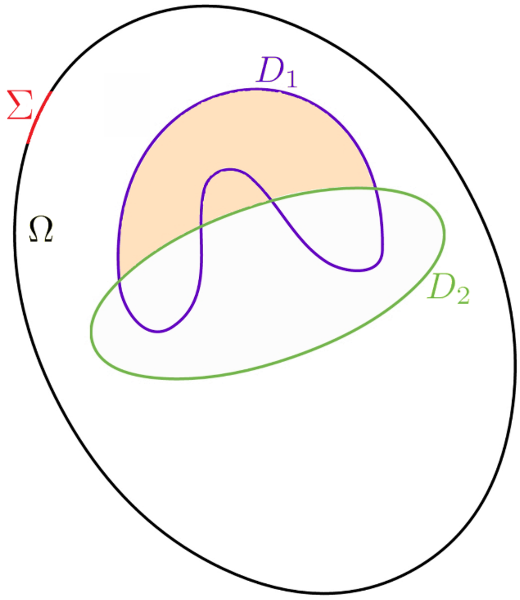

Figure 3. A section of the set $\tilde{D}$ (highlighted in light orange).

integrating the equation for w_2 we get

$$w_2(x,t) = \int_0^t \mathrm{e}^{-c_1(t-s)} g_1(u_2)\,\mathrm{d}s$$

and plugging it in the first partial differential equation we get

$$\partial_t u_2 - \mathrm{div}(K_0 \nabla u_2) + \tilde{a} u_2 + k_1 \int_0^t \mathrm{e}^{-c_1(t-s)} g_1(u_2)\,\mathrm{d}s = 0 \qquad \text{in } \tilde{D} \times (0,T) \tag{3.29}$$

with the boundary and initial conditions

$$K_0 \nabla u_2 \cdot \nu = 0 \quad \text{on } \partial\tilde{D} \times (0,T), \qquad u_2(\cdot,0) = 0 \quad \text{in } \tilde{D}. \tag{3.30}$$

By theorem 2.5, all the assumptions of lemma 3.3 are satisfied (notice that, in the Aliev–Panfilov model, we need to modify function g_1 with a Lipschitz function outside of the range of u_2). So, since $u_2 \in C^{2+\alpha,1+\alpha/2}(\overline{\tilde{D}} \times [0,T])$, we can apply lemma 3.3 to conclude that $u_2 \equiv 0$ on $\tilde{D} \times (0, T-\delta)$ for some $0 < \delta < T$ and, again by the unique continuation property, $u_2 \equiv 0$ in $(\Omega \backslash D_2) \times (0, T-\delta)$. Hence $u_2(x,0) = u_0(x) = 0$ for all $x \in \Omega \backslash D_2$ contradicting the assumption $u_0 \neq 0$.

□

Data availability statement

No new data were created or analysed in this study.

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