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ARTICLE TYPE

Optimal control for nonlocal reaction-diffusion system describing calcium dynamics in cardiac cell†

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Abstract

The purpose of this paper is to introduce an optimal control for a nonlocal calcium dynamic model in a cardiac cell acting on ryanodine receptors. The optimal control problem is considered as a coupled nonlocal reaction-diffusion system with a transmission boundary condition covering the sarcoplasmic reticulum and cytosolic domain. We establish the well-posedness result of the adjoint problem using Faedo-Galerkin approximation, a priori estimates and compactness arguments. The numerical discretization of direct and adjoint problems is realized by using the implicit Euler method in time and the finite element for spatial discretization. Moreover, we obtain the stability result in the L^2-norm for the direct and the adjoint discrete problems. Finally, in order to illustrate the control of our calcium dynamic model, we present some numerical experiments devoted to constant and nonlocal diffusions using the proposed numerical scheme.

KEYWORDS:
Optimal control, calcium model, nonlocal diffusion, weak solution, finite element method, first order optimality conditions, numerical simulation

1 | INTRODUCTION

Calcium ion Ca^{2+} plays a central role in the rapid responses of neurons and muscle cells. Particularly, in cardiac cells the contraction process depends mainly on calcium concentration. Experimental observations show the importance of calcium fluctuation effects on the heart's functional stability at the cellular scale (for e.g.[1,2]). The cellular signalization occurs through a complex mechanism known as calcium induced calcium release (CICR). This cellular mechanism is sensitive to various events including the activation of ion channels (ryanodine receptors, L-type, ...) and the interaction of buffering protein (calsequestrin, calmodulin, ...) with Ca^{2+}. Some pathological cases or even sudden cardiac death are caused due to the abnormal interaction of calsequestrin with ryanodine receptor[3].
The heart is essentially a muscle that contracts and pumps blood. It consists of specialized muscle cells called cardiac myocyte. The contraction of these cells is initiated by electrical impulses known as action potentials. This inhibits some ion channels (L-Type) placed on the cell membrane. Consequently, an influx of Ca^{2+} from the extracellular to intracellular occurs. If all parameters are regular, the rise of calcium in the cytosolic domain inhibits the activation of the ryanodine receptor that exists on the sarcoplasmic reticulum (SR) membrane inside the cardiac cell. This allows an influx of Ca^{2+} from the SR to the cytosolic domain due the high calcium difference between the two mediums (in cytosol $0.1\mu M$, in SR $1mM$). In some particular cases, a mutation in calsequestrin (calcium-binder existing in the SR) genes leads to perturbation in structural building of this protein

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and modifies the Ca^{2+}-binding site number on each CSQN molecule. This affects the total Ca^{2+}-binding capacity of CSQN and the interaction rate with Ca^{2+}[4]. The consequence is an anomalous calcium fluctuation in the SR. The perturbation of calcium concentration inside the SR prevents a natural calcium flux through RyR and produces abnormal low/hight calcium level in the cytoplasm[3]. An application of the present work is devoted to recover a healthy calcium profile under mutant binding capacity of CSQN by acting on RyR conductance (see system (1.1)-(1.2) below) using various types of drugs such that Trifluoperazine, flecainide and others[2].

To describe the cardiac cell behavior, many works[5,6,7,8] proposed mathematical models to simulate the cellular contraction using mechano-chemical coupling. Especially, the coupling between calcium equation and stress tensor. Various calcium dynamics models (see e.g.[9,10]) investigate the calcium diffusion in the cell medium, calcium sparks through an ionic channel (ryanodine receptor) and interactions with binding proteins. A more accurate description of calcium waves can be formulated by a concentration dependent diffusion rate[11,12]. Recently in[13] authors attract attention on the nonlocal diffusion in the context of the relation between mechano-chemical, micro-cellular structure and the total concentration dependent diffusion rate. Moreover, some real experiments[14] established the nonlinear dependence of diffusion rate with calcium concentration. In our study, we extend the local calcium model to a nonlocal model considering the diffusion dependency on the concentration of ions in the medium.

To model the nonlocal calcium dynamics in cardiac cell media, a distinction is made between the cell calcium cistern namely sarcoplasmic reticulum and the cell cytoplasm (or cytoplasmic domain). Moreover, we consider the calcium swapping between these two domains through an ionic channel (ryanodine receptor). To fulfill the requirements of the modeling part, we mention the basic molecules in the cytoplasmic domain taking part in the calcium dynamics: Nucleoside triphosphate used in the cells as a coenzyme and a Ca^{2+}-binder ATP u_2 , the multi-functional calcium binders calmudolin u_3, fluorescence u_4 and troponin u_5 in the physical cytosolic domain Ω_1. On the other hand, we mention the calsequestrin v_2 acting as the calcium binder in the physical sarcoplasmic domain Ω_2. We denote by u_1 and v_1 the calcium concentrations respectively in Ω_1 and Ω_2. The spatial calcium dynamic in the cardiac cell is governed by the following nonlocal transmission boundary problem:

$$\begin{cases} \left.\begin{aligned} &\partial_t u_i = \nabla\cdot\left(\mathrm{A}_i\Big(\int_{\Omega_1} u_i\,dx\Big)\nabla u_i\right) + f_i(\mathbf{u}) \\ &\partial_t u_5 = \varepsilon_1 \Delta u_5 + f_5(\mathbf{u}) \end{aligned}\right\} \text{ in } \Omega_{1,T} = \Omega_1\times(0,T), \\ \left.\begin{aligned} &\partial_t v_1 = \nabla\cdot\left(\mathrm{B}_1\Big(\int_{\Omega_2} v_1\,dx\Big)\nabla v_1\right) + g_1(\mathbf{v}) \\ &\partial_t v_2 = \varepsilon_2 \Delta v_2 + g_2(\mathbf{v}) \end{aligned}\right\} \text{ in } \Omega_{2,T} = \Omega_2\times(0,T), \end{cases} \tag{1.1}$$

for $i = 1,\dots,4$, where ε_1 and ε_2 are two small diffusion coefficients. We complete (1.1) with the following boundary and initial conditions

$$\begin{cases} A_1\Big(\int_{\Omega_1} u_1\,dx\Big)\nabla u_1\cdot\eta_c = -B_1\Big(\int_{\Omega_2} v_1\,dx\Big)\nabla v_1\cdot\eta_s = \mathcal{I}(v_1-u_1) & \text{on } \Gamma_{r,T} := \Gamma_r\times(0,T), \\ B_1\Big(\int_{\Omega_2} v_1\,dx\Big)\nabla v_1\cdot\eta_s = -A_1\Big(\int_{\Omega_1} u_1\,dx\Big)\nabla u_1\cdot\eta_c = \mathcal{I}_p(u_1,v_1) & \text{on } \Gamma_{p,T} := \Gamma_p\times(0,T), \\ A_1\Big(\int_{\Omega_1} u_1\,dx\Big)\nabla u_1\cdot\eta_c = \mathcal{I}_m(u_1) & \text{on } \Gamma_{m,T} := \Gamma_m\times(0,T), \\ A_i\Big(\int_{\Omega_1} u_i\,dx\Big)\nabla u_i\cdot\eta_c = \varepsilon_1\,\nabla u_5\cdot\eta_c = 0 & \text{on } \Gamma_{1,T} := \partial\Omega_1\times(0,T), \\ \varepsilon_2\,\nabla v_2\cdot\eta_s = 0 & \text{on } \Gamma_{2,T} := \partial\Omega_2\times(0,T), \\ \mathbf{u}(0,\cdot) = \mathbf{u}_0(\cdot) & \text{in } \Omega_1^5, \\ \mathbf{v}(0,\cdot) = \mathbf{v}_0(\cdot) & \text{in } \Omega_2^2, \end{cases} \tag{1.2}$$

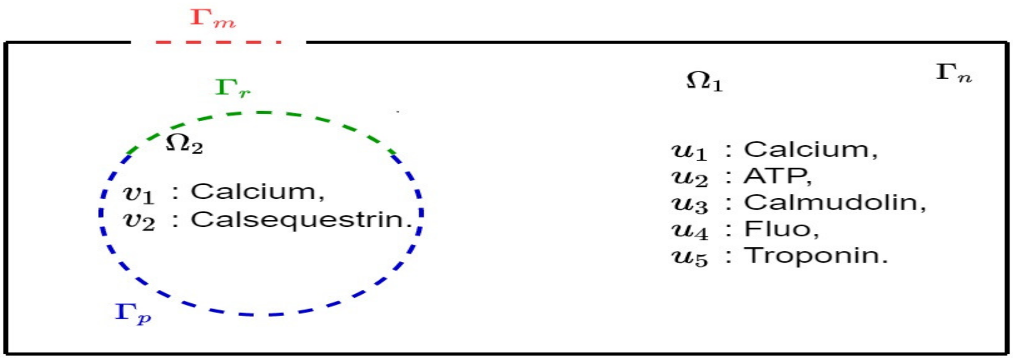

FIGURE 1 This figure shows the cell domains (cytoplasm and sarcoplasmic reticulum) boundaries describing ionic channel locations and different biochemical species.

for $i = 2, 3, 4$, where $\mathbf{v} = (v_1, v_2)$, $\mathbf{u} = (u_1, u_2, u_3, u_4, u_5)$, $\mathbf{v}_0 = (v_{1,0}, v_{2,0})$, $\mathbf{u}_0 = (u_{1,0}, u_{2,0}, u_{3,0}, u_{4,0}, u_{5,0})$, η_c and η_s are respectively the normal unit vectors on the boundaries of Ω_1 and Ω_2. The ion channels (RyR, Serca) fixed on the sarcoplasmic reticulum membrane that is represented in the model by Γ_r for RyR and Γ_p for Serca pump (see Figure 1). The L-type ion channel is represented by Γ_m in Figure 1 , it plays an essential role in launching the calcium induced-calcium release process. Here, we consider the control $\mathcal{I}$ that represents the conductance of the ionic channel RyR. An optimal conductance $\mathcal{I}$ is the best parameter that drives calcium fluctuation (u_1, v_1) to a normal state. The non flux condition is considered on the rest of the cytoplasmic boundary represented by Γ_n. The diffusion functions A_i and B_1 are continuous bounded functions that model the diffusion rates with respect to calcium's total concentration in the media. We denote by f_i and g_j the interaction terms for $i = 1, ..., 5$ and $j = 1, 2$, representing the mathematical description of mass action law that models different chemical reaction between calcium and other buffers:

$$\begin{cases} f_1(\mathbf{u}) = -\sum_{i=2}^{5} R_i(u_1, u_i), \\ f_i(\mathbf{u}) = R_i(u_1, u_i), \text{ for } i = 2, \dots, 5, \\ g_1(\mathbf{v}) = -g_2(\mathbf{v}) = -R_5(v_1, v_2), \\ R_i(t, s) = k_i^{on} t(B_i - s) - k_i^{off} s \text{ for } i = 1, \dots, 5. \end{cases} \tag{1.3}$$

We denote by $\mathcal{I}_p$ the calcium influx to the sarcoplasmic reticulum. Regarding Figure 1 , remark that we have simplified the geometry of the cytosolic and sarcoplasmic domains for numerical and implementation issues. Note that the consideration of more realistic domains requires sophisticated imaging techniques and advanced 3D reconstruction algorithms. This simplification helps to accomplish the heavy requirements of optimal control computations.

The nonlocal diffusion equations, has been studied in the literature by many authors, we mention here some works [15,16,17] where the well-posedness result and asymptotic behavior (of solution) are studied. Moreover, there are some extensions to nonlocal $p-$Laplacian diffusion, where the existence and the uniqueness results can be found in [18]. From the numerical point of view, a rigorous study of the convergence of a finite volume scheme to an epidemic model with a nonlocal diffusion was established in [19]. Note that the nonlocal system has been intensively studied only for some direct problems (there is no optimal control problem under some nonlocal PDE constraints).

In this paper, we are interested in the mathematical and numerical analysis of a nonlocal optimal control of calcium fluctuations in a cardiac cell. To our knowledge, there are no studies in the context of controlling a nonlocal transmission boundary value problem. Here, we study the derived nonlocal adjoint state system, and we prove its well-posedness. We present a numerical scheme of the direct and adjoint system based on a finite element discretization in space and implicit Euler method in time. Moreover, we propose the stability result in the L^2-norm of our discrete schemes with respect to the control $\mathcal{I}$. We support our stability analysis by various numerical experiments showing the convergence of our numerical schemes. Furthermore, we consider a set of numerical simulations dedicated to study the abnormal binding capacity of calsequestrin (CSQN) in interaction with ryanodine receptor (RyR) behavior.

This work presents strict mathematical analysis and numerical convergence results applied in bio-medicine. We establish a mathematical optimal control problem that studies the RyR ion channels under anomalous Ca^{2+}-buffering in a PDE framework.

Moreover, we propose a nonlocal model that describes the weighted-mean diffusion coefficient as shown experimentally in [14]. The well-posedness study of the adjoint system requires some regularity results from the direct system solution. Finally, we choose the finite element scheme with the implicit Euler method to discretize both direct and adjoint systems. We establish a stability result for our discrete scheme, and we provide numerical experiments proving the convergence of the discrete solution. The structure of the paper is organized as follows: In Section 2, we recall the well-posedness of the direct problem and some regularity results that will serve to prove the existence of the adjoint problem. Section 3 is devoted to the optimal control. Here, we introduce the cost functional related to calcium normal fluctuation recovery with the minimization problem. Next, we prove the well-posedness result (existence and uniqueness) of the control. We introduce the Lagrangian formulation, the derivation of the adjoint problem and the optimality conditions. We dedicate Section 4 to the well-posedness result for the adjoint problem solution. In Section 5, we introduce the numerical discretization of the direct-adjoint problem, and we prove the stability result in the L^2-norm under control. In Section 6, we present a numerical comparison between local and nonlocal diffusion cases. We conclude this section by various numerical simulations for our optimal control calcium model and some numerical tests showing the convergence of our numerical scheme.

2 | MATHEMATICAL ANALYSIS OF THE DIRECT PROBLEM

We start this section by making the following assumptions on our data. We assume that $A_i, B_1 : \mathbb{R} \to \mathbb{R}$ are of class C^1 functions, satisfying:

$$0 < D_{min} \leq A_i(r), B_1(r) \leq D_{max} \text{ for } i = 1, \cdots, 4 \text{ and and } r \in \mathbb{R}, \tag{2.1}$$

where D_{min} and D_{max} are two constant in $\mathbb{R}$. The functions $\mathcal{I}_p : \mathbb{R}^2 \to \mathbb{R}$ and $\mathcal{I}_m : \mathbb{R} \to \mathbb{R}$ are of class C^2 such that

$$\mathcal{I}_p(0, \xi_2) \leq 0 \text{ for all } \xi_2 > 0,\ \mathcal{I}_p(\xi_1, 0) \geq 0 \text{ and } \mathcal{I}_m(\xi_1) \geq 0 \text{ for all } \xi_1 > 0. \tag{2.2}$$

Moreover, there exist constants $G_p, G_m > 0$ such that

$$\mathcal{I}_p(\xi_1, \xi_2) \leq G_p \left|\xi_1\right|^2 \text{ and } \mathcal{I}_m(\xi_1) \leq G_m \left|\xi_1\right| \text{ for all } \xi_1, \xi_2 \in \mathbb{R}, \tag{2.3}$$

and there exists a function $\hat{\mathcal{I}}_p : \mathbb{R}^2 \to \mathbb{R}$ of class C^1 such that

$$\begin{cases} d\hat{\mathcal{I}}_p(u, v) = \mathcal{I}_p(u, v)dv - \mathcal{I}_p(u, v)du \quad \text{and} \quad \left|\mathcal{I}_{p,u_1}(u_1, v_1)\right|, \left|\mathcal{I}_{p,v_1}(u_1, v_1)\right| \leq C \\ 0 \leq \hat{\mathcal{I}}_p(\xi_1, \xi_2) \leq C\xi_1\xi_2 \quad \text{and} \quad 0 \leq \hat{\mathcal{I}}_m(\xi_1) := \int_0^{\xi_1} \mathcal{I}_m(s)\, ds \leq C\xi_1^2 \quad \text{for all } \xi_1, \xi_2 \geq 0, \end{cases} \tag{2.4}$$

for some constant $C > 0$, where $\mathcal{I}_{p,u_1}$ and $\mathcal{I}_{p,v_1}$ are the partial derivatives of $\mathcal{I}_p$ with respect to u_1 and v_1 respectively.

Observe that the functions f_i and g_j given in (1.3) satisfy the following condition:

$$\begin{cases} f_i \in C^1(\mathbb{R}^5, \mathbb{R}) \text{ and } g_j \in C^1(\mathbb{R}^2, \mathbb{R}), \\ \left|f_i(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5)\right| \leq G_f(1 + \sum_{k=1}^5 |\xi_k|^2), \\ \left|g_j(\xi_1, \xi_2)\right| \leq G_g(1 + \sum_{k=1}^2 |\xi_k|^2), \\ \partial_{\xi_k} f_i(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5) \leq L_f(1 + \sum_{l=1}^5 \left|\xi_l\right|) \text{ for } k = 1, ..., 5, \\ \partial_{\xi_k} g_j(\xi_1, \xi_2) \leq L_g(1 + \sum_{l=1}^2 \left|\xi_l\right|) \text{ for } k = 1, 2, \\ f_i(\dots, \chi_{i-1}, 0, \chi_{i+1}, \dots) \geq 0 \quad g_1(0, \chi_2), g_2(\chi_1, 0) \geq 0, \end{cases} \tag{2.5}$$

for all $\xi_i \in \mathbb{R}$, $\chi_i \geq 0$ and for all $i = 1, \dots, 5$, $j = 1, 2$, where G_f, G_g, L_f, L_g are some positive constants. Next, we consider the functional spaces $\mathbf{L}_i^p = L^p(\Omega_i)$, $\mathbf{H}_i^m = H^m(\Omega_i)$ and $\mathbf{L}_{i,T}^p = L^p(\Omega_{i,T})$ for $1 \leq m, p \leq +\infty$ and $i = 1, 2$. Moreover, we denote by

$$\mathcal{A}_{i,u_i} = A_i\left(\int_{\Omega_1} u_i(t, x)\, dx\right), \mathcal{B}_{j,v_j} = B_j\left(\int_{\Omega_2} v_j(t, x)\, dx\right) \tag{2.6}$$

and we use the following notations

$$\mathcal{A}^p_{i,u_i} = A'_i\left(\int_{\Omega_1} u_i(t,x)\,dx\right), \mathcal{B}^p_{j,v_j} = B'_j\left(\int_{\Omega_2} v_j(t,x)\,dx\right). \tag{2.7}$$

Note that A'_i and B'_j are the derivatives of the real functions $A_i : \mathbb{R} \to \mathbb{R}$ and $B_j : \mathbb{R} \to \mathbb{R}$. To simplify the computation and without loss of generality, we note $A_5(\int_{\Omega_1} u_5(t,x)\,dx) := \varepsilon_1$, $B_2(\int_{\Omega_2} v_2(t,x)\,dx) := \varepsilon_2$ and we have $\mathcal{A}^p_{5,u_5} = \mathcal{B}^p_{2,v_2} = 0$.

Remark 2.1. The assumptions (2.1)-(2.2) has been used to prove the solution of the problem (1.1)-(1.2) (for more details see[20]). Assumption (2.4) is used to prove the regularity Proposition 2.1 and the existence of weak solution of adjoint problem 3.5-(3.6) below.

Definition 2.1. A weak solution of (1.1)-(1.2) is a seven-tuple function $U = (u_1,u_2,u_3,u_4,u_5,v_1,v_2)$ such that $v_j \in \mathbf{L}^\infty_{2,T} \cap L^2\left(0,T;\mathbf{H}^1_1\right)$, $\partial_t v_j \in L^2\left(0,T;\left(\mathbf{H}^1_2\right)'\right)$, $u_i \in \mathbf{L}^\infty_{1,T} \cap L^2\left(0,T;\mathbf{H}^1_1\right)$ and $\partial_t u_i \in L^2\left(0,T;\left(\mathbf{H}^1_1\right)'\right)$ for $i = 1,\cdots,5$, $j = 1,2$ and satisfying

$$\begin{aligned}
&\sum_{i=1}^{5} \iint_{\Omega_{1,T}} \partial_t u_i\, \varphi_i\, dx\,dt + \sum_{j=1}^{2} \iint_{\Omega_{2,T}} \partial_t v_j\, \phi_j\, dx\,dt + \sum_{i=1}^{5} \iint_{\Omega_{1,T}} \mathcal{A}_{i,u_i} \nabla u_i \cdot \nabla \varphi_i\, dx\,dt + \sum_{j=1}^{2} \iint_{\Omega_{2,T}} \mathcal{B}_{j,v_j} \nabla v_j \cdot \nabla \phi_j\, dx\,dt \\
&\quad + \iint_{\Gamma_{r,T}} \mathcal{I}(v_1 - u_1)(\phi_1 - \varphi_1) d\sigma dt + \iint_{\Gamma_{p,T}} \mathcal{I}_p(u_1, v_1)(\phi_1 - \varphi_1) d\sigma dt + \iint_{\Gamma_{m,T}} \mathcal{I}_m(u_1)\varphi_1 d\sigma dt \\
&= \sum_{i=1}^{5} \iint_{\Omega_{1,T}} f_i(\mathbf{u})\phi_i\, dx\,dt + \sum_{i=1}^{2} \iint_{\Omega_{2,T}} g_j(\mathbf{v})\phi_j\, dx\,dt,
\end{aligned} \tag{2.8}$$

for all $\varphi_i \in L^2\left(0,T;\mathbf{H}^1_1\right)$, $\phi_j \in L^2\left(0,T;\mathbf{H}^1_2\right)$.

Remark 2.2. To obtain (2.8), we multiply each equation of system (1.1) by some test functions, integrating over Ω_1 and Ω_2 and summing them up. To simplify the computations, we have chosen to arrange variational equations related to (1.1)-(1.2) in one weak formulation. Furthermore, such an arrangement clarifies the relation between u_1 and v_1 through transmission boundary condition. Note that, modulo choice of a test function, we can recover from (2.8) each equation of system (1.1) (take for instance $\phi_i = 1$ and other test function as null values to recover the equation of u_i).

