

NUMERICAL ANALYSIS OF FINITE ELEMENT METHODS FOR THE CARDIAC EXTRACELLULAR-MEMBRANE-INTRACELLULAR MODEL: STEKLOV–POINCARÉ OPERATOR AND SPATIAL ERROR ESTIMATES

DIANE FOKOUÉ AND YVES BOURGAULT*

Abstract. The extracellular-membrane-intracellular (EMI) model consists in a set of Poisson equations in two adjacent domains, coupled on interfaces with nonlinear transmission conditions involving a system of ODEs. The unusual coupling of PDEs and ODEs on the boundary makes the EMI models challenging to solve numerically. In this paper, we reformulate the problem on the interface using a Steklov–Poincaré operator. We then discretize the model in space using a finite element method (FEM). We prove the existence of a semi-discrete solution using a reformulation as an ODE system on the interface. We derive stability and error estimates for the FEM. Finally, we propose a manufactured solution and use it to perform numerical tests. The order of convergence of the numerical method agrees with what is expected on the basis of the theoretical analysis of the convergence.

Mathematics Subject Classification. 65M12, 65M15, 65M60, 35K57, 92C37.

Received July 13, 2022. Accepted June 5, 2023.

1. INTRODUCTION

The electrical activity of the heart is a well-studied process. Several mathematical models are available for the simulation of the cardiac electrical activity at various scales. For instance, the bidomain model that is based on a homogenization process represents the cardiac action potential at the organ level, see *e.g.* [16, 31, 32, 46, 48]. For studying propagation between a smaller group of myocytes, the extracellular-membrane-intracellular (EMI) model is based on an explicit representation of individual cells. The cardiac tissue can be viewed as two separate domains: the intracellular and extracellular domains, Ω_i and Ω_e , respectively, the cellular membranes Γ are represented as separate geometrical spaces [15, 39, 45, 49, 50, 52]. The EMI model is of increasing importance, since it is well suited to study the impact of some types of intercellular couplings and connections on the cardiac action potential (AP).

In the literature, several authors have studied and used the EMI model. Some of them consider the flow of current through cardiomyocytes using an analogy with electrical circuits. Sperelakis *et al.* [34, 41, 42] used this approach to investigate the mechanism for transmission of excitation from one cell to the next within cardiac

Keywords and phrases. Extracellular-membrane-intracellular model, Numerical methods, Manufactured solution, Steklov–Poincaré operator, Semi-implicit backward differentiation formula, Cardiac electrophysiology.

Department of Mathematics and Statistics, University of Ottawa, Ottawa, Canada.

*Corresponding author: ybourg@uottawa.ca

tissue by considering a circuit diagram along a strand of cells. More recently, Keener *et al.* [9, 23–25] followed the same framework to study the electrical coupling of cardiac cells in the absence of gap junctions.

In contrast, several other authors consider a EMI model based on potential equations [5, 15, 19, 21, 39, 45, 50–52]. Tveito *et al.* [19] derived the bidomain model from the cell-based model and highlighted both similarities and differences between the models. To study at the microscopic level the relationship between tissue morphology and the propagation of the depolarization wave, and to investigate the role of the distributions of the extracellular space around cells on the conduction velocity, Stinstra *et al.* [43–45] introduced a 3D model of cardiac tissue. Spiteri *et al.* [12] used the cell-based model to simulate the effects of a cardiac condition called long QT syndrome (LQTS). They compared simulations from data from healthy cells, cells that exhibit the syndrome, and cells that have been treated with a drug to restore healthy heart function. Veneroni [52] proved the existence of a solution for the EMI model with two choices for the ionic current, that are the classical Hodgkin–Huxley model [18] and the Phase-I Luo–Rudy model [28]. In the same vein, Franzone and Savaré [15] derive, adapting the tools of abstract evolution equations in Hilbert spaces, existence, uniqueness and some regularity results for the model. They consider the FitzHugh–Nagumo model as a membrane model for ionic currents. Mori *et al.* [30] used the electrodiffusion model [17] to study the effect of gap junctions on the propagation of cardiac action potential.

From the mathematical standpoint, the EMI model consists in a set of Poisson equations in two adjacent domains, coupled on interfaces with nonlinear transmission conditions involving a system of ODEs. The unusual coupling of PDEs and ODEs on the boundary makes the EMI models challenging to solve numerically. Few numerical methods have been proposed in the literature for the EMI model [2, 5, 12, 19–22, 50, 51]. Agudelo-Toro and Neef [2] presented numerical methods allowing detailed simulations of the electric activity of excitable cells and their interaction with extracellular potentials. They introduced an implicit time iteration scheme based on the Crank–Nicolson method and studied the numerical stability of the method. To assess the computational challenges of the EMI modeling framework, Tveito *et al.* [50] solved the model using a finite difference method (FDM) and two types of mixed finite element methods (FEM) [6, 36]. In addition, they assess the accuracy of these numerical methods. Bécue [5] studied in his Ph.D. thesis the impact of the presence and absence of different gap junctions models on the propagation of the AP. He developed a computational model of AP propagation through hand-crafted two- and three-dimensional networks of cells. He discretized the model in time using the Forward Backward Euler scheme. Tveito *et al.* [22] described the spatial operator splitting algorithm for splitting the model into separate equations. They outlined a finite difference discretization for the splitting approach and investigated the accuracy of the spatial splitting method.

In all the reviewed literature, few numerical methods are proposed and tested with simple test cases. The numerical analysis (*e.g.*, stability, error estimates) is not yet available for any discretization method applied to the EMI model. The goal of our paper is to perform the numerical analysis of a finite element method for the EMI model. In Section 2, we reformulate the problem on the interface Γ using a Steklov–Poincaré operator. We introduce the Steklov–Poincaré operator and show that it is well-defined. We write two variational formulations of the problem and show that these are equivalent. In Section 3, we discretize the model in space using finite element methods (FEM). We reformulate the discrete problem using the Steklov–Poincaré operator. In Section 4, we prove the existence of semi-discrete solution using formulation as an ODE system on the interface Γ . We derive stability of the semi-discrete solution and error estimates for the FEM. In Section 7, we perform numerical tests with a manufactured solution to verify that the order of convergence of the numerical method agrees with what is expected on the basis of the theoretical analysis of the convergence. Section 7 concludes the paper.

2. ANALYSIS OF THE CONTINUOUS PROBLEM

2.1. The cardiac EMI model

We consider the EMI model [15, 52]

$$-\nabla \cdot (\sigma_i \nabla u_i) = I_{i,\text{stim}} \quad \text{in } \Omega_i, \quad (1)$$

$$-\nabla \cdot (\sigma_e \nabla u_e) = I_{e,\text{stim}} \quad \text{in } \Omega_e, \tag{2}$$

$$I_m := C_m \frac{\partial v}{\partial t} + f(v, w) \quad \text{on } \Gamma, \tag{3}$$

$$\sigma_e \nabla u_e \cdot n_e = -\sigma_i \nabla u_i \cdot n_i = I_m \quad \text{on } \Gamma, \tag{4}$$

$$[u] = u_i - u_e = v \quad \text{on } \Gamma, \tag{5}$$

$$\sigma_e \nabla u_e \cdot n_e = g_e \quad \text{on } \Gamma_e, \tag{6}$$

where $\Omega = \Omega_i \cup \Omega_e \cup \Gamma \subset \mathbb{R}^q$, $q = 2, 3$, $I_{i,\text{stim}}$ and $I_{e,\text{stim}}$ are the given stimulation currents applied on Ω_i and Ω_e , respectively, f represents the ionic current through the cellular membrane Γ and g_e is a given function on $\Gamma_e = \partial\Omega_e \setminus \Gamma$. The model is coupled with the following system of ordinary differential equations describing the electrochemical process behind the opening/closing of the ionic channels through the membrane of the cell

$$\frac{\partial w}{\partial t} = g(v, w) \quad \text{on } \Gamma, \tag{7}$$

where g models the dynamics of the gating variable, w . The following initial conditions are needed to close the system:

$$v(0) = v_0, \quad w(0) = w_0 \quad \text{on } \Gamma. \tag{8}$$

For the sake of simplicity, we assume below that $f = f(v)$ and $g = g(w)$ are independent from the gating variable w and membrane potential v , respectively. There are no essential difficulties in taking $f = f(v, w)$ and $g = g(v, w)$, only appropriate assumptions must be made about the dependance of f and g on the variables w and v , respectively, see [5]. We take $C_m = 1$.