The following theorem proposes the existence and uniqueness of the solution in the sense of Definition 2.1. The proof can be adapted from results given in[20] to the nonlocal case. Here, we omit it.

Theorem 2.1. Assume that condition (2.1)-(2.5) holds. If $\mathbf{u}_0 \in L^\infty(\Omega_1)^5$, $\mathbf{v}_0 \in L^\infty(\Omega_2)^2$ and $\mathcal{I} \in L^\infty(\Gamma_{r,T})$, then the system (1.1)-(1.2) possesses a unique weak solution in sense of Definition 2.1.

In the proofs of Proposition 2.1, Theorem 4.1, Lemma 5.1 and Proposition 5.1 (below), we will use frequently the positive constant ϑ that will be chosen in each proof. Now, to study the adjoint-problem, we need the following result.

Proposition 2.1. Assume that conditions (2.1)-(2.5) hold. If $\mathbf{u}_0 \in \left(\mathbf{H}^1_1\right)^5$, $\mathbf{v}_0 \in \mathbf{H}^2_2$ and $\mathcal{I} \in C^1(\Gamma_{r,T})$, then, the solution $U = (u_1,u_2,u_3,u_4,u_5,v_1,v_2)$ given in Definition 2.1 satisfies

$$\partial_t u_i \in \mathbf{L}^2_{1,T}, \quad \partial_t v_j \in \mathbf{L}^2_{2,T}, \quad \nabla u_i \in L^\infty(0,T;\mathbf{L}^2_1) \text{ and } \nabla v_j \in L^\infty(0,T;\mathbf{L}^2_2), \tag{2.9}$$

for $i = 1,\ldots,5$ and $j = 1,2$.

Proof. To prove (2.9), we consider the Faedo Galerkin approximation of (2.8) shown in[20]. Herein, we take $\varphi_i = \partial_t u_i^m$ and $\phi_j = \partial_t v_j^m$ in (2.8) where u_i and v_j are replaced by u_i^m and v_j^m respectively, for $i = 1,\ldots,5$ and $j = 1,2$. The result is (recall the definition of $\mathcal{A}_{i,u}$ and $\mathcal{B}_{j,v}$ from (2.6)-(2.7))

$$\begin{aligned}
&\sum_{i=1}^{5}\|\partial_t u_i^m\|^2_{\mathbf{L}^2_{1,T}} + \sum_{j=1}^{2}\left\|\partial_t v_j^m\right\|^2_{\mathbf{L}^2_{2,T}} + \frac{1}{2}\sum_{i=1}^{5}\int_0^T \mathcal{A}_{i,u_i}\frac{d}{dt}\|\nabla u_i^m\|^2_{\mathbf{L}^2_1}\,dt + \frac{1}{2}\sum_{j=1}^{2}\int_0^T \mathcal{B}_{j,v_j^m}\frac{d}{dt}\|\nabla v_1^m\|^2_{\mathbf{L}^2_2}\,dt \\
&\quad + \iint_{\Gamma_{m,T}} \mathcal{I}_m(u_1^m)\partial_t u_1 d\sigma\,dt + \iint_{\Gamma_{r,T}} \mathcal{I}(v_1^m - u_1^m)(\partial_t v_1^m - \partial_t u_1^m)d\sigma\,dt + \iint_{\Gamma_{p,T}} \mathcal{I}_p(u_1^m, v_1^m)(\partial_t v_1^m - \partial_t u_1^m)d\sigma\,dt \\
&\quad = \sum_{i=1}^{5}\iint_{\Omega_{1,T}} f_i(\mathbf{u}^m)\partial_t u_i^m\,dx\,dt + \sum_{j=1}^{2}\iint_{\Omega_{2,T}} g_1(\mathbf{v}^m)\partial_t v_j^m\,dx\,dt.
\end{aligned} \tag{2.10}$$

For the transmission terms, we use Young inequality and trace embedding theorem (see for e.g.[21]) to have

$$\begin{aligned}
&\iint_{\Gamma_{r,T}} \mathcal{I}\left(u_1^m(t) - v_1^m(t)\right)\left(\partial_t u_1^m(t) - \partial_t v_1^m(t)\right)d\sigma\,dt = \frac{1}{2}\iint_{\Gamma_{r,T}} \frac{d}{dt}\left(\mathcal{I}(u_1^m(t) - v_1^m(t))^2\right)d\sigma - \frac{1}{2}\iint_{\Gamma_{r,T}} \partial_t\mathcal{I}\left(u_1^m(t) - v_1^m(t)\right)^2 d\sigma \\
&\qquad \geq \frac{1}{2}\iint_{\Gamma_{r,T}} \frac{d}{dt}\left(\mathcal{I}(u_1^m(t) - v_1^m(t))^2\right)d\sigma - \frac{\|\partial_t\mathcal{I}\|_{L^\infty(\Gamma_{r,T})}}{2}\|u_1^m(t) - v_1^m(t)\|^2_{L^2(\Gamma_{r,T})} \\
&\qquad \geq \frac{1}{2}\int_{\Gamma_r} \mathcal{I}\left(u_1^m(t) - v_1^m(t)\right)^2 d\sigma - \frac{1}{2}\int_{\Gamma_r} \mathcal{I}(0)\left(u_1(0) - v_1(0)\right)^2 d\sigma - \|\mathcal{I}\|_{W^{1,\infty}(\Gamma_r)}\left(\|u_1^m\|^2_{L^2(0,T;\mathbf{H}^1_1)} + \|u_1^m\|^2_{L^2(0,T;\mathbf{H}^1_2)}\right) \\
&\qquad \geq -C_p\left(\|u_{1,0}\|^2_{\mathbf{H}^1_1} + \|v_{1,0}\|^2_{\mathbf{H}^1_2} + \|u_1^m\|^2_{L^2(0,T;\mathbf{H}^1_1)} + \|u_1^m\|^2_{L^2(0,T;\mathbf{H}^1_2)}\right),
\end{aligned} \tag{2.11}$$

where C_p is a positive constant. Exploiting assumptions (2.2) and (2.4), we deduce

$$\begin{aligned}
&\int_0^T\int_{\Gamma_p} \mathcal{I}_p(u_1^m(t), v_1^m(t))(\partial_t v_1^m(t) - \partial_t u_1^m(t))d\sigma\,dt = \int_0^T\int_{\Gamma_p} \frac{d}{dt}\hat{\mathcal{I}}_p(u_1^m(t), v_1^m(t))d\sigma\,dt \\
&\quad = \int_{\Gamma_p} \hat{\mathcal{I}}_p(u_1^m(T), v_1^m(T))d\sigma - \int_{\Gamma_p} \hat{\mathcal{I}}_p(u_1(0), v_1(0))d\sigma \\
&\quad \geq \int_{\Gamma_p} \hat{\mathcal{I}}_p(u_1^m(t), v_1^m(t))d\sigma - C_1\int_{\Gamma_p} |u_{1,0}|\,|v_{1,0}|\,d\sigma \geq -C_2\left(\|u_{1,0}\|^2_{L^2(\Gamma_p)} + \|v_{1,0}\|^2_{L^2(\Gamma_p)}\right) \geq -C_3\left(\|u_{1,0}\|^2_{\mathbf{H}^1_1} + \|v_{1,0}\|^2_{\mathbf{H}^1_2}\right),
\end{aligned} \tag{2.12}$$

for some constants $C_1, C_2, C_3 > 0$. It is not difficult to see that

$$\int_0^T\int_{\Gamma_m} \frac{d}{dt}\hat{\mathcal{I}}_m(u_1^m)d\sigma\,dt = \int_{\Gamma_m} \hat{\mathcal{I}}_m(u_1^m(T))d\sigma - \int_{\Gamma_m} \hat{\mathcal{I}}_m(u_{1,0})d\sigma \geq -C_4\|u_{1,0}\|^2_{\mathbf{H}^1_1}, \tag{2.13}$$

for some constant $C_4 > 0$. For the reaction terms, we use Young inequality to get

$$\left|\iint_{\Omega_{1,T}} f_i(\mathbf{u}^m(t,x))\partial_t u_i^m(t,x)\,dx\,dt\right| \leq \frac{1}{2}\|f_i(\mathbf{u}^m)\|^2_{\mathbf{L}^2_{1,T}} + \frac{1}{2}\|\partial_t u_i^m\|^2_{\mathbf{L}^2_{1,T}} \tag{2.14}$$

and

$$\left|\iint_{\Omega_2} g_j(\mathbf{v}^m(t,x))\partial_t v_j(t,x)\,dx\,dt\right| \leq \frac{1}{2}\|g_1(\mathbf{v}^m)\|^2_{\mathbf{L}^2_{2,T}} + \frac{1}{2}\left\|\partial_t v_j^m\right\|^2_{\mathbf{L}^2_{2,T}}. \tag{2.15}$$

Now, collecting the results (2.10)-(2.15), we conclude

$$\frac{1}{2}\left(\sum_{i=1}^{5}\|\partial_t u_i^m\|^2_{\mathbf{L}^2_{1,T}}+\sum_{j=1}^{2}\|\partial_t \upsilon_1^m\|^2_{\mathbf{L}^2_{2,T}}\right)+\frac{1}{2}\sum_{i=1}^{5}\int_0^T \mathcal{A}_{i,u_i^m}\frac{d}{dt}\|u_i^m\|^2_{\mathbf{H}^2_1}\,dt+\frac{1}{2}\sum_{j=1}^{2}\int_0^T \mathcal{B}_{j,\upsilon_j^m}\frac{d}{dt}\left\|\upsilon_j^m\right\|^2_{\mathbf{H}^2_2}\,dt$$
$$\leq \frac{1}{2}\left(\sum_{i=1}^{5}\int_0^T\|f_i(\mathbf{u}^m)(t)\|^2_{\mathbf{L}^2_1}+\sum_{j=1}^{2}\int_0^T\left\|g_j(\mathbf{v}^m)(t)\right\|^2_{\mathbf{L}^2_2}\right)+C_5\left(\sum_{i=1}^{5}\|u_{i,0}\|^2_{\mathbf{H}^1_1}+\sum_{j=1}^{2}\left\|\upsilon_{j,0}\right\|^2_{\mathbf{H}^1_2}\right)+C_6\left(\sum_{i=1}^{5}\|u_i^m\|^2_{\mathbf{H}^1_1}\,dt+\sum_{j=1}^{2}\left\|\upsilon_j^m\right\|^2_{\mathbf{H}^1_2}\right), \tag{2.16}$$

for some constants $C_5, C_6 > 0$. We denote by $\mathcal{U}_i(t) := \|u_i^m\|^2_{\mathbf{H}^1_1}$, $\mathcal{V}_j(t) := \left\|\upsilon_j^m\right\|^2_{\mathbf{H}^1_2}$, $a_i(t) = \mathcal{A}_{i,u_i^m(t)}$, $b_j(t) = \mathcal{B}_{j,\upsilon_j^m(t)}$, $C_7 := \sum_{i=1}^5\|f_i(\mathbf{u}^m)(t)\|^2_{\mathbf{L}^2_{1,T}} + \sum_{j=1}^2\left\|g_j(\mathbf{v}^m)(t)\right\|^2_{\mathbf{L}^2_{2,T}} + 2\ C_5\Big(\sum_{i=1}^5\|u_{i,0}\|^2_{\mathbf{H}^1_1} + \sum_{j=1}^2\left\|\upsilon_{j,0}\right\|^2_{\mathbf{H}^1_2}\Big)$ and $C_8 := 2C_6\left(\sum_{i=1}^5\|u_i^m\|^2_{\mathbf{H}^1_1}\,dt+\sum_{j=1}^2\left\|\upsilon_j^m\right\|^2_{\mathbf{H}^1_2}\right)$ we get

$$\sum_{i=1}^{5}a_i(t)\frac{d}{dt}\mathcal{U}_i(t)+\sum_{j=1}^{2}b_j(t)\frac{d}{dt}\mathcal{V}_j(t)\leq C_7+C_8\Big(\sum_{i=1}^{5}\mathcal{U}_i(t)+\sum_{j=1}^{2}\mathcal{V}_j(t)\Big). \tag{2.17}$$

This implies

$$\begin{aligned}
\sum_{i=1}^{5}\frac{d}{dt}\left(a_i(t)\mathcal{U}_i(t)\right)+\sum_{j=1}^{2}\frac{d}{dt}\left(b_j(t)\mathcal{V}_j(t)\right) &\leq C_7+\sum_{i=1}^{5}\left(\frac{d}{dt}a_i(t)+C_8\right)\mathcal{U}_i(t)+\sum_{j=1}^{2}\left(\frac{d}{dt}b_j(t)+C_8\right)\mathcal{V}_j(t)\\
&= C_7+\sum_{i=1}^{5}\frac{\left(\frac{d}{dt}a_i(t)+C_8\right)}{a_i(t)}\mathcal{U}_i(t)a_i(t)+\sum_{j=1}^{2}\frac{\left(\frac{d}{dt}b_j(t)+C_8\right)}{b_j(t)}\mathcal{V}_j(t)b_j(t)\\
&= C_7+\sum_{i=1}^{5}\left(\frac{d}{dt}\ln(a_i(t))+C_8D_{min}^{-1}\right)\mathcal{U}_i(t)a_i(t)+\sum_{j=1}^{2}\left(\frac{d}{dt}\ln(b_j(t))+C_8D_{min}^{-1}\right)\mathcal{V}_j(t)b_j(t)\\
&\leq C_7+\left(\max_{i=1,\dots,5,\,j=1,2}\left\{\frac{d}{dt}\ln(a_i(t)),\frac{d}{dt}\ln(b_j(t))\right\}+C_8D_{min}^{-1}\right)\left(\sum_{i=1}^{5}a_i(t)\mathcal{U}_i(t)+\sum_{j=1}^{2}b_j(t)\mathcal{V}_j(t)\right).
\end{aligned} \tag{2.18}$$

Using Grönwall inequality, we get

$$\begin{aligned}
\sum_{i=1}^{4}a_i(t)\mathcal{U}_i(t)+\sum_{j=1}^{2}b_j(t)\mathcal{V}_j(t) &\leq C_7\exp\left(\max_{i=1,\dots,5,j=1,2}\left\{\int_0^t\frac{d}{dt}\ln(a_i(s))\,ds,\int_0^t\frac{d}{dt}\ln(b_j(s))\,ds\right\}+C_8D_{min}^{-1}t\right)\\
&= C_7\exp\left(\max_{i=1,\dots,5,j=1,2}\left\{\ln(a_i(t))-ln(a_i(0)),\ln(b_j(t))-\ln(b_j(0))\right\}+C_8D_{min}^{-1}t\right)\\
&\leq C_7\exp\left(\ln\left(\frac{D_{max}}{D_{min}}\right)+C_8D_{min}^{-1}t\right)\leq C_7\frac{D_{max}}{D_{min}}\exp(C_8D_{min}^{-1}t).
\end{aligned} \tag{2.19}$$

Therefore, we arrive to

$$\sum_{i=1}^{5}\mathcal{U}_i(t)+\sum_{j=1}^{2}\mathcal{V}_j(t)\leq C_7\frac{D_{max}}{D_{min}^2}\exp(C_8D_{min}^{-1}t). \tag{2.20}$$

Hence, using the L^∞ boundedness of interaction terms $f_i(\mathbf{u})$ and $g_1(\mathbf{v})$, we conclude

$$\sum_{i=1}^{5}\|\partial_t u_i^m\|^2_{\mathbf{L}^2_{1,T}}+\sum_{j=1}^{2}\left\|\partial_t \upsilon_j^m\right\|^2_{\mathbf{L}^2_{2,T}}+\sum_{i=1}^{5}\sup_{t\in(0,T)}\|\nabla u_i^m(t)\|^2_{\mathbf{L}^2_1}+\sum_{j=1}^{2}\sup_{t\in(0,T)}\left\|\nabla \upsilon_j^m(t)\right\|^2_{\mathbf{L}^2_2}\leq Const. \tag{2.21}$$

Finally, we use the convergence shown in[20] to deduce (2.9). This concludes the proof of Proposition 2.1. ■

3 | THE OPTIMAL CONTROL PROBLEM

In this section, we formulate the optimal control problem applied to our nonlocal model (1.1)-(1.2). Our goal is to minimize the difference between regular calcium and anomalous calcium profiles by acting on the conductance of RyR (denoted by $\mathcal{I}$). The derivation of the optimality conditions including the adjoint system requires unusual computations of the nonlocal terms. Moreover, we deal with a transmission boundary control. Consequently, the gradient of the cost functional will be defined only on the common side of sarcoplasmic reticulum membrane with the cytosolic domain. To give the mathematical formulation of the control problem, we define the cost functional and the associated minimization problem. We establish the existence result to the optimization problem. We finish by deriving the adjoint state system and the optimality condition.
Now, we consider the following optimal control problem:

$$\begin{cases} \min_{\mathcal{I}\in\mathcal{U}} \left[J(\mathcal{I}) = \frac{\alpha_1}{2} \|u_1 - u_d\|^2_{\mathbf{L}^2_{1,T}} + \frac{\alpha_2}{2} \|v_1 - v_d\|^2_{\mathbf{L}^2_{2,T}} + \frac{\alpha_3}{2} \|\mathcal{I}\|^2_{L^2(\Gamma_{r,T})} \right], \\ \text{subject to the coupled CICR system (1.1),} \end{cases} \tag{3.1}$$

where α_1, α_2 and α_3 are the regularization parameters, (u_d, v_d) is the desired state and $\mathcal{U}$ is defined by

$$\mathcal{U} := \{\mathcal{I} \in L^2(\Gamma_{r,T}) \text{ such that for } (t,x) \in \Gamma_{r,T} \text{ we have } 0 \le \mathcal{I}(t,x) \le \mathcal{I}_{max}\}.$$

Recall that the trasmission boundary control $\mathcal{I}$ on Γ_r acts on the dynamics of calcium in the cytosolic domain Ω_1 and sarcoplasmic domain Ω_2. Precisely, an optimal conductance $\mathcal{I}$ aims to drive the calcium state described by (1.1)-(1.2) in Ω_1 and Ω_2 to the desired state (u_d, v_d).

The existence of an optimal solution described by (3.1) is given in the following lemma.

Lemma 3.1. Assume that $\mathbf{u}_0 \in L^\infty(\Omega_1)^5$, $\mathbf{v}_0 \in L^\infty(\Omega_2)^2$, $u_d \in \mathbf{L}^2_{1,T}$ and $v_d \in \mathbf{L}^2_{2,T}$ hold. Then, there exists a solution $\mathcal{I}^* \in \mathcal{U}$ of the optimal control problem (3.1).

Proof. Let $\mathcal{I}_n$ be a minimizing sequence of J such that

$$\inf_{\mathcal{I}\in\mathcal{U}}\{J\} \le J(\mathcal{I}_n) \le \inf_{\mathcal{I}\in\mathcal{U}}\{J\} + \frac{1}{n}.$$

Using the definition of J, we deduce the boundedness on the sequence $\mathcal{I}_n$ in $L^2(\Gamma_r)$. Hence, we obtain the weak convergence of $\mathcal{I}_n$ to a candidate solution $\mathcal{I}^*$. Let $\mathbf{u}_n = (u_1^n, u_2^n, u_3^n, u_4^n, u_5^n)$ and $\mathbf{v}_n = (v_1^n, v_2^n)$ be a solution to the direct problem (1.1) with respect to the control $\mathcal{I}_n$. Similarly to[20], we have the following a priori estimates

$$\sum_{i=1}^{5} \|u_i^n\|^2_{L^\infty(0,T;\mathbf{L}^2_1)} + \sum_{j=1}^{2} \left\|v_j^n\right\|^2_{L^\infty(0,T;\mathbf{L}^2_2)} + D_{min} \left(\sum_{i=1}^{5} \|u_i^n\|^2_{L^2(0,T;\mathbf{H}^1_1)} + \sum_{j=1}^{2} \left\|v_j^n\right\|^2_{L^2(0,T;\mathbf{H}^1_2)} \right) \le C, \tag{3.2}$$

for some constant C>0. Using estimates (3.2) and Aubin compactness result[22], we get the following convergences

$$\begin{aligned} (\mathbf{u}_n, \mathbf{v}_n) &\to (\mathbf{u}, \mathbf{v}) && \text{strongly in } \left(\mathbf{L}^2_{1,T}\right)^5 \times \mathbf{L}^2_{2,T}, \\ (\mathbf{u}_n, \mathbf{v}_n) &\to (\mathbf{u}, \mathbf{v}) && \text{weakly in } L^2(0,T;\mathbf{H}^1_1)^5 \times L^2(0,T;\mathbf{H}^1_2)^2, \\ \partial_t(\mathbf{u}_n, \mathbf{v}_n) &\to \partial_t(\mathbf{u}, \mathbf{v}) && \text{weakly in } L^2\left(0,T;\left(\mathbf{H}^1_1\right)'\right)^5 \times L^2\left(0,T;\left(\mathbf{H}^1_2\right)'\right)^2. \end{aligned} \tag{3.3}$$

Hence, by exploiting the strong convergence of $(u_1^n, u_2^n, u_3^n, u_4^n, u_5^n)$ and (v_1^n, v_2^n) combined with the weak lower semi-continuity of J we arrive to

$$J(\mathcal{I}^*) \le \liminf J(\mathcal{I}_n) \le \inf_{\mathcal{I}\in\mathcal{U}}\{J(\mathcal{I})\} = J(\mathcal{I}^*).$$