2.2. Variational formulation

We define a functional framework within which we derive the variational formulation of the problem (1)–(6). We set

$$u(x) = \begin{cases} u_i(x), & x \in \Omega_i, \\ u_e(x), & x \in \Omega_e, \end{cases} \quad \sigma(x) = \begin{cases} \sigma_i(x), & x \in \Omega_i, \\ \sigma_e(x), & x \in \Omega_e, \end{cases} \quad I_{\text{stim}}(x) = \begin{cases} I_{i,\text{stim}}(x), & x \in \Omega_i, \\ I_{e,\text{stim}}(x), & x \in \Omega_e. \end{cases}$$

The intracellular and extracellular conductivities, $\sigma_i(x)$ and $\sigma_e(x)$, are symmetric and positive definite matrices, respectively. They satisfy

$$m|y|^2 < y^T \sigma_{i,e}(x)y < M|y|^2 \quad \forall y \in \mathbb{R}^q, \quad \forall x \in \Omega_{i,e}, \tag{9}$$

for some constants $M > m > 0$, $q = 2, 3$.

We define the space

$$W = \left\{ u \in L^2(\Omega) : u|_{\Omega_i} \in H^1(\Omega_i), u|_{\Omega_e} \in H^1(\Omega_e), \int_{\Omega_e} u_e \, dx = 0 \right\}, \tag{10}$$

equipped with the norm:

$$\|u\|_W = \left(\|u\|_{H^1(\Omega_i)}^2 + \|u\|_{H^1(\Omega_e)}^2 \right)^{\frac{1}{2}}.$$

In the paper, $\|\cdot\|_{H^1(\Omega_i)}$, $\|\cdot\|_{L^2(\Omega_i)}$, $\|\cdot\|_{L^2(\Gamma)}$, $\|\cdot\|_{H^{\frac{1}{2}}(\Gamma)}$, $\|\cdot\|_{H^{-\frac{1}{2}}(\Gamma)}$, etc, stand for the usual norm associated to the space given in each respective subscript. Then, W is a Hilbert space. Following ([52], Thm. 1.1), we assume that (1)–(6) admits a unique solution with

$$u \in L^2(0, T; W), \quad v = [u] \in H^1(0, T; L^2(\Gamma)) \cap L^2\left(0, T; H^{\frac{1}{2}}(\Gamma)\right), \quad I_{\text{stim}} \in L^2(0, T; L^2(\Omega)), \tag{11}$$

$$\sigma \in L^\infty(\Omega), \quad v_0 \in L^2(\Gamma), \quad w_0 \in L^2(\Gamma), \quad g_e \in L^2(0, T; H^{-\frac{1}{2}}(\Gamma_e)).$$

Multiplying the PDEs (1) and (2) by a test function $\varphi \in W$, integrating over Ω , and using the Green formula yield

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi_i + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi_e + \int_{\Gamma} \frac{\partial [u]}{\partial t} [\varphi] + \int_{\Gamma} f([u])[\varphi] = \int_{\Omega} I_{stim} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)}, \quad (12)$$

for a.e. $t \in [0, T]$, where $[u] = u|_{\Omega_i} - u|_{\Omega_e} = u_i - u_e$, $[\varphi] = \varphi|_{\Omega_i} - \varphi|_{\Omega_e} = \varphi_i - \varphi_e$ and $\frac{\partial [u]}{\partial t}$ is the weak derivative of $[u]$ in $\mathcal{D}'(0, T)$.

2.3. Reformulation of the continuous problem using the Steklov–Poincaré operator

The difficulty of proving the existence and uniqueness of the solution of (12) comes from the time derivative term over Γ . We will reformulate the problem (12) into a variational formulation defined only on Γ . To do this, we will use the Steklov–Poincaré operator which links the potentials u_i and u_e with the transmembrane potential v . As such, we split (1)–(7) into two coupled problems:

$$-\nabla \cdot (\sigma_i \nabla u_i) = I_{i,stim} \quad \text{in } \mathcal{D}'(\Omega_i), \quad (13)$$

$$-\nabla \cdot (\sigma_e \nabla u_e) = I_{e,stim} \quad \text{in } \mathcal{D}'(\Omega_e), \quad (14)$$

$$\sigma_e \nabla u_e \cdot n_e = -\sigma_i \nabla u_i \cdot n_i \quad \text{in } H^{-\frac{1}{2}}(\Gamma), \quad (15)$$

$$\sigma_e \nabla u_e \cdot n_e = g_e \quad \text{in } H^{-\frac{1}{2}}(\Gamma_e), \quad (16)$$

$$[u] = u_i - u_e = v, \quad \text{in } H^{\frac{1}{2}}(\Gamma) \quad (17)$$

$$\int_{\Omega_e} u_e \, dx = 0, \quad (18)$$

and

$$\frac{\partial v}{\partial t} + f(v) = -\sigma_i \nabla S_i(v) \cdot n_i \quad \text{on } \Gamma, \quad (19)$$

where S is an operator defined as follows:

$$S: H^{\frac{1}{2}}(\Gamma) \longrightarrow W \quad (20)$$

$$v \longmapsto S(v) := (S_i(v), S_e(v)) = u,$$

where $S_i(v) = u_i$, $S_e(v) = u_e$ and u the solution of the problem (13)–(18).

There exists a linear lifting operator, see *e.g.* [13, 35]

$$R_i: H^{\frac{1}{2}}(\Gamma) \longrightarrow H^1(\Omega_i), \quad (21)$$

$$\varphi \longmapsto R_i(\varphi),$$

such that $R_i(\varphi)|_{\Gamma} = \varphi$ for all $\varphi \in H^{\frac{1}{2}}(\Gamma)$ and

$$\|R_i(\varphi)\|_{H^1(\Omega_i)} \leq C \|\varphi\|_{H^{\frac{1}{2}}(\Gamma)}. \quad (22)$$

For a.e. $t \in]0, T[$, fix $v(\cdot, t) \in H^{\frac{1}{2}}(\Gamma)$ and define $R_i(v)$ a lifting of $v(\cdot, t)$ in $H^1(\Omega_i)$ as follows:

$$u_v = \begin{cases} R_i(v) & \text{in } \Omega_i, \\ 0 & \text{in } \Omega_e, \\ v & \text{on } \Gamma. \end{cases} \quad (23)$$

Define

$$W(v) = \left\{ u \in L^2(\Omega) : u|_{\Omega_i} \in H^1(\Omega_i), u|_{\Omega_e} \in H^1(\Omega_e), [u]|_{\Gamma} = v, \int_{\Omega_e} u_e \, dx = 0 \right\},$$

where $[u]_{|\Gamma} = u_i - u_e$ on Γ . Then $W(v) \neq \emptyset$ since $u_v \in W(v)$. The space $W(v)$ can be written

$$W(v) = u_v + W(0).$$

Therefore, $W(v)$ is an affine space with vector space $W(0) \subset H^1(\Omega)$. The proposed variational formulation for (13)–(18) is:

$$\begin{cases} \text{Seek } u \in L^2(0, T; W(v)) \text{ such that, for a.e. } t \in]0, T[, \\ \int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi_i + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi_e = \int_{\Omega} I_{\text{stim}} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)}, \\ \text{for all } \varphi \in W(0). \end{cases} \tag{24}$$

To show existence and uniqueness of the solution, we must first reformulate (24) on a vector subspace of $H^1(\Omega)$ since it is defined on an affine subspace. We set $\tilde{u} = u - u_v \in W(0)$. The problem (24) becomes

$$\begin{cases} \text{Seek } \tilde{u} \in L^2(0, T; W(0)) \text{ such that, for a.e. } t \in]0, T[, \\ \int_{\Omega} \sigma \nabla \tilde{u} \cdot \nabla \varphi = \int_{\Omega} I_{\text{stim}} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)} - \int_{\Omega_i} \sigma \nabla u_v \cdot \nabla \varphi_i, \text{ for all } \varphi \in W(0). \end{cases} \tag{25}$$

Proposition 2.1. *Under the hypothesis that $I_{\text{stim}} \in L^2(0, T; L^2(\Omega))$ and $g_e \in L^2(0, T; L^2(\Gamma_e))$, the problem (25) has a unique solution.*

Proof. For a.e. $t \in]0, T[$, set

$$\begin{cases} a(\tilde{u}, \varphi) = \int_{\Omega} \sigma \nabla \tilde{u} \cdot \nabla \varphi. \\ l(\varphi) = \int_{\Omega} I_{\text{stim}} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)} - \int_{\Omega_i} \sigma \nabla u_v \cdot \nabla \varphi_i, \text{ for all } \varphi \in W(0). \end{cases} \tag{26}$$

We want to show that $a(\cdot, \cdot)$ and $l(\cdot)$ satisfy the conditions of the Lax-Milgram theorem. Obviously, $a(\cdot, \cdot)$ is a continuous bilinear form on $W(0) \times W(0)$ and $l(\cdot)$ is a linear form on $W(0)$. We show that:

(i) The bilinear form $a(\cdot, \cdot)$ is coercive on $W(0)$. The set $\Omega_e \subset \Omega$ is of non-zero measure. Define

$$\mathbb{E} = \left\{ u \in H^1(\Omega) : \frac{1}{\text{meas}(\Omega_e)} \int_{\Omega_e} u_e \, dx = 0 \right\}.$$

Then \mathbb{E} is a closed subspace of $H^1(\Omega)$ and there exists a constant C such that

$$C \|u\|_{H^1(\Omega)} \leq \|\nabla u\|_{L^2(\Omega)}, \quad \forall u \in \mathbb{E}, \tag{27}$$

thanks to the Poincaré–Friedrichs inequality, see ([13], [Lemma B.66]). Let $u \in W(0)$. Taking into account (27) we have

$$a(u, u) = \int_{\Omega} \sigma |\nabla u|^2 \geq \text{ess inf}_{x \in \Omega} \sigma \|\nabla u\|_{L^2(\Omega)}^2 \geq \nu \|u\|_{H^1(\Omega)}^2 = \nu \|u\|_W^2,$$

for some constants $\nu > 0$. It follows that the bilinear form $a(\cdot, \cdot)$ is coercive on $W(0)$.

(ii) The linear form $l(\cdot)$ is continuous on $W(0)$. Using Cauchy–Schwarz inequality, the continuity of the trace operators, and equations (22) and (23), we have

$$\begin{aligned} |l(\varphi)| &\leq C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{H^{-\frac{1}{2}}(\Gamma_e)}^2 + \|u_v\|_{L^2(\Omega_i)}^2 \right)^{\frac{1}{2}} \|\varphi\|_{1,\Omega} \\ &= C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{H^{-\frac{1}{2}}(\Gamma_e)}^2 + \|R_i(v)\|_{H^1(\Omega_i)}^2 \right)^{\frac{1}{2}} \|\varphi\|_{1,\Omega} \\ &= C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{H^{-\frac{1}{2}}(\Gamma_e)}^2 + \|v\|_{H^{\frac{1}{2}}(\Gamma)}^2 \right)^{\frac{1}{2}} \|\varphi\|_{1,\Omega}. \end{aligned}$$

For the sake of simplicity, $C > 0$ represents some constant that may change from one line to the next.

Therefore, the variational formulation problem (25) has a unique solution \tilde{u} thanks to the Lax-Milgram theorem. Moreover, the solution \tilde{u} satisfies:

$$\|\tilde{u}\|_W \leq C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{H^{-\frac{1}{2}}(\Gamma_e)}^2 + \|v\|_{H^{\frac{1}{2}}(\Gamma)}^2 \right)^{\frac{1}{2}}. \tag{28}$$

The solution exists and satisfies (28) for a.e. $t \in]0, T[$. Squaring this inequality and integrating on $]0, T[$ give the result. \square

Proposition 2.2. *Under the hypothesis that $I_{\text{stim}} \in L^2(0, T; L^2(\Omega))$, $g_e \in L^2(0, T; H^{-\frac{1}{2}}(\Gamma_e))$ and $v \in L^2(0, T; H^{\frac{1}{2}}(\Gamma))$, the problem (24) has a unique solution. Moreover, the solution u satisfies:*

$$\|u\|_{L^2(0, T; W)} \leq C \left(\|I_{\text{stim}}\|_{L^2(0, T; L^2(\Omega))} + \|g_e\|_{L^2(0, T; H^{-\frac{1}{2}}(\Gamma_e))} + \|v\|_{L^2(0, T; H^{\frac{1}{2}}(\Gamma))} \right). \tag{29}$$

Proof. From Proposition 2.1, there exists at least one solution $u = \tilde{u} + u_v \in W(v)$. We show that the solution u is unique and independent from the lifting function u_v . Take $u^1, u^2 \in W(v)$ two solutions of (24). Then $u^1 - u^2 \in W(0)$ since $[u^1 - u^2] = 0$ and is the solution of the problem

$$\int_{\Omega} \sigma \nabla(u^1 - u^2) \cdot \nabla \varphi = 0, \quad \forall \varphi \in W(0),$$

and from (28) we obtain $u^1 = u^2$. Therefore the problem (24) has a unique solution.

We have that

$$\left| \|u\|_W - \|u_v\|_{H^1(\Omega_i)} \right| \leq \|u - u_v\|_W = \|\tilde{u}\|_W.$$

It follows from (22) and (28) that, for a.e. $t \in]0, T[$,

$$\|u\|_W \leq \|\tilde{u}\|_W + \|u_v\|_{1, \Omega_i} \leq C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{H^{-\frac{1}{2}}(\Gamma_e)}^2 + \|v\|_{H^{\frac{1}{2}}(\Gamma)}^2 \right)^{\frac{1}{2}}.$$

We deduce that the problem (24) is well-posed and satisfies (29). \square

The next step consists of verifying that the solution of (24) is also a solution of (13)–(18) in the weak sense.

Proposition 2.3. *If u solves (24), then u solves the problem (13)–(18) for a.e. $t \in]0, T[$.*

Proof. Let $\varphi \in \mathcal{D}(\Omega)$, $\varphi = 0$ in Ω_e . Let u be a solution of the problem (24). Hence,

$$\langle -\nabla \cdot (\sigma \nabla u), \varphi \rangle_{\mathcal{D}'(\Omega_i), \mathcal{D}(\Omega_i)} = \langle \sigma \nabla u, \nabla \varphi \rangle_{\mathcal{D}'(\Omega_i), \mathcal{D}(\Omega_i)} = \int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi = \int_{\Omega_i} I_{i, \text{stim}} \varphi.$$

We deduce that $-\nabla \cdot (\sigma_i \nabla u_i) = I_{i, \text{stim}}$ in $\mathcal{D}'(\Omega_i)$ and (13) follows. Similarly, taking $\varphi \in \mathcal{D}(\Omega)$, $\varphi = 0$ in Ω_i we deduce (14). Let $\varphi \in \mathcal{D}(\bar{\Omega})$, $\varphi \neq 0$ on Γ_e , $\varphi = 0$ in Γ and $\varphi = 0$ in Ω_i . Green’s formula and problem (24) give,

$$-\int_{\Omega_e} \nabla \cdot (\sigma_e \nabla u_e) \varphi + \langle \sigma_e \nabla u_e \cdot n_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)} = \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi = \int_{\Omega_e} I_{e, \text{stim}} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)}.$$

It follows that

$$\langle \sigma_e \nabla u_e \cdot n_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)} = \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)},$$

thanks to (14). Thus $\sigma_e \nabla u_e \cdot n_e = g_e$ on $H^{-\frac{1}{2}}(\Gamma_e)$ which implies (16). We have

$$u \in W(v) \Rightarrow u_i - u_e = v \text{ on } \Gamma \text{ and } \int_{\Omega_e} u_e = 0 \Leftrightarrow (17) \text{ and } (18).$$

Let us take $\varphi \in \mathcal{D}(\Omega)$, $\varphi = 0$ on $\partial\Omega \setminus \Gamma$ and $\varphi \neq 0$ on Γ . From Green’s formula and problem (24) we have,

$$\begin{aligned} & - \int_{\Omega_i} \nabla \cdot (\sigma_i \nabla u_i) \varphi - \int_{\Omega_e} \nabla \cdot (\sigma_e \nabla u_e) \varphi + \langle \sigma_e \nabla u_e \cdot n_e + \sigma_i \nabla u_i \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} \\ & = \int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi = \int_{\Omega} I_{\text{stim}} \varphi. \end{aligned}$$

This implies that for $\varphi \in W$,

$$\langle \sigma_e \nabla u_e \cdot n_e + \sigma_i \nabla u_i \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = 0 \implies \sigma_e \nabla u_e \cdot n_e = -\sigma_i \nabla u_i \cdot n_i \text{ on } H^{-\frac{1}{2}}(\Gamma).$$

Thus, (15) holds. Therefore the problem (24) is equivalent to the transmission problem (13)–(18). □

We are now interested in the problem (19). Let u be a solution of the problem (24). The variational formulation for (19) reads: find $v \in H^1(0, T; L^2(\Gamma)) \cap L^2(0, T; H^{\frac{1}{2}}(\Gamma))$ such that

$$\int_{\Gamma} \frac{\partial v}{\partial t} \varphi + \int_{\Gamma} f(v) \varphi + \langle \sigma_i \nabla S_i(v) \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = 0, \quad \forall \varphi \in H^{\frac{1}{2}}(\Gamma), \tag{30}$$

$$v(0) = v_0, \quad v_0 \in H^{\frac{1}{2}}(\Gamma), \tag{31}$$

where equation (30) is satisfied in $\mathcal{D}'(0, T)$, and from the definition of the duality product $\langle \cdot, \cdot \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)}$,

$$\langle \sigma_i \nabla S_i(v) \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = \int_{\Omega_i} \sigma_i \nabla S_i(v) \cdot \nabla R_i(\varphi) - \int_{\Omega_i} I_{i, \text{stim}} R_i(\varphi), \quad \forall \varphi \in H^{\frac{1}{2}}(\Gamma), \tag{32}$$

with S and R_i defined as in (20) and (21), respectively. We show that v and u solve (30) and (24), respectively, if and only if u solves (12).