This implies the existence result of our optimal control solution (3.1). ∎

Now, in order to derive the optimality condition, we consider the following Lagrangian (see e.g.[23,24,25])

$$
\begin{aligned}
\mathcal{L}(\mathbf{u},\mathbf{v},\mathbf{p},\mathbf{q},\mathcal{I}) = {} & \frac{\alpha_1}{2}\left\|u_1-u_d\right\|^2_{\mathbf{L}^2_{1,T}} + \frac{\alpha_2}{2}\left\|v_1-v_d\right\|^2_{\mathbf{L}^2_{2,T}} + \frac{\alpha_3}{2}\left\|\mathcal{I}\right\|^2_{L^2(\Gamma_{r,T})} - \iint\limits_{\Gamma_{m,T}} \mathcal{I}_m(u_1)p_1\,d\sigma\,dt + \iint\limits_{\Gamma_{r,T}} \mathcal{I}(v_1-u_1)(q_1-p_1)\,d\sigma\,dt \\
& + \sum_{i=1}^{5}\iint\limits_{\Omega_{1,T}} p_i\partial_t u_i\,dx\,dt + \sum_{j=1}^{2}\iint\limits_{\Omega_{2,T}} q_j\partial_t v_j\,dx\,dt + \iint\limits_{\Gamma_{p,T}} \mathcal{I}_p(u_1,v_1)(q_1-p_1)\,d\sigma\,dt - \sum_{i=1}^{5}\iint\limits_{\Omega_{1,T}} f_i(\mathbf{u})p_i\,dx\,dt \\
& - \sum_{j=1}^{2}\iint\limits_{\Omega_{2,T}} g_j(\mathbf{v})q_j\,dx\,dt + \sum_{i=1}^{5}\iint\limits_{\Omega_{1,T}} \mathcal{A}_{i,u_i}\nabla u_i(t,x)\cdot\nabla p_i(t,x)\,dx\,dt + \sum_{j=1}^{2}\iint\limits_{\Omega_{2,T}} \mathcal{B}_{j,v_j}\nabla v_j(t,x)\cdot\nabla q_j(t,x)\,dx\,dt,
\end{aligned}
$$

where $\mathbf{p} := (p_1,\dots,p_5)$ and $\mathbf{q} := (q_1,q_2)$. The first order optimality system characterizing the adjoint variables, is given by the Lagrange multipliers which result from computing the derivatives of $\mathcal{L}$ with respect to u_i and v_j (for $i=1,...,5$ and $j=1,2$). First, we derive the Lagrangian $\mathcal{L}$ with respect to u_1

$$
\begin{aligned}
\left\langle \frac{d\mathcal{L}}{du_1}(\mathbf{u},\mathbf{v},\mathbf{p},\mathbf{q},\mathcal{I}),\varphi_1\right\rangle = {} & \iint\limits_{\Omega_{1,T}} \alpha_1(u_1-u_d)\varphi_1\,dx\,dt - \iint\limits_{\Omega_{1,T}} \partial_t p_1\varphi_1\,dx\,dt - \iint\limits_{\Gamma_{r,T}} \mathcal{I}(t,\sigma)(q_1-p_1)\varphi_1\,d\sigma\,dt \\
& + \iint\limits_{\Gamma_{p,T}} \mathcal{I}_{p,u_1}(u_1,v_1)(q_1-p_1)\varphi_1\,d\sigma\,dt - \iint\limits_{\Gamma_{m,T}} \mathcal{I}_{i,u_1}(u_1)p_1\varphi_1\,d\sigma\,dt + \iint\limits_{\Omega_{1,T}} A_1\left(\int\limits_{\Omega_1} u_1\,dy\right)\nabla\varphi_1\cdot\nabla p_1\,dx\,dt \\
& + \iint\limits_{\Omega_{1,T}} A_1'\left(\int\limits_{\Omega_1} u_1(t,y)\,dy\right)\varphi_1(t,y)\left(\int\limits_{\Omega_1}\nabla u_1(t,x)\cdot\nabla p_1(t,x)\,dx\right)dy\,dt - \sum_{i=1}^{5}\iint\limits_{\Omega_{1,T}} f_{i,u_1}(\mathbf{u})p_i\varphi_1\,dx\,dt.
\end{aligned}
\tag{3.4}
$$

Similarly to (3.4), we obtain $\dfrac{d\mathcal{L}}{du_i}$ and $\dfrac{d\mathcal{L}}{dv_j}$ for $i=2,...,5$ and $j=1,2$. Therefore, we obtain the following adjoint-state system:

$$
\begin{cases}
\left.\begin{aligned}
& -\partial_t p_1 - \mathcal{A}_{1,u_1}\Delta p_1 + \mathcal{A}^p_{1,u_1}\int\limits_{\Omega_1}\nabla u_1\cdot\nabla p_1 + \alpha_1(u_1-u_d) = \sum_{k=1}^{5} f_{k,u_1}(\mathbf{u})p_k \\
& -\partial_t p_i - \mathcal{A}_{i,u_i}\Delta p_i + \mathcal{A}^p_{i,u_i}\int\limits_{\Omega_1}\nabla u_i\cdot\nabla p_i = \sum_{k=1}^{5} f_{k,u_i}(\mathbf{u})p_k
\end{aligned}\right\} \text{ in } \Omega_{1,T}, \\
\left.\begin{aligned}
& -\partial_t q_1 - \mathcal{B}_{1,v_1}\Delta q_1 + \mathcal{B}^p_{1,v_1}\int\limits_{\Omega_2}\nabla v_1\cdot\nabla q_1 + \alpha_2(v_1-v_d) = \sum_{k=1}^{2} g_{k,v_1}(\mathbf{v})q_k \\
& -\partial_t q_2 - \mathcal{B}_{2,v_2}\Delta q_2 + \mathcal{B}^p_{2,v_2}\int\limits_{\Omega_2}\nabla v_2\cdot\nabla q_2 = \sum_{k=1}^{2} g_{k,v_2}(\mathbf{v})q_k
\end{aligned}\right\} \text{ in } \Omega_{2,T},
\end{cases}
\tag{3.5}
$$

for $i=2,\dots,5$, completed with the following boundary and final conditions:

$$
\begin{cases}
\mathcal{A}_{1,u_1}\nabla p_1\cdot\eta = -\mathcal{B}_{1,v_1}\nabla q_1\cdot\eta = -\mathcal{I}(p_1-q_1) \quad \text{and} \quad \mathcal{B}_{1,v_1}\nabla q_1\cdot\eta = \mathcal{I}_{p,v_1}(u_1,v_1)(q_1-p_1) & \text{on } \Gamma_{r,T}, \\
\mathcal{A}_{1,u_1}\nabla p_1\cdot\eta = \mathcal{I}_{p,u_1}(u_1,v_1)(q_1-p_1) & \text{on } \Gamma_{p,T}, \\
\mathcal{B}_{1,v_1}\nabla q_1\cdot\eta = \mathcal{I}_{p,v_1}(u_1,v_1)(q_1-p_1) & \text{on } \Gamma_{r,T}, \\
\mathcal{A}_{1,u_1}\nabla p_1\cdot\eta = \mathcal{I}_{m,u_1}(u_1)p_1 & \text{on } \Gamma_{m,T}, \\
\mathbf{p}(\cdot,T) = \mathbf{p}_T = 0 & \text{in } \Omega_1^5, \\
\mathbf{q}(\cdot,T) = \mathbf{q}_T = 0 & \text{in } \Omega_2^2.
\end{cases}
\tag{3.6}
$$

Note that f_{k,u_i} (resp. g_{k,v_j}) is the derivative of f_k (resp. g_k) with respect to the component u_i for $i,k=1,\dots,5$ (resp. to v_j for $j,k=1,2$). For the transmission terms, we denote by $\mathcal{I}_{p,u_1}$ (resp. $\mathcal{I}_{p,v_1}$) the derivative of $\mathcal{I}_p$ with respect to u_1 (resp. v_1), while $\mathcal{I}_{m,u_1}$ is the derivative of $\mathcal{I}_m$ with respect to u_1.

Next, to find the optimality conditions, we compute the gradient of the cost functional

$$\left\langle \frac{\partial \mathcal{L}}{\partial \mathcal{I}}, \delta\mathcal{I} \right\rangle = \iint\limits_{\Gamma_{r,T}} (\alpha_3 \mathcal{I} + (v_1 - u_1)(q_1 - p_1))\delta\mathcal{I} d\sigma\, dt \qquad \text{and} \qquad \nabla J(\mathcal{I}) = \frac{\partial \mathcal{L}}{\partial \mathcal{I}}.$$

It is easy to see that the optimality condition can be written as follows

$$\nabla J(\mathcal{I}) = 0 \Rightarrow \alpha_3 \mathcal{I} + (v_1^{\mathcal{I}} - u_1^{\mathcal{I}})(q_1^{\mathcal{I}} - p_1^{\mathcal{I}}) = 0 \text{ a.e. on } \Gamma_{r,T}.$$

Remark 3.1. Note that the derivation of the nonlocal terms give rise to unusual terms in the adjoint problem. Moreover, we observe that in the case where the diffusion functions A_i and B_j are constant, the third term in all equations of system (3.5) vanish and we get the usual adjoint state problem.

4 | WELL-POSEDNESS RESULT OF THE ADJOINT PROBLEM (EXISTENCE AND UNIQUENESS)

In this section, we prove the existence of the weak solution for the adjoint problem (3.5)-(3.6) by using the Faedo-Galerkin method. The existence is based on the regularity of the direct solution given in Theorem 2.1, a priori estimates, and then passing to the limit in the approximate solutions using monotonicity and compactness arguments.
Similarly to Definition 2.1, let us define the notion of weak solution to adjoint system (3.5)-(3.6):

Definition 4.1 (Weak solution)**.** A weak solution of (3.5)-(3.6) is a seven-tuple $(p_1, p_2, p_3, p_4, p_5, q_1, q_2)$ such that $q_j \in L^2(0,T;\mathbf{H}_2^1)$, $\partial_t q_j \in L^2\left(0,T;(\mathbf{H}_2^1)'\right)$, $p_i \in L^2(0,T;\mathbf{H}_1^1)$, $\partial_t p_i \in L^2\left(0,T;(\mathbf{H}_1^1)'\right)$ for $i = 1, \cdots, 5$ and $j = 1, 2$ satisfying

$$\begin{aligned}
&-\sum_{i=1}^{5}\int_0^T \langle \partial_t p_i, \varphi_i \rangle_{\mathbf{H}_1^{-1},\mathbf{H}_1^1}\, dt - \sum_{j=1}^{2}\int_0^T \left\langle \partial_t q_j, \phi_j \right\rangle_{\mathbf{H}_2^{-1},\mathbf{H}_2^1}\, dt + \iint\limits_{\Gamma_{r,T}} \mathcal{I}(p_1 - q_1)(\varphi_1 - \phi_1) d\sigma dt \\
&\quad + \iint\limits_{\Gamma_{p,T}} \left(\mathcal{I}_{p,u_1}(u_1, v_1)\varphi_1 + \mathcal{I}_{p,v_1}(u_1, v_1)\phi_1\right)(q_1 - p_1) d\sigma\, dt + \iint\limits_{\Gamma_{m,T}} \mathcal{I}_{m,u_1}(u_1) p_1 \varphi_1 d\sigma\, dt \\
&\quad + \sum_{i=1}^{5}\iint\limits_{\Omega_{1,T}} \mathcal{A}_{i,u_i} \nabla\varphi_i \cdot \nabla p_i\, dx\, dt + \sum_{i=1}^{4}\iint\limits_{\Omega_{1,T}} \Big(\int\limits_{\Omega_1} \mathcal{A}_i^p\left(u_1\right)\varphi_i(t,y)\, dy\Big)\nabla u_i \cdot \nabla p_i\, dx\, dt \\
&\quad + \sum_{j=1}^{2}\iint\limits_{\Omega_{2,T}} \mathcal{B}_{j,v_j}\nabla\phi_j \cdot \nabla q_j\, dx\, dt + \iint\limits_{\Omega_{2,T}} \Big(\int\limits_{\Omega_2} \mathcal{B}_{1,v_1}^p \phi_1(t,y)\, dy\Big)\nabla v_1 \cdot \nabla q_1\, dx\, dt \\
&= \sum_{i=1}^{5}\sum_{k=1}^{5}\iint\limits_{\Omega_{1,T}} f_{k,u_i}(\mathbf{u}) p_k \varphi_i\, dx\, dt + \sum_{j=1}^{2}\sum_{k=1}^{2}\iint\limits_{\Omega_{1,T}} g_{k,v_j}(\mathbf{v}) q_k \phi_j\, dx\, dt - \alpha_1 \iint\limits_{\Omega_{1,T}} (u_1 - u_d)\varphi_1\, dx\, dt - \alpha_2 \iint\limits_{\Omega_{2,T}} (v_1 - v_d)\phi_1\, dx\, dt,
\end{aligned} \tag{4.1}$$

for all $\varphi_1, \cdots, \varphi_5 \in L^2(0,T;\mathbf{H}_1^1)$ and $\phi_1, \phi_2 \in L^2(0,T;\mathbf{H}_2^1)$. Herein, $\langle\cdot,\cdot\rangle_{H_i^{-1},H_i^1}$ is the duality product for $i = 1, 2$.

The main result in this section is the following theorem.

Theorem 4.1. Assume that condition (2.1)-(2.5) holds and $\mathcal{I} \in C^1(\Gamma_{r,T})$, then the system (3.5)-(3.6) possesses a unique weak solution in sense of Definition 4.1.

4.1 | Existence of weak solution

To prove the existence of the weak solution for the adjoint problem (3.5)-(3.6), we use Galerking approximation of the system (3.5)-(3.6). Following the same arguments in[20], we prove easily the existence result for the approximated Galerkin system.

Note that our approximate adjoint solution satisfies the following weak formulation for all $t \in (0,T)$.

$$
\begin{aligned}
&-\sum_{i=1}^{5}\iint_{\Omega_{1,t,T}} \partial_t p_i^m \varphi_i^m \,dx\,ds-\sum_{j=1}^{2}\iint_{\Omega_{2,t,T}} \partial_t q_j^m \phi_j^m \,dx\,ds+\int_{\Gamma_{r,t,T}} \mathcal{I}(p_1^m-q_j^m)(\varphi_1^m-\phi_1^m)d\sigma ds\\
&+\iint_{\Gamma_{p,t,T}}\Big(\mathcal{I}_{p,v_1}(u_1,v_1)\phi_1^m+\mathcal{I}_{p,u_1}(u_1,v_1)\varphi_1^m\Big)(q_1^m-p_1^m)d\sigma\,ds+\iint_{\Gamma_{m,t,T}}\mathcal{I}_{m,u_1}(u_1)\varphi_1^m p_1^m d\sigma\,ds\\
&+\sum_{i=1}^{5}\iint_{\Omega_{1,t,T}}\mathcal{A}_{i,u_i}\nabla\varphi_i^m\cdot\nabla p_i^m\,dx\,ds+\sum_{i=1}^{5}\iint_{\Omega_{1,t,T}}\Big(\int_{\Omega_1}\mathcal{A}_{i,u_1}^p\varphi_i^m(t,y)\,dy\Big)\nabla u_i\cdot\nabla p_i^m\,dx\,ds\\
&+\sum_{j=1}^{2}\iint_{\Omega_{2,t,T}}\mathcal{B}_{j,v_j}\nabla\phi_j^m\cdot\nabla q_j^m\,dx\,ds+\sum_{j=1}^{2}\iint_{\Omega_{2,t,T}}\Big(\int_{\Omega_2}\mathcal{B}_{j,v_j}^p\phi_1^m(t,y)\,dy\Big)\nabla v_j\cdot\nabla q_j^m\,dx\,ds
\end{aligned}
\tag{4.2}
$$

$$
=\sum_{i=1}^{5}\sum_{k=1}^{5}\iint_{\Omega_{1,t,T}} f_{k,u_i}(\mathbf{u})p_k^m\varphi_i^m\,dx\,ds+\sum_{j=1}^{2}\sum_{k=1}^{2}\iint_{\Omega_{1,t,T}} g_{k,v_j}(\mathbf{v})q_k^m\phi_j^m\,dx\,ds-\alpha_1\iint_{\Omega_{1,t,T}}(u_1-u_d)\varphi_1^m\,dx\,ds-\alpha_2\iint_{\Omega_{2,t,T}}(v_1-v_d)\phi_1^m\,dx\,ds,
$$

for all $\varphi_i^m \in L^2(0,T;V_{1,m})$ and $\phi_j^m \in L^2(0,T;V_{2,m})$ for $i=1,\cdots,5$ and $j=1,2$, where $\Omega_{j,t,T} := \Omega_j\times(t,T)$, $\Gamma_{l,t,T} := \Gamma_l\times(t,T)$ for $j=1,2$ and $l=r,p,m$.

Now, we need the following energy lemma in order to pass to the limit of the approximate adjoint solution.

Lemma 4.2. Assume that conditions (2.1)-(2.5) hold. Then, there exists a constant $C>0$ not dependent on m such that

$$
\sum_{i=1}^{5}\left\|p_i^m\right\|_{L^\infty(0,T;\mathbf{L}_1^2)}+\sum_{j=1}^{2}\left\|q_j^m\right\|_{L^\infty(0,T;\mathbf{L}_2^2)}+\sum_{i=1}^{5}||\nabla p_i^m||_{\mathbf{L}_{1,T}^2}+\sum_{j=1}^{2}||\nabla q_j^m||_{\mathbf{L}_{2,T}^2}\le C,
$$

and

$$
\sum_{i=1}^{5}\left\|\partial_t p_i^m\right\|_{L^2(0,T;(\mathbf{H}_1^1)')}+\sum_{j=1}^{2}\left\|\partial_t q_j^m\right\|_{L^2(0,T;(\mathbf{H}_2^1)')}\le C.
$$

Proof. First, observe that $u_i \to \mathcal{A}_{i,u_i}^p$ and $v_j \to \mathcal{B}_{j,v_j}^p$ are continuous, while u_i and v_j are uniformly bounded in $\mathbf{L}_1^\infty$ and $\mathbf{L}_2^\infty$ respectively. Consequently, $\mathcal{A}_{i,u_i}^p$ and $\mathcal{B}_{1,v_1}^p$ are uniformly bounded in L^∞.

Now, we choose $\phi_i^m = p_i^m$ and $\phi_j^m = q_j^m$ in (4.2) to obtain (recall that $\mathbf{p}(T)=\mathbf{q}(T)=0$)

$$
\begin{aligned}
&\sum_{i=1}^{5}\frac{1}{2}||p_i^m(t)||_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\frac{1}{2}||q_j^m(t)||_{\mathbf{L}_2^2}^2+D_{min}\left(\sum_{i=1}^{5}||\nabla p_i^m||_{\mathbf{L}_{1,t,T}^2}^2+\sum_{j=1}^{2}||\nabla q_j^m||_{\mathbf{L}_{2,t,T}^2}^2\right)\\
&\le\underbrace{-\iint_{\Gamma_{p,t,T}}\left(\mathcal{I}_{p,v_1}(u_1,v_1)q_1^m+\mathcal{I}_{p,u_1}(u_1,v_1)p_1^m\right)(q_1^m-p_1^m)d\sigma\,ds}_{I_1}\underbrace{-\iint_{\Gamma_{m,t,T}}\mathcal{I}_{m,u_1}(u_1)|p_1^m|^2d\sigma\,ds}_{I_2}-\iint_{\Gamma_{r,t,T}}\mathcal{I}(p_1^m-q_1^m)^2d\sigma\,ds\\
&\quad+C_0\sum_{i=1}^{4}\underbrace{\int_t^T\int_{\Omega_1}\left|\int_{\Omega_1}\nabla u_i\cdot\nabla p_i^m\,dx\right|\left|p_i^m(s,y)\right|\,dy\,ds}_{I_{3,i}}+C_0\underbrace{\int_t^T\int_{\Omega_2}\left|\int_{\Omega_2}\nabla v_1\cdot\nabla q_1^m\,dx\right|\left|q_1^m(s,y)\right|\,dy\,ds}_{I_4}\\
&\quad+\sum_{i=1}^{5}\sum_{k=1}^{5}\underbrace{\iint_{\Omega_{1,t,T}} f_{k,u_i}(\mathbf{u})|p_k^m|^2\,dx\,ds}_{I_{5,k,i}}+\sum_{j=1}^{2}\sum_{k=1}^{2}\underbrace{\iint_{\Omega_{2,t,T}} g_{k,v_j}(\mathbf{v})|q_k^m|^2\,dx\,ds}_{I_{6,k,j}}-\alpha_1\iint_{\Omega_{1,T}}(u_1-u_d)p_1^m\,dx\,ds-\alpha_2\iint_{\Omega_{2,T}}(v_1-v_d)q_1^m\,dx\,ds,
\end{aligned}
\tag{4.3}
$$

for some constant $C_0 = \max\left\{ \sup_t\{\left|\mathcal{A}^p_{i,u_i(t)}\right|\}, \sup_t\{\left|\mathcal{B}^p_{j,v_j(t)}\right|\}\right\} > 0$.
We start by controlling the transmission terms I_1 and I_2, we use Young inequality and trace embedding theorem[26]

$$
\begin{aligned}
\left|I_1\right| &\le \iint_{\Gamma_{p,t,T}} \left|\mathcal{I}_{p,v_1}(u_1,v_1)\right| |q_1^m|^2 d\sigma\, ds + \iint_{\Gamma_{p,t,T}} \left|\mathcal{I}_{p,u_1}(u_1,v_1)\right| |p_1^m|^2 d\sigma\, ds + \iint_{\Gamma_{p,t,T}} |\mathcal{I}_{p,v_1}(u_1,v_1) + \mathcal{I}_{p,u_1}(u_1,v_1)||q_1^m p_1^m| d\sigma\, ds \\
&\le C_{10}\vartheta\left(\|\nabla p_1^m\|^2_{\mathbf{L}^2_{1,t,T}} + \|\nabla q_1^m\|^2_{\mathbf{L}^2_{2,t,T}}\right) + C_{10}\vartheta^{-1}\left(\|p_1^m\|^2_{\mathbf{L}^2_{1,t,T}} + \|q_1^m\|^2_{\mathbf{L}^2_{2,t,T}}\right)
\end{aligned}
\tag{4.4}
$$

and similarly we deduce

$$
\left|I_2\right| \le C\left\|p_1^m\right\|_{L^2(\Gamma_{m,T})} \le C_{10}\vartheta\left\|\nabla p_1^m\right\|_{\mathbf{L}^2_1} + C_{10}\vartheta^{-1}\left\|p_1^m\right\|_{\mathbf{L}^2_1},
$$

for some constant $C_9, C_{10} > 0$. Regarding the nonlocal term $\mathcal{O}_i$, we have

$$
\begin{aligned}
\left|I_{3,i}\right| &\le \frac{\vartheta}{2}\int_t^T\left(\int_{\Omega_1} \nabla u_i \cdot \nabla p_i^m\, dx\right)^2 ds + \frac{1}{2\vartheta}\int_t^T\left(\int_{\Omega_1} p_i^m(s,y)\, dy\right)^2 ds \\
&\le \frac{\vartheta}{2}\int_t^T\Big(\int_{\Omega_1} |\nabla u_i|^2\, dx\Big)\Big(\int_{\Omega_1} |\nabla p_i^m|^2\, dx\Big) ds + \frac{|\Omega_1|}{2\vartheta}\int_t^T\int_{\Omega_1} |p_i^m(s,y)|^2\, dy\, ds \\
&\le \frac{\vartheta}{2}\sup_{s\in(t,T)}\int_{\Omega_1} |\nabla u_i(s,x)|^2\, dx\left(\iint_{\Omega_{1,t,T}} |\nabla p_i^m|^2\, dx\, ds\right) + \frac{|\Omega_1|}{2\vartheta}\int_t^T\int_{\Omega_1} |p_i^m(s,y)|^2\, dy\, ds,
\end{aligned}
$$

Similarly, we get for I_4

$$
\left|I_4\right| \le \frac{\vartheta}{2}\sup_{s\in(t,T)}\int_{\Omega_2} |\nabla v_1(s,x)|^2\, dx\left(\iint_{\Omega_{2,t,T}} |\nabla q_1^m|^2\, dx\, ds\right) + \frac{|\Omega_2|}{2\vartheta}\iint_{\Omega_{2,t,T}} |q_1^m(t,y)|^2\, dy\, ds.
$$

By L^∞ bound of the direct solution shown in Theorem 2.1 along with the continuity of $f_{k,u_i}(\cdot)$ and $g_{k,v_j}(\cdot)$, we have $f_{k,u_i}(\mathbf{u}) \in L^\infty(\Omega_{1,T})$ and $g_{k,v_j}(\mathbf{v}) \in L^\infty(\Omega_{2,T})$. Hence, we get

$$
\left|I_{5,k,i}\right| \le ||f_{k,u_i}(\mathbf{u})||_{L^\infty(\Omega_{1,T})}\iint_{\Omega_{1,t,T}} |p_k^m|^2\, dx\, ds \text{ and } \left|I_{6,k,j}\right| \le ||g_{k,v_j}(\mathbf{v})||_{L^\infty(\Omega_{2,T})}\iint_{\Omega_{2,t,T}} |q_k^m|^2\, dx\, ds.
$$

Collecting the estimates on $I_1, I_2, I_{3,i}, I_4, I_{5,k,i}, I_{6,k,j}$ and choosing $\vartheta \le \frac{D_{min}}{C_{10}}$, we get

$$
\begin{aligned}
&\sum_{i=1}^5 \frac{1}{2}\int_{\Omega_1} |p_i^m(t)|^2\, dx + \sum_{j=1}^2 \frac{1}{2}\int_{\Omega_2} |q_j^m(t)|^2\, dx + \left(D_{min} - C_{10}\vartheta\right)\left(\sum_{i=1}^5 \iint_{\Omega_{1,t,T}} |\nabla p_i^m|^2\, dx\, ds + \sum_{j=1}^2 \iint_{\Omega_{2,t,T}} |\nabla q_j^m|^2\, dx\, ds\right) \\
&\le \sum_{i=1}^5\sum_{k=1}^5 ||f_{k,u_i}(\mathbf{u})||_{L^\infty(\Omega_{1,t,T})}\int_t^T ||p_k^m||^2_{\mathbf{L}^2_1}\, ds + \sum_{j=1}^2 ||g_{k,v_j}(\mathbf{u})||_{L^\infty(\Omega_{2,t,T})}\int_t^T ||q_k^m||_{\mathbf{L}^2_2}\, ds \\
&\quad + \frac{\alpha_1}{2}||u_1 - u_d||^2_{\mathbf{L}^2_{1,t,T}} + \frac{\alpha_1}{2}\int_t^T ||p_1||^2_{\mathbf{L}^2_1}\, ds + \frac{\alpha_2}{2}||v_1 - v_d||^2_{\mathbf{L}^2_{2,t,T}} + \frac{\alpha_2}{2}\int_t^T ||q_1||^2_{\mathbf{L}^2_2}\, ds + C_{11}\left(\sum_{i=1}^4\int_t^T ||p_k^m||^2_{\mathbf{L}^2_1}\, ds + \int_t^T ||q_1^m||^2_{\mathbf{L}^2_2}\, ds\right),
\end{aligned}
$$

for some constant $C_{11} > 0$. Therefore, an application of Grönwall inequality, we arrive to

$$
\sum_{i=1}^5 \left\|p_i^m\right\|^2_{L^\infty(t,T;\mathbf{L}^2_1)} + \sum_{j=1}^2 \left\|q_j^m\right\|^2_{L^\infty(t,T;\mathbf{L}^2_2)} \le C \text{ and } \sum_{i=1}^5 ||\nabla p_i^m||^2_{\mathbf{L}^2_{1,t,T}} + \sum_{j=1}^2 ||\nabla q_j^m||^2_{\mathbf{L}^2_{2,t,T}} \le C,
$$

for every $t \in (0,T)$.
In order to derive the necessary estimates on $\partial_t p_i$ and $\partial_t p_j$ for $i = 1, ..., 5$ and $j = 1, 2$, we choose test function in (4.2) such that

$||\phi_j||_{\mathbf{H}_2^1} = 1$ and $||\varphi_i||_{\mathbf{H}_1^1} = 1$ for $i = 1, \cdots, 5$ and $j = 1, 2$. Using Young inequality, trace embedding theorem and Theorem 2.1, we obtain

$$\begin{aligned}
&\sum_{i=1}^{5}\left|\int_0^T \left\langle \partial_t p_i^m, \varphi_i \right\rangle_{\mathbf{H}_1^{-1},\mathbf{H}_1^1} dt\right| + \sum_{j=1}^{2}\left|\int_0^T \left\langle \partial_t q_j^m, \phi_j \right\rangle_{\mathbf{H}_2^{-1},\mathbf{H}_2^1} dt\right| \\
&\quad \le D_{max}\left(\sum_{i=1}^{5}\left\|\nabla p_i^m\right\|_{\mathbf{L}^2_{1,T}} + \sum_{j=1}^{2}\left\|\nabla q_j^m\right\|_{\mathbf{L}^2_{2,T}}\right) + C_p\left\|p_1^m + q_1^m\right\|_{L^2(\Gamma_{p,T})}\left\|\phi_1 - \varphi_1\right\|_{L^2(\Gamma_{p,T})} + C_m||p_1^m||_{L^2(\Gamma_{m,T})}||\varphi_1||_{L^2(\Gamma_{m,T})} \\
&\quad + \|\mathcal{I}\|_{L^\infty(\Gamma_{r,T})}\left\|p_1^m - q_1^m\right\|_{L^2(\Gamma_{r,T})}\left\|\phi_1 - \varphi_1\right\|_{L^2(\Gamma_{r,T})} + C_{12}\sum_{j=1}^{2}\sum_{k=1}^{2}||g_{i,v_k}(\mathbf{v})||_{\mathbf{L}^2_{1,T}}||q_k^m||_{\mathbf{L}^2_{2,T}} + C_{13}\sum_{i=1}^{5}\sum_{k=1}^{5}||f_{i,u_k}(\mathbf{u})||_{\mathbf{L}^2_{1,T}}||p_k^m||_{\mathbf{L}^2_{1,T}} \\
&\quad + \left(\left\|u_d\right\|_{\mathbf{L}^2_{1,T}} + \left\|u_1\right\|_{\mathbf{L}^2_{1,T}}\right)\left\|\varphi_1\right\|_{\mathbf{L}^2_{1,T}} + \left(\left\|v_d\right\|_{\mathbf{L}^2_{2,T}} + \left\|v_{1,T}\right\|_{\mathbf{L}^2_2}\right)\left\|\phi_1\right\|_{\mathbf{L}^2_{2,T}} \\
&\quad + \sum_{i=1}^{5} C_{14}\left\|\nabla u_i\right\|_{L^\infty(0,T;\mathbf{L}^2_1)}\int_0^T\int_{\Omega_1}\left|\varphi_i(t,y)\right| dy||\nabla p_i^m||_{\mathbf{L}^2_1} dt + \sum_{j=1}^{2} C_{15}||\nabla v_j||_{L^\infty(0,T;\mathbf{L}^2_2)}\int_0^T\int_{\Omega_1}\left|\phi_j(t,y)\right| dy||\nabla q_j^m||_{\mathbf{L}^2_2} dt \\
&\quad \le C_{18}\left(\sum_{i=1}^{4}\left\|p_i^m\right\|_{L^2(0,T;\mathbf{H}_1^1)} + ||q_1^m||_{L^2(0,T;\mathbf{H}_2^1)}\right) + \left\|u_d\right\|_{\mathbf{L}^2_{1,T}} + \left\|v_d\right\|_{\mathbf{L}^2_{2,T}} \le C_{19},
\end{aligned} \tag{4.5}$$

for some constants $C_{12}, \cdots, C_{19} > 0$. This implies

$$\sum_{i=1}^{5}\sup_{||\varphi_i||_{\mathbf{H}_1^1}=1}\int_0^T \left\langle \partial_t p_i^m, \varphi_i \right\rangle_{\mathbf{H}_1^{-1},\mathbf{H}_1^1} dt + \sum_{j=1}^{2}\sup_{||\phi_j||_{\mathbf{H}_2^1}=1}\int_0^T \left\langle \partial_t q_j^m, \phi_j \right\rangle_{\mathbf{H}_2^{-1},\mathbf{H}_2^1} dt \le C_{19}.$$

Hence, we conclude the proof of Lemma 4.2. ∎

In view of Lemma 4.2 and the compactness criterion (see[22] for more details), there exist limit functions $\mathbf{p} := (p_1, \ldots, p_5)$ and $\mathbf{q} := (q_1, q_2)$ such that

$$\begin{aligned}
&(\mathbf{p}^m, \mathbf{q}^m) \to (\mathbf{p}, \mathbf{q}) && \text{strongly in } \left(\mathbf{L}^2_{1,T}\right)^5 \times \left(\mathbf{L}^2_{2,T}\right)^2, \\
&(\mathbf{p}^m, \mathbf{q}^m) \to (\mathbf{p}, \mathbf{q}) && \text{weakly in } L^2(0,T;\mathbf{H}_1^1)^5 \times L^2(0,T;\mathbf{H}_2^1)^2, \\
&(\partial_t\mathbf{p}^m, \partial_t\mathbf{q}^m) \to (\partial_t\mathbf{p}, \partial_t\mathbf{q}) && \text{weakly in } L^2\left(0,T;\left(\mathbf{H}_1^1\right)^p\right)^5 \times L^2\left(0,T;\left(\mathbf{H}_2^1\right)^p\right)^2.
\end{aligned} \tag{4.6}$$

Using (4.6) and sending m to $+\infty$ in the weak formulation (4.2), we conclude the existence of the weak solution in the sense of Definition 4.1.

4.2 | Uniqueness of weak solution

Regarding the uniqueness result, we assume two different weak solutions $(\mathbf{p}, \mathbf{q})$ and $(\mathbf{p}_*, \mathbf{q}_*)$ in the sense of Definition 4.1, where $\mathbf{p} := (p_1, \ldots, p_5)$, $\mathbf{p}_* := (p_1^*, \ldots, p_5^*)$, $\mathbf{q} := (q_1, q_2)$ and $\mathbf{q}_* := (q_1^*, q_2^*)$. Now, the difference of the two weak solutions $((\mathbf{p}, \mathbf{q})$ and $(\mathbf{p}_*, \mathbf{q}_*))$ are denoted by $\mathbf{P} = (\mathbf{p} - \mathbf{p}_*) = (P_1, P_2, P_3, P_4, P_5)$ and $\mathbf{Q} = (\mathbf{q} - \mathbf{q}_*) = (Q_1, Q_2)$. Next, we substracte the weak formulations (4.1) corresponding to $(\mathbf{p}, \mathbf{q})$ and $(\mathbf{p}_*, \mathbf{q}_*)$ without integrating over (t, T), with $\varphi_i = P_i$ and $\phi_j = Q_j$ (for

$i = 1, ..., 5$ and $j = 1, 2$) to get

$$
\begin{aligned}
&-\sum_{i=1}^{5} \frac{1}{2}\frac{d}{ds}\left\|P_i\right\|^2_{\mathbf{L}^2_1} - \sum_{j=1}^{2} \frac{1}{2}\frac{d}{ds}\left\|Q_j\right\|^2_{\mathbf{L}^2_2} + D_{min}\left(\sum_{i=1}^{5}\left\|\nabla P_i\right\|^2_{\mathbf{L}^2_1} + \sum_{j=1}^{2} ||\nabla Q_j||^2_{\mathbf{L}^2_2}\right) + \int_{\Gamma_r} \mathcal{I}(P_1 - Q_1)^2 d\sigma \\
&\leq -\int_{\Gamma_p} \left(\mathcal{I}_{p,v_1}(u_1, v_1)Q_1 - \mathcal{I}_{p,u_1}(u_1, v_1)P_1\right)(Q_1 - P_1)d\sigma - \int_{\Gamma_m} \mathcal{I}_{m,u_1}(u_1)|P_1|^2 d\sigma \\
&\quad + C_0 \sum_{i=1}^{4} \int_{\Omega_1}\left(\left|\int_{\Omega_1} \nabla u_i(t,x)\nabla P_i(t,x)\, dx\right|\right)\left|P_i(t,y)\right|\, dy + \sum_{i=1}^{5}\sum_{k=1}^{5}\int_{\Omega_1} f_{k,u_i}(\mathbf{u})|P_k|^2\, dx \\
&\quad + C_0 \int_{\Omega_2}\left(\left|\int_{\Omega_2} \nabla v_1(t,x)\nabla Q_1(t,x)\, dx\right|\right)\left|Q_1(t,y)\right|\, dy + \sum_{j=1}^{2}\sum_{k=1}^{2}\int_{\Omega_2} g_{k,v_j}(\mathbf{v})|Q_k|^2\, dx \\
&\quad - \alpha_1 \int_{\Omega_1} (u_1 - u_d)P_1\, dx - \alpha_2 \int_{\Omega_2} (v_1 - v_d)Q_1\, dx := I_1 + I_2 + I_3 + I_4 + I_5 + I_6 + I_7 + I_8,
\end{aligned}
$$

where $C_0 = \max\left\{\sup_{t\in(0,T)}\{\left|\mathcal{A}^p_{i,u_i}\right|\}, \sup_{t\in(0,T)}\{\left|\mathcal{B}^p_{j,v_j}\right|\}\right\} > 0$. Next, we use the same techniques applied to $\mathcal{O}_i, X, Y, \mathcal{F}_{i,k}$ and $\mathcal{G}_{j,k}$ in the proof of Lemma 4.2 to deduce

$$
-\frac{d}{ds}\sum_{i=1}^{5}\left\|P_i(s)\right\|^2_{\mathbf{L}^2_1} - \frac{d}{ds}\sum_{j=1}^{2}\left\|Q_i(s)\right\|^2_{\mathbf{L}^2_2} \leq C_{20}\left(\sum_{i=1}^{5}\left\|P_i(s)\right\|^2_{\mathbf{L}^2_1} + \sum_{j=1}^{2}\left\|Q_j(s)\right\|^2_{\mathbf{L}^2_2}\right). \tag{4.7}
$$

for some constant $C_{20} > 0$. Therefore, an application of Grönwall inequality to (4.7) for $s \in [t, T]$, we get:

$$
\sum_{i=1}^{5}\left\|P_i(t)\right\|^2_{\mathbf{L}^2_1} + \left\|Q_i(t)\right\|^2_{\mathbf{L}^2_2} \leq \exp((T-t)C_{20})\left(\sum_{i=1}^{5}\left\|P_i(T)\right\|^2_{\mathbf{L}^2_1} + \sum_{j=1}^{2}\left\|Q_j(T)\right\|^2_{\mathbf{L}^2_2}\right) = 0. \tag{4.8}
$$

This completes the proof.

5 | STABILITY OF THE DISCRETE OPTIMAL CONTROL SCHEME

In this section, we propose a finite element method with implicit Euler type discretization to our direct and adjoint problems. We obtain a priori estimates on the approximated solution in order to prove the stability result of our direct and adjoint discrete schemes with respect to the control.

First, we start by defining our numerical scheme. Let $\mathcal{T}_{i,h}$ be a regular partition of $\bar{\Omega}_i$ into tetrahedra K_i of maximum diameter h for $i = 1, 2$. Given an integer $k \geq 0$ and $S \subset \mathbb{R}^3$, by $P_k(S)$ we denote the space of polynomial functions defined in S of total degree up to k, and define the following finite element subspaces

$$
\mathbf{V}_{i,h} = \left\{m_h \in H^1(\Omega_i) : m_h|_K \in P_1(K)\ \ \forall K \in \mathcal{T}_{i,h}\right\},
$$

for $i = 1, 2$. respectively.

Let J_i be the set of nodes of $\mathcal{T}_{i,h}$ and $\{P_j\}_{j\in J}$ the coordinates of these nodes. Let $\{\varphi_j\}_{j\in J}$ (Resp. $\{\phi_j\}$) be the finite element basis for $\mathbf{V}_{1,h}$ (resp. for $\mathbf{V}_{2,h}$). Using implicit Euler integration with time step $\tau = T/N$. This produces the following fully discrete scheme: Find $(\mathbf{u}_h, \mathbf{p}_h, \mathbf{v}_h, \mathbf{q}_h)$ such that

$$
(\mathbf{u}_h, \mathbf{v}_h, \mathbf{p}_h, \mathbf{q}_h) = \sum_{n=1}^{N}(\mathbf{u}^n_h, \mathbf{v}^n_h, \mathbf{p}^n_h, \mathbf{q}^n_h)(x)\mathbf{1}_{[(n-1)\tau, n\tau]}(t)
$$

satisfying the following discrete direct and adjoint systems

$$\sum_{i=1}^{5}\Big(\frac{u_{i,h}^{n+1}-u_{i,h}^{n}}{\tau},\varphi_i\Big)_{\Omega_1}+\sum_{j=1}^{2}\Big(\frac{v_{j,h}^{n+1}-v_{j,h}^{n}}{\tau},\phi_j\Big)_{\Omega_2}+\sum_{j=1}^{2}(\mathcal{B}_{j,v_{j,h}^{n+1}}\nabla v_{j,h}^{n+1},\nabla\phi_j)_{\Omega_2}+\sum_{i=1}^{5}(\mathcal{A}_{i,u_{i,h}^{n+1}}\nabla u_{i,h}^{n+1},\nabla\varphi_i)_{\Omega_1}+(\mathcal{I}_m(u_1^{n+1}),\varphi_1)_{\Gamma_m}$$
$$+(\mathcal{I}(v_{1,h}^{n+1}-u_{1,h}^{n+1}),\phi_1-\varphi_1)_{\Gamma_r}+(\mathcal{I}_p(u_{1,h}^{n+1},v_{1,h}^{n+1}),\phi_1-\varphi_1)_{\Gamma_p}=\sum_{i=1}^{5}(f_i(\mathbf{u}_h^{n+1}),\varphi_i)_{\Omega_1}+\sum_{i=1}^{2}(g_j(\mathbf{v}_h^{n+1}),\phi_j)_{\Omega_2},\tag{5.1}$$

and

$$\sum_{i=1}^{5}\Big(\frac{p_{i,h}^{n}-p_{i,h}^{n+1}}{\tau},\varphi_i\Big)_{\Omega_1}+\sum_{j=1}^{2}\Big(\frac{q_{i,h}^{n}-q_{i,h}^{n+1}}{\tau},\phi_j\Big)_{\Omega_1}+\Big(\mathcal{I}_{p,v_{1,h}}(u_{1,h}^n,v_{1,h}^n)\phi_1-\mathcal{I}_{p,u_1}(u_{1,h}^n,v_{1,h}^n)\varphi_1,q_{1,h}^n-p_{1,h}^n\Big)_{\Gamma_p}$$
$$+(\mathcal{I}(p_{1,h}^n-q_{1,h}^n),\varphi_1-\phi_1)_{\Gamma_r}+\Big(\mathcal{I}_{m,u_1}(u_{1,h}^n)p_{1,h}^n,\varphi_1\Big)_{\Gamma_m}+\sum_{i=1}^{5}(\mathcal{A}_{i,u_{i,h}^n}\nabla p_{i,h}^n,\nabla\varphi_i)_{\Omega_1}+\sum_{j=1}^{2}(\mathcal{B}_{j,v_{j,h}^n}\nabla q_{j,h}^n,\nabla\phi_j)_{\Omega_2}$$
$$+\sum_{i=1}^{4}\Big(\nabla u_{i,h}^n\cdot\nabla p_{i,h}^n,\int_{\Omega_1}\mathcal{A}_{i,u_{i,h}^n}^p\left(u_{1,h}^n\right)\varphi_i(t,y)\,dy\Big)_{\Omega_1}+\Big(\nabla v_{1,h}^n\cdot\nabla q_{1,h}^n,\int_{\Omega_2}\mathcal{B}_{1,v_{1,h}^n}^p\phi_1(t,y)\,dy\Big)_{\Omega_2}\tag{5.2}$$
$$=\sum_{i=1}^{5}\sum_{k=1}^{5}(f_{k,u_i}(\mathbf{u}_h^n)p_{k,h}^n,\varphi_i)_{\Omega_1}+\sum_{j=1}^{2}\sum_{k=1}^{2}(g_{k,v_j}(\mathbf{v}_h^n)q_{k,h}^n,\phi_j)_{\Omega_1}-\alpha_1(u_{1,h}^n-u_d^n,\varphi_1)_{\Omega_1}-\alpha_2(v_{1,h}^n-v_d^n,\phi_1)_{\Omega_2},$$

for all $\varphi_1,\cdots,\varphi_5\in\mathbf{V}_{1,h}$, $\phi_1,\phi_2\in\mathbf{V}_{2,h}$ and for all $n=1,...,N$.