Proposition 2.4. *The problem (12), with u in the spaces given in (11), is equivalent to problems (24) and (30).*

Proof. Let u be a solution of (12). Let us take $\varphi \in W$, $\varphi|_{\Omega_e} = 0$ and $\varphi|_{\Omega_i} = \varphi$. We have

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi + \int_{\Gamma} \frac{\partial [u]}{\partial t} \varphi + \int_{\Gamma} f([u]) \varphi = \int_{\Omega} I_{i, \text{stim}} \varphi.$$

By considering (32), we deduce that

$$\int_{\Gamma} \frac{\partial [u]}{\partial t} \varphi + \int_{\Gamma} f([u]) \varphi + \langle \sigma_i \nabla S_i([u]) \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = 0,$$

where $[u] = u_i - u_e = v$. Then, the problem (30) follows. Let $\varphi \in W$, $\varphi|_{\Omega_e} = \varphi_e$ and $\varphi|_{\Omega_i} = \varphi_i$ such that $[\varphi] = \varphi_i - \varphi_e = 0$ on Γ . Then, $[u] = v$ which implies $u \in W(v)$. We have

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi_i + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi_e = \int_{\Omega} I_{\text{stim}} \varphi + \langle g_e, \varphi_e \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)}.$$

Therefore, we obtain the problem (24).

Conversely, let $v \in H^{\frac{1}{2}}(\Gamma)$ and $u \in W(v)$ be the solutions of (30) and (24), respectively. Let $\varphi \in W$, $\varphi|_{\Omega_e} = \varphi_e$ and $\varphi|_{\Omega_i} = \varphi_i$. There exists an extension $\tilde{\varphi} \in H^1(\Omega)$ such that $\tilde{\varphi}|_{\Omega_e} = \varphi_e$ and $[\tilde{\varphi}] = 0$ on Γ , see e.g. [7]. Then $\tilde{\varphi} = \varphi_e$ on Γ . Let us define $\tilde{\varphi}_i = \varphi_i - \tilde{\varphi}$ in Ω_i . The problem (24) and (30) give, respectively,

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \tilde{\varphi} + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \tilde{\varphi} = \int_{\Omega} I_{\text{stim}} \tilde{\varphi} + \langle g_e, \tilde{\varphi} \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)}. \tag{33}$$

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \tilde{\varphi}_i + \int_{\Gamma} \frac{\partial [u]}{\partial t} \tilde{\varphi}_i + \int_{\Gamma} f([u]) \tilde{\varphi}_i = \int_{\Omega} I_{i,\text{stim}} \tilde{\varphi}_i. \tag{34}$$

By adding up equations (33) and (34) we obtain

$$\int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \varphi_i + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \nabla \varphi_e + \int_{\Gamma} \frac{\partial [u]}{\partial t} [\varphi] + \int_{\Gamma} f([u])[\varphi] = \int_{\Omega} I_{\text{stim}} \varphi + \langle g_e, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma_e), H^{\frac{1}{2}}(\Gamma_e)},$$

since $\tilde{\varphi}_i = \varphi_i - \tilde{\varphi} = \varphi_i - \varphi_e$ on Γ . Then the problem (12) follows. □

We will need the following results later.

Proposition 2.5. *The operator S defined in (20) is Lipschitzian, that is, there exists $L > 0$ such that*

$$\|S(v_1) - S(v_2)\|_{\mathbb{W}} \leq L \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)}, \quad \forall v_1, v_2 \in H^{\frac{1}{2}}(\Gamma). \tag{35}$$

Proof. Fix $v_1, v_2 \in H^{\frac{1}{2}}(\Gamma)$ and consider $u^1 \in W(v_1)$ and $u^2 \in W(v_2)$ solution of the problem (24) both with the same I_{stim} and g_e . Hence, $[u^1 - u^2] = v^1 - v^2$. We have that $u^1 - u^2 \in W(v_1 - v_2)$ solves the problem

$$\int_{\Omega_i} \sigma_i \nabla (u_i^1 - u_i^2) \cdot \nabla \varphi_i + \int_{\Omega_e} \sigma_e \nabla (u_e^1 - u_e^2) \cdot \nabla \varphi_e = 0, \quad \forall \varphi \in W(0).$$

It follows from (29) that

$$\|u^1 - u^2\|_{\mathbb{W}} \leq C \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)},$$

since $\|I\|_{0,\Omega} = 0$ and $\|g_e\|_{0,\Gamma_e} = 0$. Therefore,

$$\|S(v_1) - S(v_2)\|_{\mathbb{W}} \leq L \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)}.$$

□

Let S be defined as in (20). Let us define the following map

$$\begin{aligned} \gamma_1 : H^{\frac{1}{2}}(\Gamma) &\longrightarrow H^{-\frac{1}{2}}(\Gamma) \\ v &\longmapsto \sigma_i \nabla S_i(v) \cdot n_i, \end{aligned} \tag{36}$$

where $S_i(v) = u|_{\Omega_i} = u_i$ for u solution of the problem (24).

Proposition 2.6. *The map γ_1 given in (36) is Lipschitzian, that is, there exists $\tilde{L} > 0$ such that*

$$\|\gamma_1(v_1) - \gamma_1(v_2)\|_{H^{-\frac{1}{2}}(\Gamma)} \leq \tilde{L} \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)}, \quad \forall v_1, v_2 \in H^{\frac{1}{2}}(\Gamma).$$

Proof. Fix $v_1, v_2 \in H^{\frac{1}{2}}(\Gamma)$ and $\varphi \in H^{\frac{1}{2}}(\Gamma)$. From (32) we have

$$\left| \langle \sigma_i \nabla S_i(v_1) \cdot n_i - \sigma_i \nabla S_i(v_2) \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} \right| = \left| \int_{\Omega_i} \sigma_i \nabla (S_i(v_1) - S_i(v_2)) \cdot \nabla R_i(\varphi) \right|.$$

Using (22) and (35), we have

$$\begin{aligned} \left| \int_{\Omega_i} \sigma_i \nabla (S_i(v_1) - S_i(v_2)) \cdot \nabla R_i(\varphi) \right| &\leq C \|S_i(v_1) - S_i(v_2)\|_{H^1(\Omega_i)} \|R_i(\varphi)\|_{H^1(\Omega_i)}, \\ &\leq C \|S(v_1) - S(v_2)\|_{\mathbb{W}} \|\varphi\|_{H^{\frac{1}{2}}(\Gamma)}, \\ &\leq C \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)} \|\varphi\|_{H^{\frac{1}{2}}(\Gamma)}. \end{aligned}$$

It follows that

$$\|\sigma_i \nabla S_i(v_1) \cdot n_i - \sigma_i \nabla S_i(v_2) \cdot n_i\|_{H^{-\frac{1}{2}}(\Gamma)} = \sup_{\varphi \neq 0} \frac{|\langle \sigma_i \nabla(S_i(v_1) - S_i(v_2)) \cdot n_i, \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)}|}{\|\varphi\|_{H^{\frac{1}{2}}(\Gamma)}} \leq C \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)},$$

and the map (36) is Lipschitzian. □

Proposition 2.7. *Assume that f in (30) is in $C^1(\mathbb{R})$ and satisfies a global Lipschitz condition on \mathbb{R} , then $f: H^{\frac{1}{2}}(\Gamma) \rightarrow H^{-\frac{1}{2}}(\Gamma)$ is Lipschitzian.*

Proof. Let $v \in H^{\frac{1}{2}}(\Gamma) \subset L^2(\Gamma)$ be arbitrary. We claim that $f(v) \in L^2(\Gamma)$. Indeed, the function f satisfies a global Lipschitz condition on \mathbb{R} implies for a.e $x \in \Gamma$

$$\begin{aligned} |f(v(x)) - f(0)| &\leq L_1 |v(x)| \implies |f(v(x))| \leq L_1 |v(x)| + |f(0)|, \\ &\implies \int_{\Gamma} |f(v(x))|^2 \leq L_2 \left(\|v\|_{L^2(\Gamma)}^2 + \int_{\Gamma} |f(0)|^2 \right) < \infty. \end{aligned} \tag{37}$$

Therefore $f(v) \in L^2(\Gamma)$. Furthermore, f is Lipschitzian in $L^2(\Gamma)$, that is,

$$\|f(v_1) - f(v_2)\|_{L^2(\Gamma)} \leq L_3 \|v_1 - v_2\|_{L^2(\Gamma)}, \quad \forall v_1, v_2 \in L^2(\Gamma), \tag{38}$$

for some constant $L_3 > 0$.