Lemma 5.1. Assume that $\mathbf{u}_0\in\left(\mathbf{H}_1^1\right)^5$, $\mathbf{v}_0\in\left(\mathbf{H}_2^1\right)^2$, $p_0\in\left(\mathbf{L}_1^2\right)^5$ and $\mathbf{q}_0\in\mathbf{L}_2^2$, then, the following estimates hold: there exists a constant $C>0$ not depending on τ and h such that

$$\sum_{i=1}^{5}\max_{0\le k\le N}\left\|u_{i,h}^k\right\|_{\mathbf{L}_1^2}+\sum_{j=1}^{2}\max_{0\le k\le N}\left\|v_{j,h}^k\right\|_{\mathbf{L}_2^2}+\tau\sum_{j=1}^{2}\sum_{i=1}^{N}\left\|v_{j,h}^k\right\|_{\mathbf{H}_2^1}+\tau\sum_{i=1}^{5}\sum_{i=1}^{N}\left\|u_{i,h}^k\right\|_{\mathbf{H}_1^1}\le C\tag{5.3}$$

and

$$\sum_{i=1}^{5}\max_{0\le k\le N}\left\|p_{i,h}^k\right\|_{\mathbf{L}_1^2}+\sum_{i=1}^{2}\max_{0\le k\le N}\left\|q_{j,h}^k\right\|_{\mathbf{L}_2^2}+\tau\sum_{j=1}^{2}\sum_{i=1}^{N}\left\|q_{j,h}^k\right\|_{\mathbf{H}_2^1}+\tau\sum_{i=1}^{5}\sum_{i=1}^{N}\left\|p_{i,h}^k\right\|_{\mathbf{H}_1^1}\le C.\tag{5.4}$$

Proof. The proof of estimates (5.3) is given in[20]. Now, in the discrete adjoint problem (5.2), we take $\varphi_i=\tau p_{i,h}^n$, $\phi_j=\tau q_{j,h}^n$ and we use assumption (2.5) to get

$$\sum_{i=1}^{5}\left\|p_{i,h}^n\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^n\right\|_{\mathbf{L}_2^2}^2+2\tau D_{min}\left(\sum_{i=1}^{5}\left\|p_{i,h}^n\right\|_{\mathbf{H}_1^1}+\sum_{j=1}^{2}\left\|v_{j,h}^n\right\|_{\mathbf{H}_2^2}^2\right)+2\tau\int_{\Gamma_r}\mathcal{I}^n(p_{1,h}^n-q_{1,h}^n)^2d\sigma$$
$$\le 2\tau\int_{\Gamma_p}\left|\mathcal{I}_{p,v_1}(u_{1,h}^n,v_{1,h}^n)\right|\left|q_{1,h}^n\right|^2d\sigma+2\tau\int_{\Gamma_p}\left|\mathcal{I}_{p,u_1}(u_{1,h}^n,v_{1,h}^n)+\mathcal{I}_{p,v_1}(u_{1,h}^n,v_{1,h}^n)\right|\left|q_{1,h}^np_{1,h}^n\right|d\sigma$$
$$+2\tau\int_{\Gamma_p}\left|\mathcal{I}_{p,u_1}(u_{1,h}^n,v_{1,h}^n)\right|\left|p_{1,h}^n\right|^2d\sigma+2\tau C_1\int_{\Gamma_m}\left|p_{1,h}^n\right|^2d\sigma$$
$$+2\tau\sum_{i=1}^{4}\frac{\vartheta C_0}{2}\left(\sup_{k=1,...,N}\left\|\nabla u_{i,h}^k\right\|_{\mathbf{L}_1^2}^2\right)\left\|\nabla p_{i,h}^n\right\|_{\mathbf{L}_1^2}^2+2\tau\frac{\vartheta C_0}{2}\left(\sup_{k=1,...,N}\left\|\nabla v_{1,h}^k\right\|_{\mathbf{L}_2^2}^2\right)\left\|\nabla q_{1,h}^n\right\|_{\mathbf{L}_2^2}^2\tag{5.5}$$
$$+2\tau\sum_{i=1}^{4}\frac{C_0}{2\vartheta}|\Omega_1|^2\left\|p_{i,h}^n\right\|_{\mathbf{L}_1^2}^2+2\tau\frac{C_0}{2\vartheta}|\Omega_2|^2\left\|q_{1,h}^n\right\|_{\mathbf{L}_2^2}^2+2\tau C_2\left(\sum_{i=1}^{5}\left\|p_{i,h}^n\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^n\right\|_{\mathbf{L}_2^2}^2\right)$$
$$+2\tau\left\|u_{d,h}^n\right\|_{\mathbf{L}_1^2}^2+2\tau\left\|v_{d,h}^n\right\|_{\mathbf{L}_2^2}^2+\sum_{i=1}^{5}\left\|p_{i,h}^{n+1}\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^{n+1}\right\|_{\mathbf{L}_2^2}^2.$$

Observe that the fourth term in the first line of (5.5) is positive. We use similar arguments as in (4.4) to deal with the second line and the first term in the third line of (5.5) (consult the estimates on I_1 and I_2 in the proof Lemma 4.2). From (5.5) we get

$$\begin{aligned}\sum_{i=1}^{5}\left\|p_{i,h}^{n}\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^{n}\right\|_{\mathbf{L}_2^2}^2+2\tau\left(D_{min}-\vartheta C_{26}\right)\left(\sum_{i=1}^{5}\left\|p_{i,h}^{n}\right\|_{\mathbf{H}_1^1}+\sum_{j=1}^{2}\left\|v_{j,h}^{n}\right\|^2\right)\\ \le 2\tau C_{27}\left(\sum_{i=1}^{5}\left\|p_{i,h}^{n}\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^{n}\right\|_{\mathbf{L}_2^2}^2\right)+\sum_{i=1}^{5}\left\|p_{i,h}^{n+1}\right\|_{\mathbf{L}_1^2}^2+\sum_{j=1}^{2}\left\|q_{j,h}^{n+1}\right\|_{\mathbf{L}_2^2}^2,\end{aligned}\tag{5.6}$$

for some constants $C_{26}, C_{27} > 0$. Finally, by an application of Grönwall inequality to (5.6), we conclude the proof of (5.4). ∎

Remark 5.1. In the previous proof, we have assumed that the gradient of the discrete direct solution is bounded in L^∞ in time as shown in Theorem 2.1 (for the continuous case). Similar result can be obtained in the discrete case, so we omit the details.

In the following step, we establish the stability result with respect to the control $\mathcal{I}$. We consider the discrete systems (5.1) and (5.2) with two different controls $\mathcal{I}$ and $\mathcal{I}^*$. We try to establish some estimates on the difference between solutions $(\mathbf{u},\mathbf{v}) = (\mathbf{u}(\mathcal{I}),\mathbf{v}(\mathcal{I}))$ (resp $(\mathbf{p},\mathbf{q}) = (\mathbf{p}(\mathcal{I}),\mathbf{q}(\mathcal{I}))$) and $(\mathbf{u}_*,\mathbf{v}_*) = (\mathbf{u}(\mathcal{I}^*),\mathbf{v}(\mathcal{I}^*))$ (resp $(\mathbf{p}_*,\mathbf{q}_*) = (\mathbf{p}(\mathcal{I}^*),\mathbf{q}(\mathcal{I}^*))$ for given controls $\mathcal{I}$ and $\mathcal{I}^*$.
Now, we need some inequalities based on trace inequalities[27,21]. There exists a constant $C > 0$ such that

$$\|U_h - V_h\|_{L^2(\Gamma_r)}^2 \le Ch^{-1}\left(\|U_h\|_{\mathbf{L}_1^2}^2 + \|V_h\|_{\mathbf{L}_2^2}^2\right),\tag{5.7}$$

$$\|U_h - V_h\|_{L^4(\Gamma_r)}^2 \le \|U_h\|_{\mathbf{H}_1^1}^2 + \|V_h\|_{\mathbf{H}_2^1}^2,\tag{5.8}$$

$$\|W_h\|_{L^2(\Omega_i)}^2 \le C\left(\|W_h - X_h\|_{L^2(\Omega_i)}^2 + \|X_h\|_{L^2(\Omega_i)}^2\right),\tag{5.9}$$

(5.10)

for all $U_h \in \mathbf{V}_{1,h}$, $V_h \in \mathbf{V}_{2,h}$ and $W_h, X_h \in \mathbf{V}_{i,h}$ for $i = 1, 2$.
We have the following stability results concerning our numerical solution.

Proposition 5.1. Let $(\mathbf{u}_h,\mathbf{v}_h,\mathbf{p}_h,\mathbf{q}_h,\mathcal{I})$ and $(\mathbf{u}_{*,h},\mathbf{v}_{*,h},\mathbf{p}_{*,h},\mathbf{q}_{*,h},\mathcal{I}_*)$ two different solutions of the discrete systems (5.1)-(5.2). Assume that the following CFL condition holds

$$\tau \le M/(1+h^{-1}),\tag{5.11}$$

where $M > 0$ is a constant will be defined in the proof. Then, there exists a constant $C > 0$ such that

$$\sum_{i=1}^{5}||u_{i,h} - u_{*,i,h}||_{L^2(0,T;\mathbf{H}_1^1)} + \sum_{j=1}^{2}||v_{j,h} - v_{*,j,h}||_{L^2(0,T;\mathbf{H}_2^1)} \le C||\mathcal{I} - \mathcal{I}_*||_{L^2(\Gamma_{r,T})}\tag{5.12}$$

$$\sum_{i=1}^{5}||p_{i,h} - p_{*,i,h}||_{L^2(0,T;\mathbf{H}_1^1)} + \sum_{j=1}^{2}||q_{j,h} - q_{*,j,h}||_{L^2(0,T;\mathbf{H}_2^1)} \le C||\mathcal{I} - \mathcal{I}_*||_{L^2(\Gamma_{r,T})}.\tag{5.13}$$

Proof. First, we let $U_{i,h}^n = u_{i,h}^n - u_{*,i,h}^n$ and $V_{j,h}^n = v_{j,h}^n - v_{*,j,h}^n$ for $i = 1,\dots,5$ and $j = 1, 2$. Observe that from (5.1), we get

$$\begin{aligned}&\sum_{i=1}^{5}\int_{\Omega_1}\frac{U_{i,h}^n - U_{i,h}^{n-1}}{\tau}\varphi_i\,dx + \sum_{j=1}^{2}\int_{\Omega_2}\frac{V_{j,h}^n - V_{j,h}^{n-1}}{\tau}\phi_j\,dx + \sum_{i=1}^{5}\mathcal{A}_{i,u_{i,h}^n}\int_{\Omega_1}\nabla u_{i,h}^n\cdot\nabla\varphi_i\,dx\\ &- \sum_{i=1}^{5}\mathcal{A}_{i,u_{*,i,h}^n}\int_{\Omega_1}\nabla u_{*,i,h}^n\cdot\nabla\varphi_i\,dx + \int_{\Gamma_r}\left(\mathcal{I}^n(v_{1,h}^n - u_{1,h}^n) - \mathcal{I}_*^n(v_{*,1,h}^n - u_{*,1,h}^n)\right)(\phi_1 - \varphi_1)d\sigma\\ &+ \sum_{j=1}^{2}\mathcal{B}_{j,v_{j,h}^n}\int_{\Omega_2}\nabla v_{j,h}^n\cdot\nabla\phi_j\,dx - \sum_{j=1}^{2}\mathcal{B}_{j,v_{*,j,h}^n}\int_{\Omega_2}\nabla v_{*,j,h}^n\cdot\nabla\phi_j\,dx\\ &+ \int_{\Gamma_p}\left(\mathcal{I}_p(u_{1,h}^n, v_{1,h}^n) - \mathcal{I}_p(u_{*,1,h}^n, v_{*,1,h}^n)\right)(\varphi_1 - \phi_1)d\sigma - \int_{\Gamma_p}\left(\mathcal{I}_m(u_{1,h}^n) - \mathcal{I}_m(u_{*,1,h}^n)\right)\varphi_1 d\sigma\end{aligned}\tag{5.14}$$

$$= \sum_{i=1}^{5}\int_{\Omega_1}(f_i(\mathbf{u}_h^n)-f_i(\mathbf{u}_{*,h}^n))\varphi_i\,dx+\sum_{j=1}^{2}\int_{\Omega_2}(g_j(\mathbf{v}_h^n)-g_j(\mathbf{v}_{*,h}^n))\phi_j\,dx.$$

Next, we denote $\mathcal{U}_{i,n} := ||U_{i,h}^n||_{\mathbf{H}_1^1}$, $\mathcal{V}_{j,n} := ||V_{j,h}^n||_{\mathbf{H}_2^1}$, $\overline{\mathcal{U}}_{i,n} := ||U_{i,h}^n - U_{i,h}^{n-1}||_{\mathbf{L}_1^2}$ and $\overline{\mathcal{V}}_{j,n} := ||V_{j,h}^n - V_{j,h}^{n-1}||_{\mathbf{L}_2^2}$ for $i = 1,\cdots,5$ and $j = 1, 2$. We substitute $\varphi_i = \tau(U_{i,h}^n - U_{i,h}^{n-1})$ and $\phi_j = \tau(V_{j,h}^n - V_{j,h}^{n-1})$ in (5.14) to obtain

$$\begin{aligned}
&\sum_{i=1}^{5}\overline{\mathcal{U}}_{j,n}^2+\overline{\mathcal{V}}_{1,n}^2+\tau\int_{\Gamma_r}\mathcal{I}^n(V_{1,h}^n-U_{1,h}^n)(V_{1,h}^n-U_{1,h}^n-(V_{1,h}^{n-1}-U_{1,h}^{n-1}))d\sigma\\
&\quad+\tau\sum_{i=1}^{5}\mathcal{A}_{i,u_{i,h}^n}\int_{\Omega_1}\nabla U_{i,h}^n\cdot\nabla(U_{i,h}^n-U_{i,h}^{n-1})\,dx+\tau\sum_{j=1}^{2}\mathcal{B}_{j,v_{j,h}^n}\int_{\Omega_2}\nabla V_{j,h}^n\cdot\nabla(V_{j,h}^n-V_{j,h}^{n-1})\,dx\\
&=\tau\sum_{i=1}^{5}\int_{\Omega_1}(f_i(\mathbf{u}_h^n)-f_i(\mathbf{u}_{*,h}^n))(U_{i,h}^n-U_{i,h}^{n-1})\,dx+\tau\sum_{j=1}^{2}\int_{\Omega_2}(g_j(\mathbf{v}_h^n)-g_j(\mathbf{v}_{*,h}^n))(V_{j,h}^n-V_{j,h}^{n-1})\,dx\\
&\quad+\tau\int_{\Gamma_p}\left(\mathcal{I}_p(u_{1,h}^n,v_{1,h}^n)-\mathcal{I}_p(u_{*,1,h}^n,v_{*,1,h}^n)\right)(V_{1,h}^n-U_{1,h}^n-(V_{1,h}^{n-1}-U_{1,h}^{n-1}))d\sigma\\
&\quad+\tau\int_{\Gamma_r}(\mathcal{I}^n-\mathcal{I}_*^n)(v_{*,1,h}^n-u_{*,1,h}^n)(U_{1,h}^n-U_{1,h}^{n-1}-(V_{1,h}^n-V_{1,h}^{n-1}))d\sigma-\tau\int_{\Gamma_m}\left(\mathcal{I}_m(u_{1,h}^n)-\mathcal{I}_m(u_{*,1,h}^n)\right)(U_{1,h}^n-U_{1,h}^{n-1}))d\sigma\\
&\quad+\tau\sum_{i=1}^{5}\left(\mathcal{A}_{i,u_{*,i,h}^n}-\mathcal{A}_{i,u_{i,h}^n}\right)\int_{\Omega_1}\nabla u_{*,i,h}^n\cdot\nabla(U_{i,h}^n-U_{i,h}^{n-1})\,dx+\tau\sum_{j=1}^{2}\left(\mathcal{B}_{j,v_{*,j,h}^n}-\mathcal{B}_{j,v_{j,h}^n}\right)\int_{\Omega_2}\nabla v_{*,j,h}^n\cdot\nabla(V_{j,h}^n-V_{j,h}^{n-1})\,dx\\
&:=\tau\left(\sum_{i=1}^{5}X_i^f+\sum_{j=1}^{2}X_j^g+Y+Z+\sum_{i=1}^{5}W_{A_i}+\sum_{j=1}^{2}W_{B_j}\right).
\end{aligned}$$

According to mean-value theorem, Young inequality, Sobolev embedding, assumption (2.5) and Lemma 5.1, we get

$$\begin{aligned}
\left|X_i^f\right| &:= \left|\int_{\Omega_1}(f_i(\mathbf{u}_h^n)-f_i(\mathbf{u}_{*,h}^n))(U_{i,h}^n-U_{i,h}^{n-1})\,dx\right|\\
&\le\le L_f\int_{\Omega_1}\sum_{k=1}^{5}\left|U_{k,h}^n\right|\left|U_{i,h}^n-U_{i,h}^{n-1}\right|\,dx L_f\int_{\Omega_1}(1+\sum_{i=1}^{5}\left|u_h^n\right|)\sum_{k=1}^{5}\left|U_{k,h}^n\right|\left|U_{i,h}^n-U_{i,h}^{n-1}\right|\,dx \qquad (5.15)\\
&\le\left\|1+\sum_{i=1}^{5}\left|u_{i,h}^n\right|\right\|_{\mathbf{L}_1^4}\left\|U_{k,h}^n\right\|_{\mathbf{L}_1^4}\overline{\mathcal{U}}_{i,n}\le\left\|1+\sum_{i=1}^{5}\left|u_{i,h}^n\right|\right\|_{\mathbf{H}_1^2}\left\|U_{k,h}^n\right\|_{\mathbf{H}_1^2}\overline{\mathcal{U}}_{i,n}\le\frac{\vartheta}{2}\sum_{k=1}^{5}\mathcal{U}_{k,n}^2+\frac{L_f^2}{2\vartheta}\overline{\mathcal{U}}_{i,n}^2,
\end{aligned}$$

for $i = 1,\cdots,5$. Similar estimates applies to X_j^g:

$$\left|X_j^g\right| := \left|\int_{\Omega_2}(g_j(\mathbf{v}_h^n)-g_j(\mathbf{v}_{*,h}^n))V_{1,h}^n\right|\,dx\le\frac{\vartheta}{2}\sum_{k=1}^{2}\mathcal{V}_{k,n}^2+\frac{L_g^2}{2\vartheta}\overline{\mathcal{V}}_{j,n}^2, \qquad (5.16)$$

(5.17)

for $j = 1, 2$. Now, we apply (5.7) and (2.5) to get

$$\begin{aligned}
|Y_1| &:= \left| \int_{\Gamma_p} \left(\mathcal{I}_p(u^n_{1,h}, v^n_{1,h}) - \mathcal{I}_p(u^n_{*,1,h}, v^n_{*,1,h}) \right) (V^n_{1,h} - U^n_{1,h} - (V^{n-1}_{1,h} - U^{n-1}_{1,h})) d\sigma \right| \\
&\leq \int_{\Gamma_p} L_p \left(|U^n_{1,h}| + |V^n_{1,h}| \right) \left| V^n_{1,h} - U^n_{1,h} - (V^{n-1}_{1,h} - U^{n-1}_{1,h}) \right| d\sigma \\
&\leq \frac{\vartheta}{2} ||U^n_{1,h}||^2_{L^2(\Gamma_p)} + \frac{L_p^2}{2\vartheta} ||U^n_{1,h} - U^{n-1}_{1,h}||^2_{L^2(\Gamma_p)} + \frac{\vartheta}{2} ||V^n_{1,h}||^2_{L^2(\Gamma_p)} + \frac{L_p^2}{2\vartheta} ||V^n_{1,h} - V^{n-1}_{1,h}||^2_{L^2(\Gamma_p)} \\
&\leq \vartheta C_{28} \mathcal{U}^2_{1,n} + \frac{C(\Omega_1) L_p^2 h^{-1}}{2\vartheta} \overline{\mathcal{U}}^2_{1,n} + \vartheta C_{29} \mathcal{V}^2_{1,n} + \frac{C(\Omega_2) L_p^2 h^{-1}}{2\vartheta} \overline{\mathcal{V}}^2_{1,n} \leq \vartheta C_{30} \left(\mathcal{U}^2_{1,n} + \mathcal{V}^2_{1,n} \right) + \frac{C_{31} h^{-1}}{2\vartheta} \left(\overline{\mathcal{U}}^2_{1,n} + \overline{\mathcal{V}}^2_{1,n} \right),
\end{aligned} \tag{5.18}$$

and

$$|Y_2| := \left| \int_{\Gamma_m} \left(\mathcal{I}_m(u^n_{1,h}) - \mathcal{I}_m(u^n_{*,1,h}) \right) (U^n_{1,h} - U^{n-1}_{1,h})) d\sigma \right| \vartheta C_{30} \mathcal{U}^2_{1,n} + \frac{C_{31} h^{-1}}{2\vartheta} \overline{\mathcal{U}}^2_{1,n},$$

for some positive constants $C_{28}, \dots, C_{31} > 0$. An application of Young inequality and trace embedding Theorem[21], we get

$$\begin{aligned}
|Y_3| &:= \left| \int_{\Gamma_r} (\mathcal{I}^n - \mathcal{I}^n_*)(v^n_{*,1,h} - u^n_{*,1,h})(U^n_{1,h} - U^{n-1}_{1,h} - (V^n_{1,h} - V^{n-1}_{1,h})) d\sigma \right| \\
&\leq ||\mathcal{I}^n - \mathcal{I}^n_*||_{L^2(\Gamma_r)} ||v^n_{*,1,h} - u^n_{*,1,h}||_{L^4(\Gamma_r)} ||V^n_{1,h} - U^n_{1,h} - (V^{n-1}_{1,h} - U^{n-1}_{1,h})||_{L^4(\Gamma_r)} \\
&\leq C_{32}(||v_{*,1,h}||^2_{\mathbf{H}^1_2} + ||u_{*,1,h}||^2_{\mathbf{H}^1_1}) \left(\frac{1}{2\vartheta} ||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \frac{\vartheta}{2} \mathcal{V}^2_{1,n} + \frac{\vartheta}{2} \mathcal{V}^2_{1,n-1} + \frac{\vartheta}{2} \mathcal{U}^2_{1,n} + \frac{\vartheta}{2} \mathcal{U}^2_{1,n-1} \right) \\
&\leq C_{33} (\frac{1}{2\vartheta} ||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \frac{\vartheta}{2} \mathcal{V}^2_{1,n} + \frac{\vartheta}{2} \mathcal{V}^2_{1,n-1} + \frac{\vartheta}{2} \mathcal{U}^2_{1,n} + \frac{\vartheta}{2} \mathcal{U}^2_{1,n-1} \Big),
\end{aligned} \tag{5.19}$$