Let $v_1, v_2 \in H^{\frac{1}{2}}(\Gamma)$ and $\varphi \in H^{\frac{1}{2}}(\Gamma)$ be arbitrary. Since $f(v_1), f(v_2) \in L^2(\Gamma)$ and $H^{\frac{1}{2}}(\Gamma) \subset L^2(\Gamma)$ with continuous injection, using (38) we have

$$\|f(v_1) - f(v_2)\|_{H^{-\frac{1}{2}}(\Gamma)} = \sup_{\varphi \neq 0} \frac{|\langle f(v_1) - f(v_2), \varphi \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)}|}{\|\varphi\|_{H^{\frac{1}{2}}(\Gamma)}} \leq L \|v_1 - v_2\|_{H^{\frac{1}{2}}(\Gamma)}.$$

□

3. DISCRETIZATION OF THE EMI MODEL

3.1. Space-discretization of the EMI model

We present the methods in details in the 2D case. The method can be developed in 3D and the theory presented below applies in both dimensions. To keep the presentation simple, only one cell is considered but the method works with a larger number of cells with appropriate modifications to account for the gap junctions, see [14] for an example with two cells and a gap junction. From here, we assumed that the regularity on the solution and the data functions holds for the r.h.s. in the inequalities and estimates to be bounded. To simplify notations, we assume that at least $g_e \in L^2(0, T; L^2(\Gamma_e))$.

We consider a spatial discretization of the problems (24) and (30) through finite element methods. Let \mathcal{T}_h be a partition of the domain $\bar{\Omega} = \bar{\Omega}_i \cup \bar{\Omega}_e$ into triangular elements. In this context the parameter h corresponds to the maximal size of the elements in the triangulation \mathcal{T}_h . Let us assume that the partition $\mathcal{T}_h = \mathcal{T}_{ih} \cup \mathcal{T}_{eh}$, where \mathcal{T}_{ih} and \mathcal{T}_{eh} are triangular element meshes of Ω_i and Ω_e , respectively, and $\mathcal{T}_{ih} \cap \mathcal{T}_{eh} = \emptyset$. The meshes \mathcal{T}_{ih} and \mathcal{T}_{eh} can be conformal or nonconformal on the interface Γ , which means that the edges of adjacent triangles may or may not match on Γ , see Figures 1 and 2.

The \mathbb{P}_d finite element spaces associated with the meshes \mathcal{T}_{ih} and \mathcal{T}_{eh} are defined as follows

$$V_h^i = \{u_{ih} \in C(\bar{\Omega}_i) : u_{ih}|_K \in \mathbb{P}_d(K), \quad \forall K \in \mathcal{T}_{ih}\}, \tag{39}$$

$$V_h^e = \{u_{eh} \in C(\bar{\Omega}_e) : u_{eh}|_K \in \mathbb{P}_d(K), \quad \forall K \in \mathcal{T}_{eh}\}, \tag{40}$$

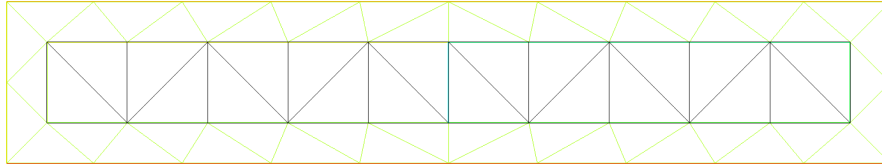


FIGURE 1. Sketch of a conformal mesh on the membrane Γ between the cell and the extracellular domain.

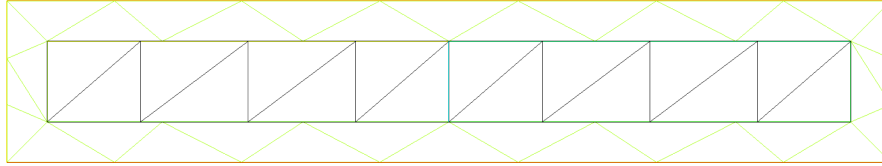


FIGURE 2. Sketch of a nonconformal mesh on the membrane Γ between the cell and the extracellular domain.

where $\mathbb{P}_d(\mathbb{K})$ is the set of polynomials in two variables, with real coefficients and of degree less than or equal to d on \mathbb{K} . The corresponding \mathbb{P}_d Lagrange interpolation operators are denoted by Π_h^i and Π_h^e , respectively. Let $u_j \in H^{l+1}(\Omega_j)$ for $1 \leq l \leq d$ and $j = i, e$. We have the following interpolation error estimates:

$$\|u_j - \Pi_h^j u_j\|_{H^1(\Omega_j)} \leq Ch^l |u_j|_{H^{l+1}(\Omega_j)}, \tag{41}$$

for some constant $C > 0$, where $|\cdot|_{H^{l+1}(\Omega)}$ stands for the $H^{l+1}(\Omega)$ -seminorm. The proof of these error estimates can be found in [8, 13, 37].

We define the following trace operators:

$$\begin{aligned} \gamma_0^j: H^1(\Omega_j) &\longrightarrow L^2(\Gamma) \\ u_j &\longmapsto u_j|_\Gamma, \quad j = i, e. \end{aligned}$$

The linear operators γ_0^j are continuous, that is,

$$\|\gamma_0^j(u_j)\|_{L^2(\Gamma)}^2 \leq C \|u_j\|_{H^1(\Omega_j)}^2 \tag{42}$$

for some constant $C > 0$ and $j = i, e$.

Now we construct a mesh, $\mathcal{T}_{\Gamma h}$, on the interface Γ for both conformal and non-conformal cases. Let \mathcal{S}_Γ^i and \mathcal{S}_Γ^e be the collection of vertices on the inner and outer sides of Γ , respectively. We have

$$\mathcal{S}_\Gamma^j = \{x_k^j, k = 1, \dots, N_j^\Gamma\},$$

where N_j^Γ , $j = i, e$, denote the total number of nodes on the inner and outer sides of Γ , respectively. For simplicity, let \mathcal{S}_Γ be the union of \mathcal{S}_Γ^i and \mathcal{S}_Γ^e . The vertices in \mathcal{S}_Γ are rearranged as follows:

$$\mathcal{S}_\Gamma = \mathcal{S}_\Gamma^i \cup \mathcal{S}_\Gamma^e = \{x_k, k = 1, \dots, N^\Gamma\}, \tag{43}$$

where N^Γ is the total number of nodes on Γ . To avoid curved boundaries, we assume that Γ is a polygonal simple curve, that is, it is the union of edges. We define the curve

$$\gamma: [0, 1] \longrightarrow \Gamma$$

$$s \mapsto \gamma(s), \quad \gamma(0) = \gamma(1),$$

and a partition $0 = s_0 < s_1 < \dots < s_{N^\Gamma} = 1$ such that $\gamma(s_j) = x_k, k = 1, \dots, N^\Gamma$. Using this ordering of the nodes on Γ , the mesh $\mathcal{T}_{\Gamma h}$ is composed of the elements $K = [x_k, x_{k+1}] \subset \mathbb{R}^2$, edges of the polygonal curve Γ , that is,

$$\mathcal{T}_{\Gamma h} = \{K : K = [x_k, x_{k+1}], x_k \in \mathcal{S}_\Gamma, k = 1, \dots, N^\Gamma\}.$$

For a conformal interface Γ , $\mathcal{S}_\Gamma = \mathcal{S}_\Gamma^j = \{x_k, k = 1, \dots, N^\Gamma\}$ for $j = i, e$. The \mathbb{P}_l finite element space associated to $\mathcal{T}_{\Gamma h}$ reads:

$$V_h^\Gamma = \gamma_0^j(V_h^j), \tag{44}$$

where $\gamma_0^j, j = i, e$, are the trace operators defined in (42).

For a nonconformal interface Γ , we define

$$V_h^\Gamma = \left\{ v_h = u_{ih} - u_{eh} \in C([0, 1]) : u_{ih} \in V_{h|\Gamma}^i, u_{eh} \in V_{h|\Gamma}^e, v_{h|K} \in \mathbb{P}_d(K), K \in \mathcal{T}_{\Gamma h} \right\}. \tag{45}$$

For both cases, we have $v_h = u_{ih|\Gamma} - u_{eh|\Gamma} \in V_h^\Gamma$ for $u_{ih} \in V_h^i$ and $u_{eh} \in V_h^e$.

We are now in position to define the discrete version of the spaces W and $W(v)$. Define

$$W_h = \left\{ u_h \in L^2(\Omega) : u_{h|\Omega_i} \in V_h^i, u_{h|\Omega_e} \in V_h^e, \int_{\Omega_e} u_{eh} \, dx = 0 \right\},$$

$$W_h(v_h) = \left\{ u_h \in L^2(\Omega) : u_{h|\Omega_i} \in V_h^i, u_{h|\Omega_e} \in V_h^e, [u_h] = v_h, \int_{\Omega_e} u_{eh} \, dx = 0 \right\},$$

where $[u_h] = u_{ih|\Gamma} - u_{eh|\Gamma} \in V_h^\Gamma, u_{h|\Omega_i} = u_{ih}$ and $u_{h|\Omega_e} = u_{eh}$.