for some constants $C_{32}, C_{33} > 0$. Thanks to Theorem 2.1, we deduce from (5.9)

$$\begin{aligned}
|W_{A_i}| &:= \left| \left(A_i \left(\int_{\Omega_1} u^n_{*,i,h} \, dx \right) - A_i \left(\int_{\Omega_1} u^n_{i,h} \, dx \right) \right) \int_{\Omega_1} \nabla u^n_{*,i,h} \nabla (U^n_{i,h} - U^{n-1}_{i,h}) \, dx \right| \\
&\leq L_A \left\| U^n_{i,h} \right\|_{\mathbf{L}^1_1} \left\| \nabla u^n_{*,i,h} \right\|_{\mathbf{L}^2_1} \left\| \nabla (U^n_{i,h} - U^{n-1}_{i,h}) \right\|_{\mathbf{L}^2_1} \leq \frac{L_A C(\Omega_1)^2 \left\| \nabla u^n_{*,i,h} \right\|^2_{\mathbf{L}^2_1}}{2\vartheta} \left\| U^n_{i,h} \right\|^2_{\mathbf{L}^2_1} + \frac{\vartheta}{2} \left\| \nabla (U^n_{i,h} - U^{n-1}_{i,h}) \right\|^2_{\mathbf{L}^2_1} \\
&\leq \frac{C_{34}}{\vartheta} \left(\left\| U^n_{i,h} - U^{n-1}_{i,h} \right\|^2_{\mathbf{L}^2_1} + \left\| U^{n-1}_{i,h} \right\|^2_{\mathbf{L}^2_1} \right) + \frac{\vartheta}{2} \left(\left\| \nabla U^n_{i,h} \right\|^2_{\mathbf{L}^2_1} + \left\| \nabla U^{n-1}_{i,h} \right\|^2_{\mathbf{L}^2_1} \right) \leq \frac{\vartheta}{2} \mathcal{U}^2_{i,n} + \left(\frac{\vartheta}{2} + \frac{C_{34}}{\vartheta} \right) \mathcal{U}^2_{i,n-1} + \frac{C_{34}}{\vartheta} \overline{\mathcal{U}}^2_{i,n},
\end{aligned} \tag{5.20}$$

for some constant $C_{34} > 0$ depending only on Ω_1, $\mathbf{u}^*_0$ and $\mathbf{u}_0$. Similarly, we obtain

$$|W_{B_1}| := \left| \left(B_1 \left(\int_{\Omega_2} v^n_{*,1,h} \, dx \right) - A_1 \left(\int_{\Omega_1} v^n_{1,h} \, dx \right) \right) \int_{\Omega_2} \nabla v^n_{*,1,h} \nabla (U^n_{1,h} - U^{n-1}_{1,h}) \, dx \right| \leq \frac{\vartheta}{2} \mathcal{V}^2_{1,n} + \left(\frac{\vartheta}{2} + \frac{C_{35}}{\vartheta} \right) \mathcal{V}^2_{1,n-1} + \frac{C_{35}}{\vartheta} \overline{\mathcal{V}}^2_{1,n},$$

for some constant $C_{35} > 0$ depending only on Ω_2, $\mathbf{u}_0$ and $\mathbf{u}_0$. Collecting the previous estimates, we arrive to

$$\begin{aligned}
&\left| \sum_{i=1}^{5} X^f_i + \sum_{j=1}^{2} X^g_j + \sum_{i=1}^{3} Y_i + \sum_{i=1}^{4} W_{A_i} + \sum_{j=1}^{2} W_{B_j} \right| \leq \vartheta C_{36} \left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n} \right) + \frac{C_{37}}{\vartheta} (1 + h^{-1}) \left(\sum_{i=1}^{5} \overline{\mathcal{U}}^2_{i,n} + \sum_{j=1}^{2} \overline{\mathcal{V}}^2_{j,n} \right) \\
&\qquad + C_{39} \left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \mathcal{V}^2_{1,n-1} \right) + C_{40} ||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^4(\Gamma_r)},
\end{aligned} \tag{5.21}$$

for some constants $C_{36}, C_{37}, C_{38} > 0$. Now, using the identity $\frac{|a_n|^2-|a_{n-1}|^2}{2} \leq a_n(a_n - a_{n-1})$, we get

$$\sum_{i=1}^{5} \mathcal{A}_{i,u^n_{*,i,h}} \left\|\nabla U^n_{i,h}\right\|^2_{\mathbf{L}^2_1} + \sum_{j=1}^{2} \mathcal{B}_{j,v^n_{*,j,h}} \left\|\nabla V^n_{j,h}\right\|^2_{\mathbf{L}^2_2} - \left(\sum_{i=1}^{5} \mathcal{A}_{i,u^n_{*,i,h}} \left\|\nabla U^{n-1}_{i,h}\right\|^2_{\mathbf{L}^2_1} + \sum_{j=1}^{2} \mathcal{B}_{j,v^n_{*,j,h}} \left\|\nabla V^{n-1}_{j,h}\right\|^2_{\mathbf{L}^2_2} \right) + \int_{\Gamma_r} \mathcal{I}^n \left(V^n_{1,h} - U^n_{1,h}\right)^2 - \int_{\Gamma_r} \mathcal{I}^n \left(V^{n-1}_{1,h} - U^{n-1}_{1,h}\right)^2$$
$$\leq 2\sum_{i=1}^{5} \mathcal{A}_{i,u^n_{*,i,h}} \int_{\Omega_1} \nabla U^n_{i,h} \cdot \nabla \left(U^n_{i,h} - U^{n-1}_{i,h}\right) dx + 2\sum_{j=1}^{2} \mathcal{B}_{j,v^n_{*,j,h}} \int_{\Omega_2} \nabla V^n_{j,h} \cdot \nabla \left(V^n_{j,h} - V^{n-1}_{j,h}\right) dx + 2\int_{\Gamma_r} \mathcal{I}^n \left(V^n_{1,h} - U^n_{1,h}\right)\left(V^n_{1,h} - V^{n-1}_{1,h} - \left(U^n_{1,h} - U^{n-1}_{1,h}\right)\right).$$

This implies

$$D_{min}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n}\right) - D_{max}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n-1}\right) + \int_{\Gamma_r} \mathcal{I}^n \left(V^n_{1,h} - U^n_{1,h}\right)^2 - \int_{\Gamma_r} \mathcal{I}^n \left(V^{n-1}_{1,h} - U^{n-1}_{1,h}\right)^2$$
$$\leq 2\left(\sum_{i=1}^{5} \mathcal{A}_{i,u^n_{*,i,h}} \int_{\Omega_1} \nabla U^n_{i,h} \cdot \nabla \left(U^n_{i,h} - U^{n-1}_{i,h}\right) dx + \sum_{j=1}^{2} \mathcal{B}_{j,v^n_{*,j,h}} \int_{\Omega_2} \nabla V^n_{j,h} \cdot \nabla \left(V^n_{j,h} - V^{n-1}_{j,h}\right) dx\right) \tag{5.22}$$
$$+ 2\int_{\Gamma_r} \mathcal{I}^n \left(V^n_{1,h} - U^n_{1,h}\right)\left(V^n_{1,h} - V^{n-1}_{1,h} - \left(U^n_{1,h} - U^{n-1}_{1,h}\right)\right).$$

Using this and the previous estimates (5.21) and (5.22), we get from (5.14)-(5.22)

$$(1 - \tau\frac{C_{37}}{\vartheta}(1 + h^{-1}))\left(\sum_{i=1}^{5} \overline{\mathcal{U}}^2_{i,n} + \sum_{j=1}^{2} \overline{\mathcal{V}}^2_{j,n}\right) + \tau\left(D_{min} - \vartheta C_{36}\right)\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n}\right) + \tau\int_{\Gamma_r} \mathcal{I}^n(U^n_{1,h} - V^n_{1,h})^2$$
$$\leq \tau\int_{\Gamma_r} \mathcal{I}^n(U^{n-1}_{1,n} - V^{n-1}_{1,h})^2 + \tau C_{39}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \mathcal{V}^2_{1,n-1}\right) + \tau C_{40}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)}. \tag{5.23}$$

Now, we choose ϑ and τ such that $\vartheta \leq \dfrac{D_{min}}{C_{36}}$ and $\tau < \dfrac{C_{37} D_{min}}{C_{36}(1 + h^{-1})} =: \dfrac{M}{1 + h^{-1}}$, we obtain

$$2\tau\left(D_{min} - \vartheta C_{36}\right)\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n}\right) + \tau\int_{\Gamma_r} \mathcal{I}^n(U^n_{1,h} - V^n_{1,h})^2$$
$$\leq \tau\int_{\Gamma_r} \mathcal{I}^n(U^{n-1}_{1,n} - V^{n-1}_{1,h})^2 + \tau C_{39}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n-1}\right) + \tau C_{40}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)}$$
$$\leq \tau\int_{\Gamma_r} \mathcal{I}^{n-1}(U^{n-1}_{1,h} - V^{n-1}_{1,h})^2 + \tau\int_{\Gamma_r} (\mathcal{I}^n - \mathcal{I}^{n-1})(U^{n-1}_{1,h} - V^{n-1}_{1,h})^2 + \tau C_{40}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \tau C_{39}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n-1}\right)$$
$$\leq \tau\int_{\Gamma_r} \mathcal{I}^{n-1}(U^{n-1}_{1,h} - V^{n-1}_{1,h})^2 + 2\tau\mathcal{I}_{max}||U^{n-1}_{1,h} - V^{n-1}_{1,h}||^2_{L^2(\Gamma_r)} + \tau C_{40}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \tau C_{39}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n-1}\right)$$
$$\leq \tau\int_{\Gamma_r} \mathcal{I}^{n-1}(U^{n-1}_{1,h} - V^{n-1}_{1,h})^2 + \tau C_{41}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \tau C_{39}\left(\sum_{i=1}^{5} \mathcal{U}^2_{i,n-1} + \sum_{j=1}^{2} \mathcal{V}^2_{j,n-1}\right),$$

for some constant $C_{41} > 0$. Thanks to (5.8), we get

$$\left(\sum_{i=1}^{5}\mathcal{U}_{i,n}^2+\mathcal{V}_{1,n}^2\right)+\frac{\tau}{C_{42}}\int_{\Gamma_r}\mathcal{I}^n(U_{1,h}^n-V_{1,h}^n)^2\leq\frac{\tau}{C_{42}}\int_{\Gamma_r}\mathcal{I}^{n-1}(U_{1,h}^{n-1}-V_{1,h}^{n-1})^2+\frac{\tau C_{41}}{C_{42}}||\mathcal{I}_*^n-\mathcal{I}^n||_{L^2(\Gamma_r)}^2+\frac{\tau C_{39}}{C_{42}}\left(\sum_{i=1}^{5}\mathcal{U}_{i,n-1}^2+\mathcal{V}_{1,n-1}^2\right),$$

where $C_{42} := \min\left\{2\tau\left(D_{min}-\frac{D_{min}}{C_{36}}\right),1-\frac{C_{38}C_{37}D_{min}}{C_{36}(1+h^{-d})}\right\}>0$. By induction, we obtain

$$\left(\sum_{i=1}^{5}\mathcal{U}_{i,n}^2+\sum_{j=1}^{2}\mathcal{V}_{j,n}^2\right)\leq\left(\frac{\tau C_{39}}{C_{42}}\right)^n\left(\sum_{i=1}^{5}\mathcal{U}_{i,0}^2+\sum_{j=1}^{2}\mathcal{V}_{j,0}^2\right)+\sum_{k=1}^{n}\left(\frac{\tau C_{39}}{C_{42}}\right)^{k-1}\left(\frac{C_{41}}{C_{42}}\right)^k||\mathcal{I}_*^n-\mathcal{I}^n||_{L^2(\Gamma_r)}^2. \tag{5.24}$$

This proves (5.12).

Now, we prove (5.13). For that, we let $P_{i,h}^n = p_{i,h}^n - p_{*,i,h}^n$ and $Q_{i,h}^n = q_{i,h} - q_{*,i,h}$, $\mathcal{P}_{i,n} := ||P_{i,h}^n||_{\mathbf{H}_1^1}$, $\mathcal{Q}_{j,n} := ||Q_{j,h}^n||_{\mathbf{H}_2^1}$, $\overline{\mathcal{P}}_{i,n} := ||P_{i,h}^n - P_{i,h}^{n+1}||_{\mathbf{L}_1^2}$ and $\overline{\mathcal{Q}}_{j,n} := ||Q_{j,h}^n - Q_{j,h}^{n+1}||_{\mathbf{L}_2^2}$. Observe that from (5.2), we get

$$\begin{aligned}
&\sum_{i=1}^{5}\int_{\Omega_1}\frac{P_{i,h}^n-P_{i,h}^{n+1}}{\tau}\varphi_i\,dx+\sum_{j=1}^{2}\int_{\Omega_2}\frac{Q_{j,h}^n-Q_{j,h}^{n+1}}{\tau}\phi_j\,dx+\sum_{i=1}^{5}\mathcal{A}_{i,u_{i,h}^n}\int_{\Omega_1}\nabla P_{i,h}^n\cdot\nabla\varphi_i\,dx+\sum_{j=1}^{2}\mathcal{B}_{j,v_{j,h}^n}\int_{\Omega_2}\nabla Q_{j,h}^n\cdot\nabla\phi_j\,dx\\
&\quad+\sum_{i=1}^{4}\underbrace{\mathcal{A}_{i,u_{i,h}^n}^p\iint_{\Omega_1^2}\nabla P_{i,h}^n\cdot\nabla u_{i,h}^n\,dy\varphi_i\,dx}_{\mathcal{T}_{1,i}(\varphi_i)}+\underbrace{\mathcal{B}_{1,v_{1,h}^n}^p\iint_{\Omega_2^2}\nabla Q_{1,h}^n\cdot\nabla v_{1,h}^n\,dy\phi_1\,dx}_{\mathcal{T}_2(\phi_1)}+\underbrace{\int_{\Gamma_r}\mathcal{I}^n\left(P_{1,h}^n-Q_{1,h}^n\right)(\varphi_1-\phi_1)d\sigma}_{\mathcal{T}_3(\varphi_1,\phi_1)}\\
&=\underbrace{-\int_{\Gamma_p}\left(\mathcal{I}_{p,v_1}^n\phi_1-\mathcal{I}_{p,u_1}^n\varphi_1\right)\left(q_{1,h}^n-p_{1,h}^n\right)-\left(\mathcal{I}_{*,p,v_1}^n\phi_1-\mathcal{I}_{*,p,u_1}^n\varphi_1\right)\left(q_{*,1,h}^n-p_{*,1,h}^n\right)d\sigma}_{\mathcal{T}_4(\varphi_1,\phi_1)}-\underbrace{\int_{\Omega_1}\alpha_1(u_{*,1,h}^n-u_{1,h}^n)\varphi_1\,dx}_{\mathcal{T}_8(\varphi_1)}\\
&\quad+\underbrace{\int_{\Gamma_r}(\mathcal{I}^n-\mathcal{I}_*^n)(q_{*,1,h}^n-p_{*,1,h}^n)(\phi_1-\varphi_1)d\sigma}_{\mathcal{T}_5(\phi_1,\varphi_1)}-\underbrace{\int_{\Gamma_m}\left(\mathcal{I}_{m,u_1}^n p_{1,h}^n-\mathcal{I}_{*,m,u_1}^n p_{*,1,h}^n\right)\varphi_1 d\sigma}_{\mathcal{T}_6(\varphi_1)}-\underbrace{\int_{\Omega_1}\alpha_2(v_{*,1,h}^n-v_{1,h}^n)\phi_1\,dx}_{\mathcal{T}_{10}(\phi_1)}\\
&\quad+\sum_{i,k=1}^{5}\underbrace{\int_{\Omega_1}\left(f_{k,u_i}(\mathbf{u}_h^k)p_{k,h}^n-f_{k,u_i}(\mathbf{u}_{*,h}^k)p_{*,k,h}^n\right)\varphi_i\,dx}_{\mathcal{T}_{7,i,k}(\varphi_i)}-\sum_{j,k=1}^{2}\underbrace{\int_{\Omega_2}\left(g_{k,v_j}(\mathbf{v}_h^k)q_{k,h}^n-g_{k,v_j}(\mathbf{v}_{*,h}^k)q_{*,k,h}^n\right)\phi_j\,dx}_{\mathcal{T}_{9,j,k}(\phi_j)}\\
&\quad+\sum_{j=1}^{2}\underbrace{\left(\mathcal{B}_{j,v_{j,h}^n}-\mathcal{B}_{j,v_{*,j,h}^n}\right)\int_{\Omega_2}\nabla q_{*,j,h}^n\cdot\nabla\phi_j\,dx}_{\mathcal{T}_{11,j}(\phi_j)}+\sum_{i=1}^{5}\underbrace{\left(\mathcal{A}_{i,u_{i,h}^n}-\mathcal{A}_{i,u_{*,i,h}^n}\right)\int_{\Omega_1}\nabla p_{*,i,h}^n\cdot\nabla\varphi_i\,dx}_{\mathcal{T}_{12,i}(\varphi_i)}\\
&\quad+\sum_{i=1}^{4}\underbrace{\iint_{\Omega_1^2}\nabla\left(\mathcal{A}_{i,u_{i,h}^n}u_{i,h}^n-\mathcal{A}_{i,u_{*,i,h}^n}^p u_{*,i,h}^n\right)\cdot\nabla p_{*,i,h}^n(x)\varphi_i(y)\,dx\,dy}_{\mathcal{T}_{13,i}(\varphi_i)}\\
&\quad+\underbrace{\iint_{\Omega_2^2}\nabla\left(\mathcal{B}_{j,v_{1,h}^n}^p v_{1,h}^n-\mathcal{B}_{j,v_{*,1,h}^n}^p v_{*,1,h}^n\right)\cdot\nabla q_{*,1,h}^n(x)\phi_1(y)\,dx\,dy}_{\mathcal{T}_{14}(\phi_1)}.
\end{aligned} \tag{5.25}$$

It is not difficult to see that

$$\begin{aligned}\left|\mathcal{T}_8(P^n_{1,h}-P^{n+1}_{1,h})\right| &\le \frac{1}{2}\mathcal{U}^2_{1,n}+\frac{1}{2}\overline{\mathcal{P}}^2_{1,n}\le C_{43}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+\frac{1}{2}\overline{\mathcal{P}}^2_{1,n}\\ \left|\mathcal{T}_{10}(Q^n_{1,h}-Q^{n+1}_{1,h})\right| &\le \frac{1}{2}\mathcal{V}^2_{1,n}+\frac{1}{2}\overline{\mathcal{Q}}^2_{1,n}\le C_{43}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+\frac{1}{2}\overline{\mathcal{Q}}^2_{1,n},\end{aligned}\tag{5.26}$$

for some constant $C_{43}>0$. Using Young inequality with Lemma 5.1, we have

$$\begin{aligned}\left|\mathcal{T}_{1,i}(P^n_{i,h}-P^{n+1}_{i,h})\right| &\le C_{44}\int_{\Omega_1}\left|\int_{\Omega_1}\nabla P^n_{i,h}\cdot\nabla u^n_{i,h}\,dy\right|\left|P^n_{i,h}-P^{n+1}_{i,h}\right|\,dx\\ &\le C_{44}\left\|\nabla P^h_{i,n}\right\|_{\mathbf{L}^2_1}\left\|\nabla u^h_{i,n}\right\|_{\mathbf{L}^2_1}\left\|P^n_{i,h}-P^{n+1}_{i,h}\right\|_{\mathbf{L}^1_1}\le\frac{\vartheta C_{45}}{2}\mathcal{P}^2_{i,n}+\frac{1}{2\vartheta}\overline{\mathcal{P}}^2_{i,n}\end{aligned}\tag{5.27}$$

and

$$\left|\mathcal{T}_2(Q^n_{1,h}-Q^{n+1}_{1,h})\right|\le\frac{\vartheta C_{45}}{2}\mathcal{Q}^2_{1,n}+\frac{1}{2\vartheta}\overline{\mathcal{Q}}^2_{1,n},\tag{5.28}$$

for some constants $C_{44},C_{45}>0$. Using Lemma 5.1, (5.24) and Young inequality, we obtain