The discrete version of the problem (12) reads

$$\int_{\Omega_i} \sigma_i \nabla u_{ih} \cdot \nabla \varphi_{ih} + \int_{\Omega_e} \sigma_e \nabla u_{eh} \cdot \nabla \varphi_{eh} + \int_\Gamma \frac{\partial [u_h]}{\partial t} [\varphi_h] + \int_\Gamma f([u_h]) [\varphi_h] = \int_\Omega I_{\text{stim}} \varphi_h + \int_{\Gamma_e} g_e \varphi_h, \tag{46}$$

where $\varphi_h \in W_h, [\varphi_h] = \varphi_{ih|\Gamma} - \varphi_{eh|\Gamma} \in V_h^\Gamma, \varphi_{h|\Omega_i} = \varphi_{ih}$ and $\varphi_{h|\Omega_e} = \varphi_{eh}$. The numerical method (46) can be used for both conformal and nonconformal cases, but we will restrict our analysis to the conformal case. In the following, we thus assume that we are in the conformal case for the analysis and the numerical tests.

3.2. Reformulation of the semi-discrete problem using a Steklov–Poincaré operator

As before, we want to split the problem (46) into two problems. For this purpose, we introduce the following linear Scott-Zhang interpolation operator, see ([13], Lemma 1.130)

$$SZ_h : H^1(\Omega_i) \longrightarrow V_h^i \subset H^1(\Omega_i)$$

$$\varphi \longmapsto SZ_h(\varphi).$$

The operator SZ_h possesses two key features. It preserves boundary values on Γ , that is, $\varphi|_\Gamma = g$ implies $SZ_h(\varphi)|_\Gamma = g$ for $g \in \gamma_0^i(V_h^i)$. It satisfies $SZ_h(\varphi) = \varphi$ for all $\varphi \in V_h^i$. Furthermore, the operator SZ_h is continuous, that is,

$$\|SZ_h(\varphi)\|_{H^1(\Omega_i)} \leq C \|\varphi\|_{H^1(\Omega_i)}, \tag{48}$$

for some constant $C > 0$, independent from the mesh size h .

Further, we define the following lifting operator

$$R_{ih} : V_h^\Gamma \subset H^{\frac{1}{2}}(\Gamma) \longrightarrow V_h^i \subset H^1(\Omega_i), \tag{49}$$

$$v_h \mapsto R_{ih}(v_h) = SZ_h(R_i(v_h)),$$

where R_i is defined as in (21). We claim that R_{ih} is continuous, that is, there exists a constant $C > 0$ independent from the mesh size h such that

$$\|R_{ih}(v_h)\|_{H^1(\Omega_i)} \leq C \|v_h\|_{H^{\frac{1}{2}}(\Gamma)}. \tag{50}$$

In fact, using (48) and (22) we have

$$\|R_{ih}(v_h)\|_{H^1(\Omega_i)} = \|SZ_h(R_i(v_h))\|_{H^1(\Omega_i)} \leq C_1 \|R_i(v_h)\|_{H^1(\Omega_i)} \leq C_2 \|v_h\|_{H^{\frac{1}{2}}(\Gamma)},$$

for some constants $C_1, C_2 > 0$.

Fix $v_h \in V_h^\Gamma$ and define $u_{v_h} \in W_h(v_h)$ as follows:

$$u_{v_h} = \begin{cases} R_{ih}(v_h) = SZ_h(R_i(v_h)) & \text{in } \Omega_i, \\ 0 & \text{in } \Omega_e, \\ v_h & \text{on } \Gamma. \end{cases} \tag{51}$$

Then we have $\gamma_0^i(u_{v_h}) = v_h$ since $SZ_h(R_i(v_h)) = R_i(v_h) = v_h$ on Γ .

The space $W_h(v_h)$ can be written as

$$W_h(v_h) = u_{v_h} + W_h(0).$$

The discrete version of (24) is

$$\begin{cases} \text{Seek } u_h \in W_h(v_h) \text{ such that} \\ \int_{\Omega_i} \sigma_i \nabla u_{ih} \cdot \nabla \varphi_{ih} + \int_{\Omega_e} \sigma_e \nabla u_{eh} \cdot \nabla \varphi_{eh} = \int_{\Omega} I_{\text{stim}} \varphi_h + \int_{\Gamma_e} g_e \varphi_{eh}, \\ \text{for all } \varphi_h \in W_h(0). \end{cases} \tag{52}$$

Under the hypothesis of Proposition 2.2, one can show that the solution, $u_h = \tilde{u}_h + u_{v_h}$ of (52) is unique and independent from the lifting function u_{v_h} . Moreover, u_h satisfies

$$\|u_h\|_W \leq C \left(\|I_{\text{stim}}\|_{L^2(\Omega)}^2 + \|g_e\|_{L^2(\Gamma_e)}^2 + \|v_h\|_{H^{\frac{1}{2}}(\Gamma)}^2 \right)^{\frac{1}{2}}. \tag{53}$$

The discrete version of the operator S is

$$\begin{aligned} S_h: V_h^\Gamma &\longrightarrow W_h \\ v_h &\longmapsto S_h(v_h) := (S_{ih}(v_h), S_{eh}(v_h)) = u_h, \end{aligned} \tag{54}$$

where $S_{ih}(v_h) = u_{ih}$, $S_{eh}(v_h) = u_{eh}$ and u_h is the solution of the problem (52). Proceeding as in Proposition 2.5 and using (53) one can show that the operator S_h is Lipschitzian.

We are now in position to write the discrete version of the problem (30). Let u_h be the the solution of the problem (52). The discrete version of the problem (30) consists in finding $v_h(t) = u_{ih|_\Gamma} - u_{eh|_\Gamma} \in V_h^\Gamma$ such that

$$\int_{\Gamma} \frac{\partial v_h}{\partial t} \varphi_h + \int_{\Gamma} f(v_h) \varphi_h + \langle \sigma_i \nabla S_{ih}(v_h) \cdot n_i, \varphi_h \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = 0, \quad \forall \varphi_h \in V_h^\Gamma, \tag{55}$$

where

$$\langle \sigma_i \nabla S_i(v_h) \cdot n_i, \varphi_h \rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)} = \int_{\Omega_i} \sigma_i \nabla S_{ih}(v_h) \cdot \nabla R_{ih}(\varphi_h) - \int_{\Omega_i} I_{i,\text{stim}} R_{ih}(\varphi_h), \tag{56}$$

where R_{ih} and S_h are defined as in (49) and (54), respectively.

Proposition 3.1. *The problem (46) is equivalent to problems (52) and (55).*

The proof of this proposition uses the same arguments as those of the Proposition 2.4.

4. ANALYSIS OF THE SEMI-DISCRETE PROBLEM

4.1. Existence of the semi-discrete solution

Let $\{\Phi_{i,l}, l = 1, \dots, N_\Gamma, N_\Gamma + 1, \dots, N_{ih}\}$ and $\{\Phi_{e,k}, k = 1, \dots, N_\Gamma, N_\Gamma + 1, \dots, N_{eh}\}$ be the usual basis of \mathbb{P}_d hat functions associated with the vertices $\{x_l, 1 \leq l \leq N_{ih}\}$ and $\{x_k, 1 \leq k \leq N_{eh}\}$, respectively. Take V_h^Γ as in (44). Let $\Phi_l^\Gamma = \Phi_{i,l}|_\Gamma$, be the restriction of the basis function $\Phi_{i,l}$ on Γ , for $1 \leq l \leq N_\Gamma$. Then $\{\Phi_l^\Gamma, 1 \leq l \leq N_\Gamma\}$ is a basis for V_h^Γ for a conformal interface Γ . Write

$$v_h(t) = \sum_{k=1}^{N_\Gamma} v_k(t)\Phi_k^\Gamma. \tag{57}$$

Taking $\varphi = \Phi_l^\Gamma$ in (55) for $t > 0$ and $1 \leq l \leq N_\Gamma$ gives

$$\sum_{k=1}^{N_\Gamma} \frac{dv_k(t)}{dt} \int_\Gamma \Phi_k^\Gamma \Phi_l^\Gamma = - \left\langle \sigma_i \nabla S_{ih} \left(\sum_{k=1}^{N_\Gamma} v_k(t)\Phi_k^\Gamma \right) \cdot n_i + f \left(\sum_{k=1}^{N_\Gamma} v_k(t)\Phi_k^\Gamma \right), \Phi_l^\Gamma \right\rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)}$$

The previous equation can be written under matrix form:

$$M_\Gamma \frac{dV}{dt} = F(V), \tag{58}$$

$$V(0) = V_{0h}, \quad V_{0h} \in V_h^\Gamma, \tag{59}$$

where

$$\begin{aligned} (M_\Gamma)_{lj} &= \int_\Gamma \Phi_j^\Gamma \Phi_l^\Gamma, \quad 1 \leq j, l \leq N_\Gamma \\ V &= (v_1(t), v_2(t), \dots, v_{N_\Gamma}(t))^T, \\ (F(U))_l &= - \left\langle \sigma_i \nabla S_{ih} \left(\sum_{k=1}^{N_\Gamma} v_k(t)\Phi_k^\Gamma \right) \cdot n_i + f \left(\sum_{k=1}^{N_\Gamma} v_k(t)\Phi_k^\Gamma \right), \Phi_l^\Gamma \right\rangle_{H^{-\frac{1}{2}}(\Gamma), H^{\frac{1}{2}}(\Gamma)}. \end{aligned}$$

Proceeding as in Propositions 2.6 and 2.7 one can show that the map $v_h \mapsto \sigma_i \nabla S_{ih}(v_h) \cdot n_i$ from V_h^Γ to $H^{-\frac{1}{2}}(\Gamma)$ and the function $f : V_h^\Gamma \rightarrow H^{-\frac{1}{2}}(\Gamma)$ are Lipschitzian, respectively. In addition, the mass matrix M_Γ is invertible. Therefore, there exists $T > 0$ such that $U \in C^1([0, T]; V_h^\Gamma)$ is a unique solution of the problem (58) and (59) thanks to the Cauchy–Lipschitz Theorem, see *e.g.* [10, 33].

4.2. Stability of the semi-discrete solution

We set $E = H^{\frac{1}{2}}(\Gamma)$, $H = L^2(\Gamma)$ endowed with their usual norms. Identifying H with its dual space H' , we have the following continuous injections,

$$E \hookrightarrow H \simeq H' \hookrightarrow E',$$

where $E' = H^{-\frac{1}{2}}(\Gamma)$ denotes the dual space of E , see *e.g.* [1, 26, 27]. It follows that the duality product $\langle \cdot, \cdot \rangle_{E', E}$ and the scalar product (\cdot, \cdot) defined in H coincide, that is,

$$\langle f, g \rangle_{V, V'} = (f, g) = \int_\Omega f(x)g(x) \, dx, \quad \forall f \in H, \quad \forall g \in E. \tag{60}$$

We derive some stability estimates uniform in h . The following stability estimates hold on v_h, u_{ih} and u_{eh} .

Proposition 4.1 (Stability Estimates). *Let $T > 0$. There exist positive constants C_1, C_2, C_3 , independent from h and depending only on $T, v(0), f(0), \mathbf{I}_{\text{stim}}, g_e$, the Lipschitz constant L_f , and the coefficient functions σ_i, σ_e , such that*

$$\|v_h(t)\|_{L^2(\Gamma)}^2 \leq C_1, \quad \forall t \in [0, T], \quad (61)$$

$$\|u_{ih}\|_{L^2(0, T; H^1(\Omega_i))} + \|u_{eh}\|_{L^2(0, T; H^1(\Omega_e))} \leq C_2, \quad (62)$$

$$\|v_h\|_{L^2(0, T; H^{\frac{1}{2}}(\Gamma))} \leq C_3, \quad (63)$$

where $v_h(t) = \sum_{k=1}^{N_\Gamma} v_k(t) \Phi_k^\Gamma$ is the solution of the Cauchy problem (58) and (59), $u_{h_{1\Omega_i}}(t) = u_{ih}(t)$, and $u_{h_{1\Omega_e}}(t) = u_{eh}(t)$ are the solutions of the problem (52).

Proof. Let us prove the inequality (61). Taking $\varphi_h = u_h$ in (46) we have

$$\begin{aligned} \int_{\Omega_i} \sigma_i \nabla u_{ih} \cdot \nabla u_{ih} + \int_{\Omega_e} \sigma_e \nabla u_{eh} \cdot \nabla u_{eh} + \int_{\Gamma} \frac{\partial v_h}{\partial t} v_h + \int_{\Gamma} f(v_h) v_h &= \int_{\Omega_i} \mathbf{I}_{i, \text{stim}} u_{ih} \\ &+ \int_{\Omega_e} \mathbf{I}_{e, \text{stim}} u_{eh} + \int_{\Gamma_e} g_e u_{eh}. \end{aligned} \quad (64)$$

Thanks to the Cauchy–Schwarz inequality, we have

$$\left| \int_{\Omega_i} \mathbf{I}_{i, \text{stim}} u_{ih} \right| \leq \|\mathbf{I}_{i, \text{stim}}\|_{L^2(\Omega_i)} \|u_{ih}\|_{L^2(\Omega_i)} \leq \|\mathbf{I}_{i, \text{stim}}\|_{L^2(\Omega_i)} \|u_{ih}\|_{H^1(\Omega_i)}, \quad (65)$$

$$\left| \int_{\Omega_e} \mathbf{I}_{e, \text{stim}} u_{eh} \right| \leq \|\mathbf{I}_{e, \text{stim}}\|_{L^2(\Omega_e)} \|u_{eh}\|_{L^2(\Omega_e)} \leq \|\mathbf{I}_{e, \text{stim}}\|_{L^2(\Omega_e)} \|u_{eh}\|_{H^1(\Omega_e)}, \quad (66)$$

$$\left| \int_{\Gamma_e} g_e u_{eh} \, dx \right| \leq \|g_e\|_{L^2(\Gamma_e)} \|u_{eh}\|_{L^2(\Gamma_e)} \leq \alpha_2 \|g_e\|_{L^2(\Gamma_e)} \|u_{eh}\|_{H^1(\Omega_e)}, \quad (67)$$

where $\alpha_2 > 0$ is a constant. Furthermore,

$$\beta \left(\|\nabla u_{ih}\|_{L^2(\Omega_i)}^2 + \|\nabla u_{eh}\|_{L^2(\Omega_e)}^2 \right) \leq \int_{\Omega_i} \sigma_i \nabla u_{ih} \cdot \nabla u_{ih} + \int_{\Omega_e} \sigma_e \nabla u_{eh} \cdot \nabla u_{eh}, \quad (68)$$

where $\beta = \min(\text{ess inf}_{x \in \Omega_i} \sigma_i, \text{ess inf}_{x \in \Omega_e} \sigma_e)$. Substituting (65)–(68) in the equation (64) and using the Poincaré–Friedrichs inequality (27) and Young inequality, we obtain

$$\begin{aligned} \frac{C\beta}{2} \left(\|u_{ih}\|_{H^1(\Omega_i)}^2 + \|u_{eh}\|_{H^1(\Omega_e)}^2 \right) + \frac{1}{2} \frac{d}{dt} \|v_h\|_{L^2(\Gamma)}^2 &\leq \|f(v_h)\|_{L^2(\Gamma)} \|v_h\|_{L^2(\Gamma)} + \frac{1}{2C\beta} \|\mathbf{I}_{i, \text{stim}}\|_{L^2(\Omega_i)}^2 \\ &+ \frac{1}{C\beta} \|\mathbf{I}_{e, \text{stim}}\|_{L^2(\Omega_e)}^2 + \frac{\alpha_2^2}{C\beta} \|g_e\|_{L^2(\Gamma_e)}^2. \end{aligned} \quad (69)$$

Proceeding as in (37) for f , it follows from the Young inequality that

$$\|f(v_h)\|_{L^2(\Gamma)} \|v_h\|_{L^2(\Gamma)} \leq L_f \|v_h\|_{L^2(\Gamma)}^2 + \|f(0)\|_{L^2(\Gamma)} \|v_h\|_{L^2(\Gamma)} \leq \left(L_f + \frac{1}{2} \right) \|v_h\|_{L^2(\Gamma)}^2 + \frac{1}{2} \|f(0)\|_{L^2(\Gamma)}^2. \quad (70)$$

Plugging in (70) into (69), we deduce that

$$\frac{d}{dt} \|v_h\|_{L^2(\Gamma)}^2 \leq (2L_f + 1) \|v_h\|_{L^2(\Gamma)}^2 + \|f(0)\|_{L^2(\Gamma)}^2 + C \|\mathbf{I}_{i, \text{stim}}\|_{L^2(\Omega_i)}^2 + C \|\mathbf{I}_{e, \text{stim}}\|_{L^2(\Omega_e)}^2 + C \|g_e\|_{L^2(\Gamma_e)}^2. \quad (71)$$

Using Gronwall Lemma ([35], p. 13), we obtain

$$\begin{aligned} \|v_h(t)\|_{L^2(\Gamma)}^2 &\leq C e^{(2L_f+1)T} \left[\|v_h(0)\|_{L^2(\Gamma)}^2 + \|f(0)\|_{L^2(\Gamma)}^2 + \|\mathbf{I}_{i,\text{stim}}\|_{L^2(0,T;L^2(\Omega_i))}^2 \right] \\ &\quad + C e^{(2L_f+1)T} \left[\|\mathbf{I}_{e,\text{stim}}\|_{L^2(0,T;L^2(\Omega_e))}^2 + \|g_e\|_{L^2(0,T;L^2(\Gamma_e))}^2 \right], \end{aligned}$$

a.e. on $[0, T]$. It is worth noticing that the previous inequality implies

$$\|v_h\|_{L^\infty(0,T;L^2(\Gamma))} \leq C_1, \tag{72}$$

for some constant $C_1 > 0$.