$$\begin{aligned}\left|\mathcal{T}_{7,i,k}(P^n_{i,h}-P^{n+1}_{i,h})\right| &\le\left|\int_{\Omega_1}\left(\left(f_{k,u_i}(\mathbf{u}^n_h)-f_{k,u_i}(\mathbf{u}^n_{*,h})\right)p^n_{k,h}+f_{k,u_i}(\mathbf{u}^n_{*,h})P^n_{k,h}\right)\left(P^n_{i,h}-P^{n+1}_{i,h}\right)\right|\\ &\le\int_{\Omega_1}C_{46}\left(\sum_{l=1}^5\left|U^n_{l,h}\right|\right)\left|p^n_{k,h}\right|\left|P^n_{i,h}-P^{n+1}_{i,h}\right|+\int_{\Omega_1}\left|f_{k,u_i}(\mathbf{u}^n_{*,h})\right|\left|P^n_{k,h}\right|\left|P^n_{i,h}-P^{n+1}_{i,h}\right|\\ &\le C_{46}\left(\sum_{l=1}^5\left\|U^n_{l,h}\right\|_{\mathbf{L}^4_1}\right)\left\|p^n_{k,h}\right\|_{\mathbf{L}^4_1}\left\|P^n_{i,h}-P^{n+1}_{i,h}\right\|_{\mathbf{L}^2_1}+C_{46}\left\|f_{k,u_i}(\mathbf{u}_{*,h})\right\|_{\mathbf{L}^4_1}\left\|P^n_{k,h}\right\|_{\mathbf{L}^4_1}\left\|P^n_{i,h}-P^{n+1}_{i,h}\right\|_{\mathbf{L}^2_1}\\ &\le C_{46}\left(\sum_{l=1}^5\left\|U^n_{l,h}\right\|_{\mathbf{H}^2_1}\right)\left\|p^n_{k,h}\right\|_{\mathbf{H}^2_1}\left\|P^n_{i,h}-P^{n+1}_{i,h}\right\|_{\mathbf{L}^2_1}+C_{46}\left\|f_{k,u_i}(\mathbf{u}_{*,h})\right\|_{\mathbf{H}^2_1}\left\|P^n_{k,h}\right\|_{\mathbf{H}^2_1}\left\|P^n_{i,h}-P^{n+1}_{i,h}\right\|_{\mathbf{L}^2_1}\\ &\le\frac{C_{47}}{2}\left(\sum_{l=1}^5\mathcal{U}^2_{l,n}+\overline{\mathcal{P}}^2_{i,n}\right)+C_{47}\left(\frac{\vartheta}{2}\mathcal{P}^2_{i,n}+\frac{1}{2\vartheta}\overline{\mathcal{P}}^2_{i,n}\right)\le C_{48}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+C_{49}\vartheta\mathcal{P}^2_{k,n}+\frac{C_{50}}{\vartheta}\overline{\mathcal{P}}^2_{i,n},\end{aligned}$$

for $i,k=1,\cdots,5$ and for some constants $C_{46},\cdots,C_{50}>0$. Moreover, we have

$$\left|\mathcal{T}_{9,j,k}(Q^n_{j,h}-Q^{n+1}_{j,h})\right|\le C_{48}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+C_{49}\vartheta\mathcal{Q}^2_{k,n}+\frac{C_{50}}{\vartheta}\overline{\mathcal{Q}}^2_{j,n},\tag{5.29}$$

for $j=1,2$ and $k=1,\cdots,5$. Using similar computation as in (5.20), we get

$$\begin{aligned}\left|\mathcal{T}_{12,i}(P^n_{i,h}-P^{n+1}_{i,h})\right| &\le\left|\mathcal{A}_{i,u^n_{*,i,h}}-\mathcal{A}_{i,u^n_{*,i,h}}\right|\left|\int_{\Omega_1}\nabla p^n_{*,i,h}\cdot\nabla\left(P^n_{i,h}-P^{n+1}_{i,h}\right)\,dx\right|\\ &\le\frac{L_A C(\Omega_1)}{\vartheta}\left\|\nabla p^n_{*,i,h}\right\|_{\mathbf{L}^2_1}\left\|U_{i,h}\right\|^2_{\mathbf{L}^2_1}+\frac{\vartheta}{2}\left\|\nabla\left(P^n_{i,h}-P^{n+1}_{i,h}\right)\right\|^2_{\mathbf{L}^2_1}\le C_{51}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+\frac{\vartheta}{2}\left(\mathcal{P}^2_{i,n}+\mathcal{P}^2_{i,n+1}\right)\end{aligned}\tag{5.30}$$

and

$$\left|\mathcal{T}_{11}(Q^n_{1,h}-Q^{n+1}_{1,h})\right|\le C_{51}\left\|\mathcal{I}^n_*-\mathcal{I}^n\right\|^2_{L^2(\Gamma_r)}+\frac{\vartheta}{2}\left(\mathcal{Q}^2_{i,n}+\mathcal{Q}^2_{i,n+1}\right),\tag{5.31}$$

for some constant $C_{51} > 0$. For nonlocal transport terms, we have

$$
\begin{aligned}
\left|\mathcal{T}_{13,i}\left(P^n_{i,h} - P^{n+1}_{i,h}\right)\right| &= \left|\iint_{\Omega_1^2} \left(\nabla\left(\mathcal{A}^p_{i,u^n_{i,h}} u^n_{i,h} - \mathcal{A}^p_{i,u^n_{*,i,h}} u^n_{*,i,h}\right)\right)\cdot \nabla p^n_{*,i,h}(x)\left(P^n_{i,h} - P^{n+1}_{i,h}\right)(y)\,dx\,dy\right| \\
&\le \left\|\nabla\left(\mathcal{A}^p_{i,u^n_{i,h}} u^n_{i,h} - \mathcal{A}^p_{i,u^n_{*,i,h}} u^n_{*,i,h}\right)\right\|_{\mathbf{L}^2_1} \left\|\nabla p^n_{*,i,h}(x)\right\|_{\mathbf{L}^2_1} \left\|P^n_{i,h} - P^{n+1}_{i,h}\right\|_{\mathbf{L}^1_1} \\
&\le C(\Omega_1)\left(\left(\mathcal{A}^p_{i,u^n_{i,h}} - \mathcal{A}^p_{i,u^n_{*,i,h}}\right)\left\|\nabla u^n_{i,h}\right\|_{\mathbf{L}^2_2} + \mathcal{A}^p_{i,u^n_{*,i,h}}\left\|\nabla U^n_{i,h}\right\|_{\mathbf{L}^2_2}\right)\overline{\mathcal{P}}_{i,n} \\
&\le C(\Omega_1)\left(\left\|U^n_{i,h}\right\|_{\mathbf{L}^2_1}\left\|\nabla u^n_{i,h}\right\|_{\mathbf{L}^2_2} + \mathcal{A}^p_{i,u^n_{*,i,h}}\left\|\nabla U^n_{i,h}\right\|_{\mathbf{L}^2_2}\right)\overline{\mathcal{P}}_{1,n} \\
&\le C(\Omega_1)\left(\left\|\nabla u^n_{i,h}\right\|_{\mathbf{L}^2_2} + \mathcal{A}^p_{i,u^n_{*,i,h}}\right)\left\|\nabla U^n_{i,h}\right\|_{\mathbf{L}^2_1}\overline{\mathcal{P}}_{i,n} \le C_{52}\left\|\mathcal{I}^n_* - \mathcal{I}^n\right\|^2_{L^2(\Gamma_r)} + C_{53}\overline{\mathcal{P}}^2_{i,n}
\end{aligned} \tag{5.32}
$$

and

$$
\left|\mathcal{T}_{14}\left(Q^n_{1,h} - Q^{n+1}_{1,h}\right)\right| \le \frac{C_{54}}{2}\left\|\mathcal{I}^n_* - \mathcal{I}^n\right\|^2_{L^2(\Gamma_r)} + C_{55}\overline{\mathcal{Q}}^2_{1,n}, \tag{5.33}
$$

for some constant $C_{52}, \dots, C_{55} > 0$. Now, using similar computation as in (5.19), we obtain

$$
\mathcal{T}_3(Q^n_{1,h} - Q^{n+1}_{1,h}, P^n_{1,h} - P^{n+1}_{1,h}) \le C_{56}\left(\frac{1}{2\vartheta}\left\|\mathcal{I}^n - \mathcal{I}^n_*\right\|_{L^2(\Gamma_r)} + \frac{\vartheta}{2}\left(\mathcal{Q}^2_{1,n} + \mathcal{Q}^2_{1,n+1} + \mathcal{P}^2_{1,n} + \mathcal{P}^2_{1,n+1}\right)\right), \tag{5.34}
$$

for some constant $C_{56} > 0$. Regarding transmission terms, we have

$$
\begin{aligned}
&\left|\mathcal{T}_4(Q^n_{1,h} - Q^{n+1}_{1,h}, P^n_{1,h} - P^{n+1}_{1,h})\right| \le L_p\int_{\Gamma_p}\left((|U^n_{1,h}| + |V^n_{1,h}|)\left(\left|Q^n_{1,h} - Q^{n+1}_{1,h}\right| + \left|P^n_{1,h} - P^{n+1}_{1,h}\right|\right)\right)\left|q^n_{1,h} - p^n_{1,h}\right| d\sigma \\
&\quad + L_p\int_{\Gamma_p}\left(\left|Q^n_{1,h} - Q^{n+1}_{1,h}\right| + \left|P^n_{1,h} - P^{n+1}_{1,h}\right|\right)\left|Q^n_{1,h} - P^n_{1,h}\right| d\sigma \\
&\le L_p\left\|q^n_{1,h} - q^n_{1,h}\right\|_{L^4(\Gamma_p)}\left(\frac{1}{2\vartheta}\left(\left\|U^n_{1,h}\right\|^2_{L^4(\Gamma_p)} + \left\|V^n_{1,h}\right\|^2_{L^4(\Gamma_p)}\right)\right. \\
&\quad \left. + \frac{\vartheta}{2}\left(\left\|Q^n_{1,h}\right\|^2_{L^4(\Gamma_p)} + \left\|Q^{n+1}_{1,h}\right\|^2_{L^4(\Gamma_p)} + \left\|P^n_{1,h}\right\|^2_{L^4(\Gamma_p)} + \left\|P^{n+1}_{1,h}\right\|^2_{L^4(\Gamma_p)}\right)\right) \\
&\quad + C_{57}\left(\frac{h^{-1}}{2\vartheta}\left(\overline{\mathcal{Q}}^2_{1,n} + \overline{\mathcal{P}}^2_{1,n}\right) + \frac{\vartheta}{2}\left(\left\|Q^n_{1,h}\right\|^2_{L^4(\Gamma_p)} + \left\|P^n_{1,h}\right\|^2_{L^4(\Gamma_p)}\right)\right) \\
&\le C\left(\mathcal{U}^2_{1,n} + \mathcal{V}^2_{1,n}\right) + h^{-1}\frac{C_{57}}{\vartheta}\left(\overline{\mathcal{Q}}^2_{1,n} + \overline{\mathcal{P}}^2_{1,n}\right) + \vartheta C_{58}\left(\mathcal{Q}^2_{1,n} + \mathcal{P}^2_{1,n}\right) \\
&\le C_{59}\left\|\mathcal{I}^n_* - \mathcal{I}^n\right\|^2_{L^2(\Gamma_r)} + h^{-1}\frac{C_{57}}{\vartheta}\left(\overline{\mathcal{Q}}^2_{1,n} + \overline{\mathcal{P}}^2_{1,n}\right) + \vartheta C_{58}\left(\mathcal{Q}^2_{1,n} + \mathcal{P}^2_{1,n}\right)
\end{aligned} \tag{5.35}
$$

and

$$
\left|\mathcal{T}_{14}(P^n_{1,h} - P^{n+1}_{1,h})\right| \le C_{59}\left\|\mathcal{I}^n_* - \mathcal{I}^n\right\|^2_{L^2(\Gamma_r)} + h^{-1}\frac{C_{57}}{\vartheta}\left(\overline{\mathcal{Q}}^2_{1,n} + \overline{\mathcal{P}}^2_{1,n}\right) + \vartheta C_{58}\left(\mathcal{Q}^2_{1,n} + \mathcal{P}^2_{1,n}\right),
$$

for some constantw $C_{57}, C_{58}, C_{59} > 0$. Collecting the results (5.25)-(5.35), choosing ϑ and τ such that

$$
\vartheta < \min\left(1, \frac{D_{min}}{\max\{C_{45}, C_{49}, 1/2, C_{56}/2, C_{58}\}}\right), \quad \tau \le \frac{\max\{C_{45}, C_{49}, 1/2, C_{56}/2, C_{58}\}}{D_{min}(1 + h^{-1})} \le \frac{M}{(1 + h^{-1})}
$$

and using similar argument in (5.23)-(5.24), we get

$$
\begin{aligned}
&\left(\sum_{i=1}^{5}\mathcal{P}^2_{i,n} + \sum_{j=1}^{2}\mathcal{Q}^2_{1,n}\right) + \frac{\tau}{C_{62}}\int_{\Gamma_r}\mathcal{I}^n(P^n_{1,h} - Q^n_{1,h})^2 \\
&\qquad \le \frac{\tau}{C_{62}}\int_{\Gamma_r}\mathcal{I}^{n-1}(P^{n+1}_{1,h} - Q^{n+1}_{1,h})^2 + \frac{\tau C_{60}}{C_{62}}||\mathcal{I}^n_* - \mathcal{I}^n||^2_{L^2(\Gamma_r)} + \frac{\tau C_{61}}{C_{62}}\left(\sum_{i=1}^{5}\mathcal{P}^2_{i,n+1} + \mathcal{Q}^2_{1,n+1}\right)
\end{aligned}
$$

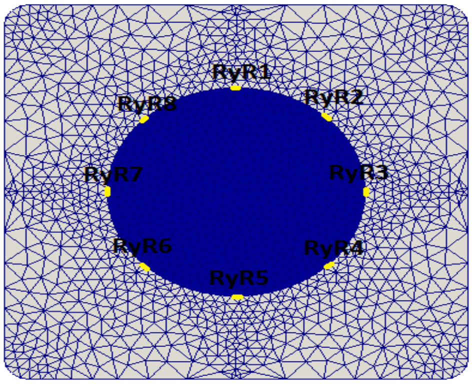

FIGURE 2 This figure shows the meshing used during the simulations.

and thus

$$\left(\sum_{i=1}^{5}\mathcal{P}_{i,n}^{2}+\mathcal{Q}_{1,n}^{2}\right)\leq\left(\frac{\tau C_{60}}{C_{62}}\right)^{n}\left(\sum_{i=1}^{5}\mathcal{P}_{i,N}^{2}+\mathcal{Q}_{1,N}^{2}\right)+\sum_{k=n}^{N-1}\left(\frac{\tau C_{60}}{C_{62}}\right)^{k-1}\left(\frac{C_{61}}{C_{62}}\right)^{k}||\mathcal{I}_{*}^{n}-\mathcal{I}^{n}||_{L^{2}(\Gamma_{r})}^{2},$$

for some constants $C_{60}, C_{61}, C_{62} > 0$. ■

6 | NUMERICAL SIMULATIONS

This section is devoted to the numerical simulation of optimal control model (3.1). In our numerical tests, we illustrate the regulation of ion channels under abnormal buffers behavior inside the sarcoplasmic domain. First, we give an explicit presentation of the algorithm used in the optimization procedure. Next, we give a comparison between the normal cell and the anomalous cell due to buffers irregularity. By applying the optimal control model, we recover the optimal conductivity, and we re-compare the simulation output with the normal cell and the regularized one. Note that the convenient way to deduce the cell regular functionality is the dynamic of calcium inside the cytosolic domain. Recall that the calcium's diffusion depends on its total mass. Therefore, we choose (see e.g.[28,11,12]):

$$A_1(r)=\epsilon+D_1\frac{r}{1+r},\qquad B_1(r)=\epsilon+D_2\frac{r}{1+r}\qquad\text{for } r\in\mathbb{R}.$$

In this case, we consider that the calcium ions diffuse rapidly if the total concentration increases in cytosolic (resp. sarcoplasmic) domain to get closer to its maximum value D_1 (resp. D_2). Moreover, we consider that the opening of RyR_1 happens at $t = 1e{-}3$. The other ion channels (see Figure 2) open when calcium concentration around them reaches $0.1\mu M$. The period opening of each ionic channel is $T_{opening} = 8e-3$. Moreover, after closing, the ryanodine receptors sensitivity to the calcium ions decreases for a period of time.

Figure 2 show the meshing of simple cardiac cell geometry. Herein, RyR_i is the location of ion channels for $i = 1, ..., 8$. We choose the time step to be $\tau = 1e - 3s$. Now, we present the calcium dynamics in a healthy cell comparing with a pathological case resulting from CSQN mutation in an abnormal cell. In our simulations we consider a slight endoplasmic flux of calcium the L-type channel. This influx occurs periodically in order to launch the CICR process repeatedly. Here, we investigate the nonlocal effect on the cardiac cell sensitivity under CSQN perturbation. Next, we study the difference between a local diffusion and a nonlocal diffusion.

In Figures 3 , we show the average calcium fluctuation with respect to the nonlocal diffusion. In the local case, we observe a similar profile to the calcium fluctuation shown in[29]. The nonlocal diffusion shows a closer dynamic to the local case in the context of a regular CSQN buffering. In an irregular CSQN profile, the linear calcium fluctuation keeps showing a periodic and responsive to stimulus behavior with higher calcium concentration. Various observations indicate that the irregularity of the CSQN produces a break-down of periodicity of calcium profile along with spontaneous calcium release which leads to tachycardia. The loss of periodicity is recovered using the nonlocal diffusion (see Figure 3). Due to the slow diffusion, the calcium stay at higher concentration even after the closing time of ryanodin receptors. This provokes an early spontaneous

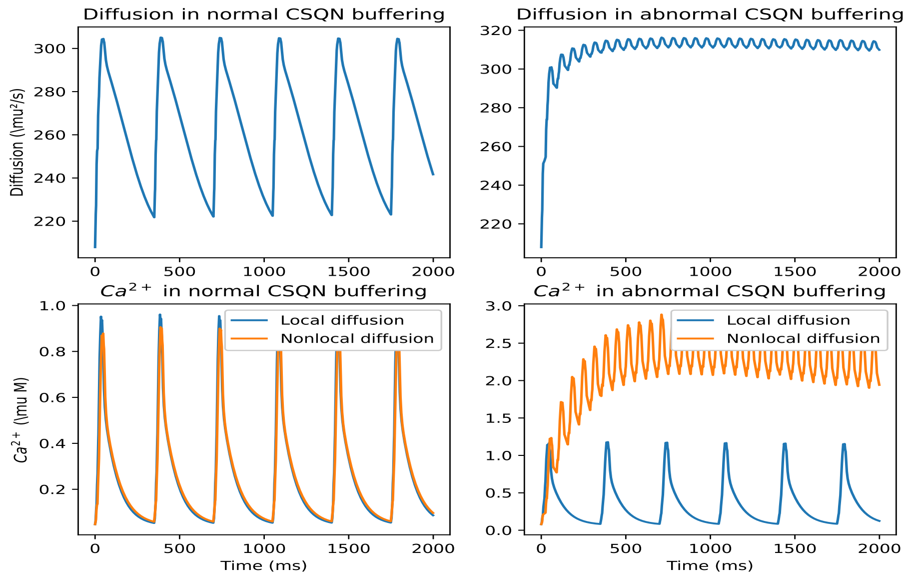

FIGURE 3 Comparison between local and nonlocal diffusion in terms of calcium average in a cardiac cell.

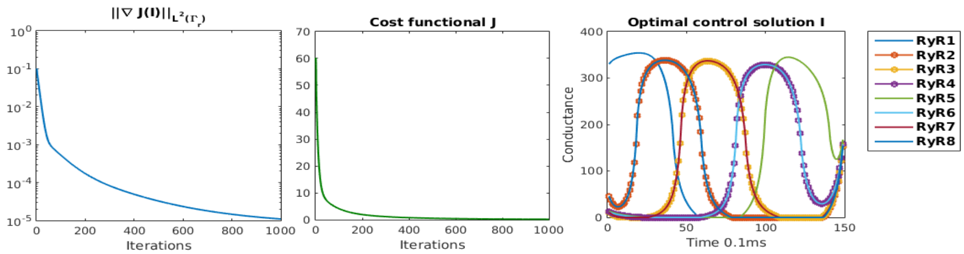

FIGURE 4 Gradient of cost functional, cost functional and optimal control solution (the regularization parameters are $\alpha_1 = 0.1$, $\alpha_2 = 0.1$ and $\alpha_3 = 10^{-4}$).

release of several high frequent calcium waves. A similar phenomenon is shown in [29,30].

Next, we present the solving procedure of the optimization problem in (3.1). We consider the implicit Euler discretization to the adjoint and direct problem. At each time step, we solve the inducing stationary problem in a finite element framework. In the following algorithm we give a sketch on the solving strategy to the optimal control problem:
We now present the ability of our optimal control procedure to recover the healthy calcium profile based on perturbed initial data. First, we start by running the direct problem under abnormal calcium initial data. Second, we recover the healthy calcium profile based on experimental data using direct problem. This calcium profile will be considered as a desired state. We run our optimal control procedure under abnormal initial data to recover the desired state. All used data will be presented in Table 1 below. The following figure depicts the optimal control solution with $\|\nabla J(\mathcal{I})\|$ and $J(\mathcal{I})$ evolution through gradient descent iterations. In Figure 4 , the L^2-norm of the gradient decreases during the gradient descent algorithm. Similarly, in the middle panel of Figure 4 , we observe that the cost functional decreases to its stability near to zero. This proves that we recover the regular profile of calcium under the anomalous initial condition. As a result, we get in the right hand side of Figure 4 the conductance behavior of Ryanodine receptors.

In Figure 5 , we observe a slower propagation of calcium and slower opening of ryanodine receptor in the abnormal case comparing with the regular case. The anomalous propagation of calcium fluctuation in the uncontrolled cell is handled using

Algorithm 1 The solving strategy of the optimal control problem.

Input: computational domains Ω_1, Ω_2, The ion channels borders Γ_r, Γ_m and Γ_p
;
Input: $\mathbf{u}_0$, $\mathbf{v}_0$, u_d, $err \leftarrow 1$
Initialize: $\mathcal{I}^0, \alpha, tol, k \leftarrow 0$

while $||\nabla J(\mathcal{I}^k)|| > tol$ **do**
  for $t = t^1, ..., t^{final}$ **do**
    Giving $\mathcal{I}^k$ Compute $\mathbf{u}^h$ and $\mathbf{v}^h$ from the direct problem 1.1;
  end for
  Compute the cost functional $J(u_1^h, \mathcal{I}^k)$
  for $t = t^{final}, ..., t^0$ **do**
    Giving $\mathcal{I}^k$, $\mathbf{u}^h$ and $\mathbf{v}^h$, compute $\mathbf{q}^h$ and $\mathbf{v}^h$ by solving the adjoint problem (3.5);
  end for
  Compute the gradient $g_{k+1} = \nabla J(\mathcal{I}^k, u_1^h, v_1^h, p_1^h, q_1^h)$;
  Compute $y_k = I^{k+1} - \mathcal{I}^k$
  Compute step length α_k
  Update the values of $\mathcal{I}$ $\quad \mathcal{I}^{k+1} = \mathcal{I}^k + \alpha_k d_k$;
  Compute $\beta^k = (y_k - 2d_k \dfrac{||y_k||^2}{d_k^T y_k})^T \dfrac{\mathcal{I}^{k+1}}{d_k^T y_k}$
  $d_k = -\mathcal{I}^k + \beta_k d_{k-1}$;
  Update the direction $d_k = \mathcal{I}^k + \beta^k d_{k-1}$
  $k \leftarrow k + 1$
end while

Diffusion coefficient	D_1	D_2	$\mathcal{A}_2$	$\mathcal{A}_3$	$\mathcal{A}_4$
Value	220	73.3	140	25	42

Off rates	k_1^{off}	k_2^{off}	k_3^{off}	k_4^{off}	k_5^{off}
Value	45	0.238	0.110	0.0196	0.065

Total concentration	B_1	B_2	B_3	B_4	B_5
Value	140	25	42	42	42

On rates	k_1^{on}	k_2^{on}	k_3^{on}	k_4^{on}	k_5^{on}
Value	255	34	110	32.7	102

TABLE 1 Total concentration, reaction and diffusion rates in a cardiac cell. The units are presented as follows: The diffusion coefficient (D_l) unit is e+3 $nm^2 ms^{-1}$ and the total mass unit (B_i) is μM. The k_i^{on} unit is e-3 $ms^{-1}\mu m^{-1}$ and k_i^{off} unit is ms^{-1}.

Algorithm 1. Therefore, we recover a healthy fluctuation as shown in the right column of Figure 5 acting only on the ryanodine receptor conductance. The calcium current through the ryanodine receptor is corrected to block or enhance the calcium flux in cytosolic domain (in order to achieve the desired state). Figure 4 shows the decreasing gradient to zero through descent gradient iterations. Furthermore, it depicts the decreasing behavior of the cost functional. This confirms that the optimal control solution (the optimal conductance of RyR) is well computed to reach the desired state.

The next test is dedicated to a pathological type namely catecholaminergic polymorphic ventricular tachycardia. Which is linked in some cases to irregular mutation in calsequestrin (CASQ2) genes (see[2] for more information). Herein, we investigate different scenarios in terms of total concentration, interaction rate and initial condition. We reproduce the calcium profile using abnormal CSQN parameters. Moreover, we look for the best RyR characteristics to reproduce the normal profile. This could regulate the pathological buffering by designing the best ion channels to handle cellular dysfunction.

Now, we consider that the desired state (healthy calcium fluctuation) is given by the direct system under regular parameters (see Table 1). In the optimal control problem, we use abnormal interaction rates of CSQN with calcium. This change of interaction parameter causes abnormal calcium fluctuation. We act on RyR conductance $\mathcal{I}$ to reform the calcium fluctuation. In Figure 6 , we plot the calcium fluctuation in cytosolic domain in three cases:

- Normal cell: We consider experimental parameters as shown in Table 1 .

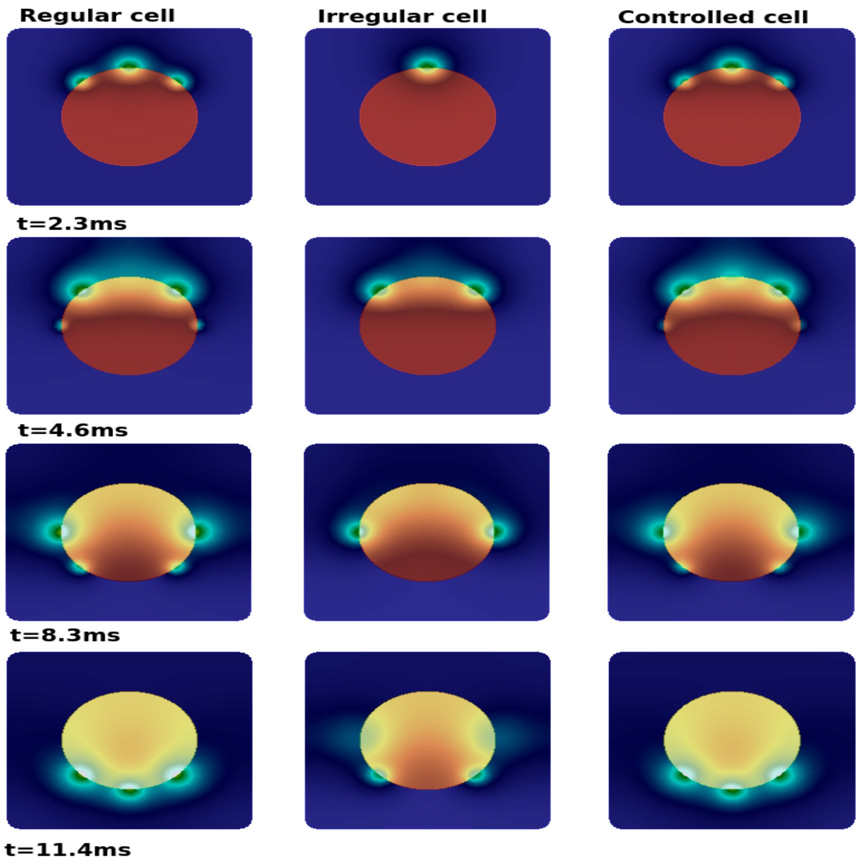

FIGURE 5 This figure shows the evolution of calcium in three cases. The left column shows the calcium dynamics in a regular states. The middle one shows the abnormal calcium profile. The right column presents the recovered calcium profile.

- Abnormal cell: We consider the same parameter considered in the abnormal cell except for $k_5^{on} = 10.2$ and $k_5^{off} = 65$[29].
- Controlled cell: The controlled cell is an abnormal cell under optimal Ryanodine receptor conductance computed using Algorithme 1.

In the abnormal cell, and due to CSQN's low binding capacity, the calcium concentration rises in sarcoplasmic reticulum which lead to high Ca^{2+} potential in the SR. This leads to an increased flux comparing to the normal cell. The Ca^{2+} flux increases Ca^{2+} concentration in cytosolic media which induces an early opening of neighbors ionic channel. This made the CICR shorter and consequently affects the contraction activity. On the microscopical scale this can be considered a CPVT syndromes[2]. Controlled cell shows a similar calcium fluctuation in cytosolic domain by acting only on the conductance of the passive ionic channel described in Figure 7 . Note that the opening time of ionic gates in the controlled cell shows identical behavior to the normal cell. Moreover, the cost functional shows smaller values at the end of the iterative process which means that the calcium in the controlled cell is much closer to the regular one.

In the last test, we present the numerical experiments related to error analysis of the control, state and adjoint variables. Here, we consider a simplified version of the original problem.

$$\min(J(\mathcal{I})) = \min\left\{ \frac{\alpha_1}{2} \iint_{\Omega_1} |u - u_d|^2 \, dx \, dt + \frac{\alpha_2}{2} \iint_{\Omega_2} |v - v_d|^2 \, dx \, dt + \frac{\alpha_3}{2} \iint_{\Gamma_{r,T}} |\mathcal{I}|^2 \, dx \, dt \right\} \tag{6.1}$$

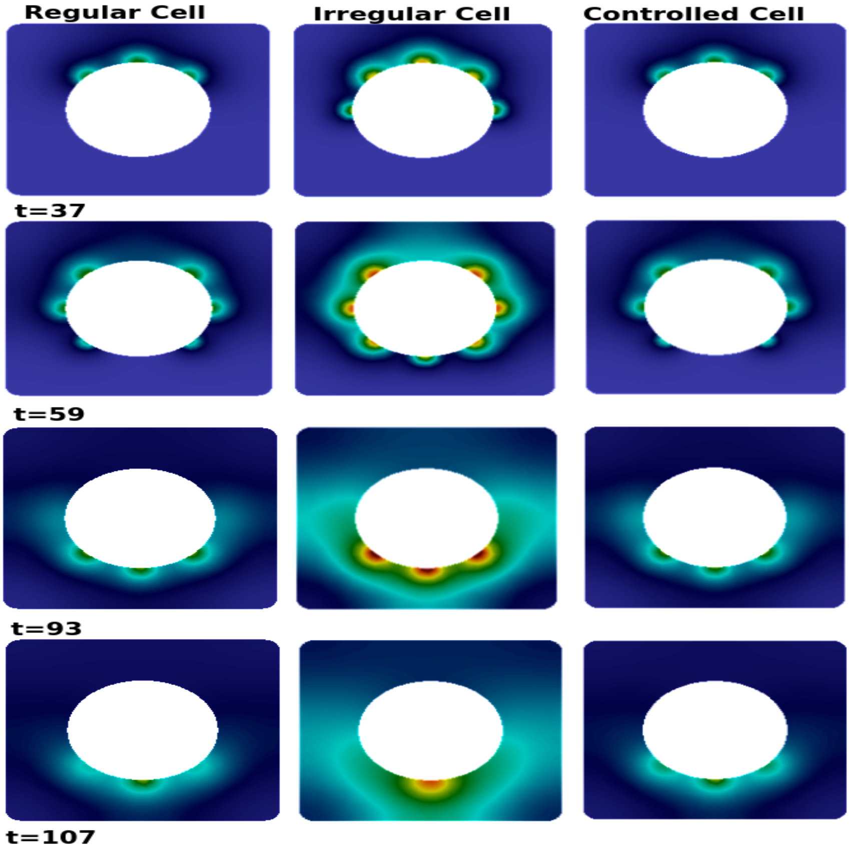

FIGURE 6 The graphical comparison between the solution with pathological parameters, normal parameters and optimal conductance.

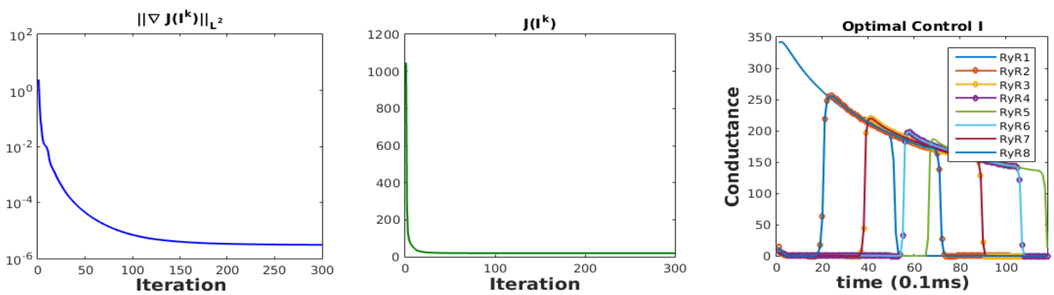

FIGURE 7 Gradient of cost functional, cost functional and optimal control solution (the regularization parameters are $\alpha_1 = 0.1$, $\alpha_2 = 0$ and $\alpha_3 = 10^{-4}$).

$$\begin{cases} \textbf{Direct problem:} \\ \partial_t u - D_1\left(\displaystyle\int_{\Omega_1} u\,dx\,dy\right)\Delta u = f \text{ in } \Omega_{1,T}, \qquad \text{and} \qquad \partial_t v - D_2\left(\displaystyle\int_{\Omega_2} v\,dx\,dy\right)\Delta v = g \text{ in } \Omega_{2,T}, \\ D_1 \nabla u \cdot \eta_1 = -\mathcal{I}(v-u) \text{ on } \Gamma_{r,T}, \qquad \text{and} \qquad D_2 \nabla v \cdot \eta_2 = \gamma \mathcal{I}(v-u) \text{ on } \Gamma_{r,T}, \end{cases} \tag{6.2}$$

Mesh h	$\mathcal{I}_h - \mathcal{I}$ $L^2(0,T;L^2(\Gamma_r))$	$U_h - U$ $L^2(0,T;L^2(\Omega_1 \times \Omega_2))$	$P_h - P$ $L^2(0,T;L^2(\Omega_1 \times \Omega_2))$
5	0.000986512	0.0271875	0.0269102
10	0.000343097	0.00662593	0.006575
15	0.000219199	0.00308125	0.00311252
20	0.000176917	0.00211467	0.00219682
25	0.000157959	0.00183901	0.00194549

TABLE 2 The convergence table for the nonlocal system

Mesh h	$\mathcal{I}_h - \mathcal{I}$ $L^2(0,T;L^2(\Gamma_r))$	$U_h - U$ $L^\infty(0,T;L^2(\Omega_1 \times \Omega_2))$	$P_h - P$ $L^\infty(0,T;L^2(\Omega_1 \times \Omega_2))$
5	0.000986512	0.0463046	0.0460935
10	0.000343097	0.0108027	0.0107176
15	0.000219199	0.00507255	0.00506748
20	0.000176917	0.00388362	0.00394111
25	0.000157959	0.00372577	0.0038133

TABLE 3 The convergence table for the nonlocal system

$$\begin{cases} \textbf{Adjoint problem:} \\ -\partial_t p - D_1\left(\int\limits_{\Omega_1} u\,dx\,dy\right)\Delta p + D_1'\left(\int\limits_{\Omega_1} u\,dx\,dy\right)\int\limits_{\Omega_1} \nabla u \cdot \nabla p\,dx\,dy = \tilde{f} \text{ in } \Omega_{1,T}, \\ -\partial_t q - D_2\left(\int\limits_{\Omega_2} v\,dx\,dy\right)\Delta q + D_2'\left(\int\limits_{\Omega_2} v\,dx\,dy\right)\int\limits_{\Omega_2} \nabla v \cdot \nabla q\,dx\,dy = \tilde{g} \text{ in } \Omega_{2,T}, \\ D_1\nabla q \cdot \eta_1 = -\mathcal{I}(q-p) \text{ on } \Gamma_{r,T}, \qquad \text{and} \qquad D_2\nabla p \cdot \eta_2 = \gamma\mathcal{I}(q-p) \text{ on } \Gamma_{r,T}. \end{cases} \tag{6.3}$$

In our simulation, we are interested only in the dynamics of calcium between Ω_1 and Ω_2. We consider a constant diffusion coefficient $D_1(r) = 2D_2(r) = 2$. Note that $D_1'(r) = 2D_2'(r) = 0$. Let $\Omega_1 = [\frac{\pi}{4}, \frac{3\pi}{4}] \times [-\pi, 0]$ and $\Omega_2 = [\frac{\pi}{4}, \frac{3\pi}{4}] \times [0, \pi]$. In this case, the exact solutions are given by:

$$\begin{cases} u(t,x,y,z) = t sin(x)\left(1 + e^{t(T-t)sin^2(x)\frac{(D_1-D_2)^3}{D_1 D_2^3} y}\right) \quad \text{and} \quad v(t,x,y,z) = t sin(x)\left(1 + \frac{D_1}{D_2} e^{t(T-t)sin^2(x)\frac{(D_1-D_2)^3}{D_1 D_2^3} y}\right), \\ p(t,x,y,z) = (T-t) sin(x)\left(1 + e^{t(T-t)sin^2(x)\frac{(D_1-D_2)^3}{D_1 D_2^3} y}\right) \quad \text{and} \quad q(t,x,y,z) = (T-t) sin(x)\left(1 + \frac{D_1}{D_2} e^{t(T-t)sin^2(x)\frac{(D_1-D_2)^3}{D_1 D_2^3} y}\right), \end{cases}$$

and the optimal control solution is stated as follow

$$\mathcal{I}(t,x) = t(t-T) sin^2(x)\left(\frac{D_1 - D_2}{D_2}\right)^2. \tag{6.4}$$

In Table 2 , we present the resulting of the numerical error estimates to the direct and adjoint state solutions. Moreover, we have the following convergence table in $L^\infty(0,T;L^2(\Omega_1 \times \Omega_2))$

In the linear example, we depict the numerical error behavior of optimal control, direct and adjoint state solution in Figure 8 . The control shows a decreasing profile with respect to mesh refinement. As shown in Proposition 5.1, the numerical error estimates of direct and adjoint solutions show stability with respect to the control in $L^2(\Omega_{1,T} \times \Omega_{2,T})$.
Now, we consider the following domains $\Omega_1 = [0, \frac{\pi}{2}] \times [-2, 0]$ and $\Omega_2 = [0, \frac{\pi}{2}] \times [0, 2]$. Moreover, we consider the nonlocal diffusions $D_2(s) = D_1(s) = s$.

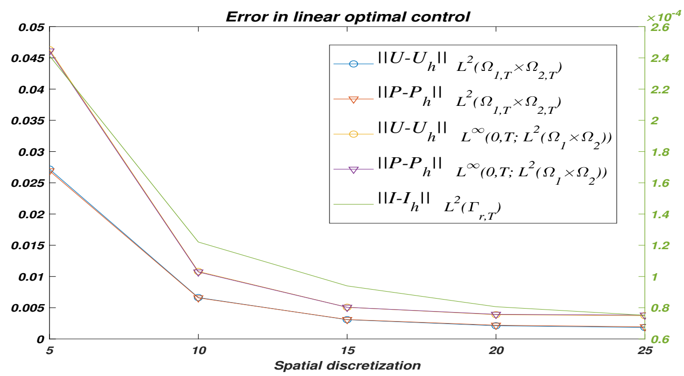

FIGURE 8 Error in linear case.

Mesh h	$\mathcal{I}_h - \mathcal{I}$ $L^2(0,T;L^2(\Gamma_r))$	$U_h - U$ $L^2(0,T;L^2(\Omega_1\times\Omega_2))$	$P_h - P$ $L^2(0,T;L^2(\Omega_1\times\Omega_2))$
5	0.000241354	0.00704769	0.0144253
10	0.000122063	0.00225455	0.00882685
15	9.39691e-05	0.00173168	0.00637899
20	8.06267e-05	0.0016516	0.00506445
25	7.51517e-05	0.001638	0.00425756

TABLE 4 The convergence table for the linear system

Mesh h	$\mathcal{I}_h - \mathcal{I}$ $L^2(0,T;L^2(\Gamma_r))$	$U_h - U$ $L^\infty(0,T;L^2(\Omega_1\times\Omega_2))$	$P_h - P$ $L^\infty(0,T;L^2(\Omega_1\times\Omega_2))$
5	0.000241354	0.0179967	0.0324155
10	0.000122063	0.00586534	0.0203745
15	9.39691e-05	0.00399715	0.0149876
20	8.06267e-05	0.00345623	0.0120445
25	7.51517e-05	0.00348877	0.0102094

TABLE 5 The convergence table for the linear system

Furthermore, the exact analytical solution of system (6.1)-(6.3) is given by:

$$\begin{cases} u(t,x,y,z) = t sin(x)\left(2 - \dfrac{(T-t)t\sin^2(x)(\gamma-1)^3}{\alpha_3\gamma^2}y\right) & \text{and } v(t,x,y,z) = t sin(x)\left(1+\dfrac{1}{\gamma} - \dfrac{(T-t)t\sin^2(x)(\gamma-1)^3}{\alpha_3\gamma^3}y\right), \\ p(t,x,y,z) = (T-t)sin(x)\left(2 - \dfrac{(T-t)t\sin^2(x)(\gamma-1)^3}{\alpha_3\gamma^2}y\right) & \text{and } q(t,x,y,z) = (T-t)sin(x)\left(1+\dfrac{1}{\gamma} - \dfrac{(T-t)t\sin^2(x)(\gamma-1)^3}{\alpha_3\gamma^3}y\right). \end{cases}$$

The optimal control solution is given by

$$\mathcal{I}(t,x) = t(t-T)sin^2(x)\left(\frac{\gamma-1}{\gamma\alpha_3}\right)^2. \tag{6.5}$$

Similarly to the linear case, experimental $L^2(0,T;L^2)$ numerical error estimates is shown in Table 4 as follow Moreover, we have the following convergence table in $L^\infty(0,T;L^2(\Omega_1\times\Omega_2))$ In Figure 9 , we present the numerical error estimates of the nonlocal optimal control computed by the proposed numerical approach. Compared to linear case, the nonlocal direct and adjoint state solutions present slower convergences in $L^\infty(L^2)$. However, the stability result shown in Proposition 5.1 holds for the nonlocal numerical experiment. The numerical direct and adjoint error estimates are still controlled by the optimal control.

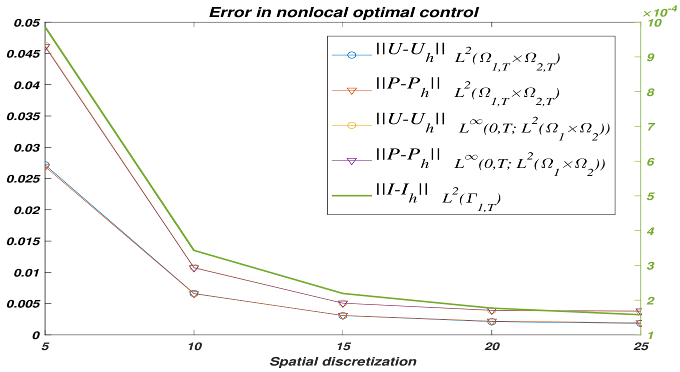

FIGURE 9 Error in nonlocal case.

CONCLUSION

In this paper, we established an optimal control to a nonlocal reaction-diffusion system modeling the calcium fluctuation in a cardiac cell. Herein, we considered the control only on the subset of a common boundary between cytoplasm and sarcoplasmic reticulum membranes. We derived the first order optimality condition of the associated minimization problem and we studied the existence and uniqueness of the adjoint solution. To approximate numerically the nonlocal optimal control solution, we proposed a finite element discretization for adjoint and direct systems. We also studied the stability results of the approximated direct and adjoint solutions with respect to the control. Based on real observations, a various numerical simulations show that the nonlocal model is more realistic than the local classical model. Using the proposed transmission optimal control approach, we developed a technique to reform the correct calcium fluctuation (from abnormal calcium) under mutant CSQN buffering acting only on RyR conductance. In our approach, we have focused on the abnormalities related to the buffering of CSQN and ionic channel behavior. More investigations can be driven including ATP and calcium buffering provided by abnormal mitochondrial function[31].

In the future work, we will study the numerical convergence of the present model with stochastic behavior of the ionic channels.

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CONFLICT OF INTEREST

This work does not have any conflicts of interest.

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