We now prove the inequality (62). Substituting (70) into (69) and integrating from 0 to T yields

$$\begin{aligned} C_2 \int_0^T \left(\|u_{ih}\|_{H^1(\Omega_i)}^2 + \|u_{eh}\|_{H^1(\Omega_e)}^2 \right) dt &\leq \|v_h(0)\|_{L^2(\Gamma)}^2 + C \int_0^T \|v_h(t)\|_{L^2(\Gamma)}^2 dt \\ &\quad + C \left(\|\mathbf{T}f(0)\|_{L^2(\Gamma)}^2 + \|\mathbf{I}_{i,\text{stim}}\|_{L^2(0,T;L^2(\Omega_i))}^2 \right) \\ &\quad + \left(\|\mathbf{I}_{e,\text{stim}}\|_{L^2(0,T;L^2(\Omega_e))}^2 + \|g_e\|_{L^2(0,T;L^2(\Gamma_e))}^2 \right). \end{aligned}$$

Thus, (62) holds using (72). Lastly, we prove the inequality (63) by noticing that

$$\|v_h\|_{H^{\frac{1}{2}}(\Gamma)} = \|u_{ih} - u_{eh}\|_{H^{\frac{1}{2}}(\Gamma)} \leq \|u_{ih}\|_{H^{\frac{1}{2}}(\Gamma)} + \|u_{eh}\|_{H^{\frac{1}{2}}(\Gamma)} \leq C(\|u_{ih}\|_{H^1(\Omega_i)} + \|u_{eh}\|_{H^1(\Omega_e)}), \tag{73}$$

thanks to the continuity of trace operators defined in (42). □

4.3. Well-posedness of the projection operator

In this section, we estimate the error between the solutions of the semidiscrete and continuous problems (46) and (12), respectively. Proceeding as in [47], we write the error as a sum of two terms which are then bounded separately:

$$u_h - u = (u_h - P_h u) + (P_h u - u) = \theta + \rho, \tag{74}$$

where P_h denotes a projection of W onto $V_h^i \times V_h^e$ defined by

$$\begin{aligned} \int_{\Omega_i} \sigma_i \nabla P_h u_i \cdot \nabla \chi_{ih} + \int_{\Omega_e} \sigma_e \nabla P_h u_e \cdot \nabla \chi_{eh} + \int_{\Gamma} (P_h u_i - P_h u_e)(\chi_{ih} - \chi_{eh}) &= \int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \chi_{ih} \\ + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \chi_{eh} + \int_{\Gamma} (u_i - u_e)(\chi_{ih} - \chi_{eh}), \quad \forall \chi \in W_h. \end{aligned} \tag{75}$$

Due to the jump on the interface Γ , P_h is not a standard projection operator.

The space W defined in (10) is equipped with the norm

$$\|u\|_W = \left(\|u_i\|_{H^1(\Omega_i)}^2 + \|u_e\|_{H^1(\Omega_e)}^2 + \|u_i - u_e\|_{L^2(\Gamma)}^2 \right)^{\frac{1}{2}}. \tag{76}$$

Before stating the main result of this section, we shall prove that the projection operator P_h is well defined. For a given $u \in W$, let us set

$$\begin{aligned} a(w_h, \chi_h) &= \int_{\Omega_i} \sigma_i \nabla w_{ih} \cdot \nabla \chi_{ih} + \int_{\Omega_e} \sigma_e \nabla w_{eh} \cdot \nabla \chi_{eh} + \int_{\Gamma} (w_{ih} - w_{eh})(\chi_{ih} - \chi_{eh}), \\ l(\chi_h) &= a(u, \chi_h) = \int_{\Omega_i} \sigma_i \nabla u_i \cdot \nabla \chi_{ih} + \int_{\Omega_e} \sigma_e \nabla u_e \cdot \chi_{eh} + \int_{\Gamma} v(\chi_{ih} - \chi_{eh}), \end{aligned}$$

where $w_h \in W_h$ and $v = u_i - u_e$. For a given $u \in W$, let us consider the following problem:

$$\begin{aligned} &\text{find } P_h u \in W_h \text{ such that} \\ &a(P_h u, \chi_h) = l(\chi_h) \text{ for all } \chi_h \in W_h. \end{aligned} \tag{77}$$

The following lemma will be useful to prove the coercivity of $a(\cdot, \cdot)$.

Lemma 4.2. *Let $w \in W$ be arbitrary. There exists a constant $\alpha > 0$ such that*

$$\alpha \|w\|_W \leq \|\nabla w_e\|_{L^2(\Omega_e)}^2 + \|\nabla w_i\|_{L^2(\Omega_i)}^2 + \|w_i - w_e\|_{L^2(\Gamma)}^2 \tag{78}$$

Proof. We consider the following three Banach spaces:

$$\begin{cases} X = W \\ Y = L^2(\Omega_i) \times L^2(\Omega_e) \times L^2(\Gamma), \\ Z = L^2(\Omega_i) \times L^2(\Omega_e). \end{cases} \tag{79}$$

Further, we consider the following operator:

$$\begin{aligned} A: X &\longrightarrow Y \\ w &\longmapsto (\nabla w_i, \nabla w_e, w_{i|\Gamma} - w_{e|\Gamma}). \end{aligned}$$

Clearly, A is a continuous linear operator. We claim that A is injective. In fact, assume that

$$\begin{cases} \nabla w_i = 0 & \text{a.e in } \Omega_i, \\ \nabla w_e = 0 & \text{a.e in } \Omega_e, \\ w_i = w_e & \text{a.e on } \Gamma. \end{cases}$$

Then,

$$\begin{cases} w_{i|\Omega_i} = C_i & \text{a.e in } \Omega_i, \\ w_{e|\Omega_e} = C_e & \text{a.e in } \Omega_e, \\ C_i = C_e & \text{a.e on } \Gamma. \end{cases}$$

where C_i and C_e are constants. Since $\int_{\Omega_e} w_e \, dx = 0$, $w_e|_{\Omega_e} = C_e$ a.e, and $\mu(\Omega_e) \neq 0$, it follows that $u_e = 0$ in Ω_e a.e. Therefore, $C_e = 0 = C_i$ and $u_i = 0$ in Ω_i a.e.

On the other hand, we consider the operator below:

$$\begin{aligned} T: X &\longrightarrow Z \\ w &\longmapsto (w_i, w_e). \end{aligned}$$

Clearly, T is a compact operator, see e.g. [1, 7]. Let us show that there exists $C > 0$ such that

$$\|w\|_W \leq \|Aw\|_Y + \|Tw\|_Z.$$

We have

$$\begin{aligned} \|w\|_W^2 &= \|w_i\|_{L^2(\Omega_i)}^2 + \|\nabla w_i\|_{L^2(\Omega_i)}^2 + \|w_e\|_{L^2(\Omega_e)}^2 + \|\nabla w_e\|_{L^2(\Omega_e)}^2 + \|w_i - w_e\|_{L^2(\Gamma)}^2 \\ &\leq (\|Aw\|_Y + \|Tw\|_Z)^2. \end{aligned}$$

Consequently,

$$\|w\|_X \leq \|Aw\|_Y + \|Tw\|_Z,$$

with $C = 1$. Thanks to Petree-Tartar ([13], Lemma A.38, p. 469), there exists $\alpha > 0$, such that

$$\alpha \|w\|_X \leq \|Aw\|_Y,$$

that is,

$$\alpha \left(\|w_i\|_{H^2(\Omega_i)}^2 + \|w_e\|_{H^1(\Omega_e)}^2 + \|w_i - w_e\|_{L^2(\Gamma)}^2 \right) \leq \|\nabla w_e\|_{L^2(\Omega_e)}^2 + \|\nabla w_i\|_{L^2(\Omega_i)}^2 + \|w_i - w_e\|_{L^2(\Gamma)}^2.$$

□

Theorem 4.3. *The problem (77) has a unique solution.*

Proof. Let us show that:

- (i) The bilinear form $a(\cdot, \cdot)$ in (77) is continuous on $W \times W$ and coercive on W .
- (ii) The linear form $l(\cdot)$ in (77) is continuous on W .

(i) Let $w, \varphi \in W$ be arbitrary, we have

$$\begin{aligned} |a(w, \varphi)| &\leq C \|\nabla w_e\|_{L^2(\Omega_e)} \|\nabla \varphi_e\|_{L^2(\Omega_e)} + C \|\nabla w_i\|_{L^2(\Omega_i)} \|\nabla \varphi_i\|_{L^2(\Omega_i)} + \|w_i - w_e\|_{L^2(\Gamma)} \|\varphi_i - \varphi_e\|_{L^2(\Gamma)}, \\ &\leq C \|w\|_W \|\varphi\|_W, \end{aligned}$$

where C is a given constant depending on $\text{ess sup}_{x \in \Omega_e} \sigma_e(x)$ and $\text{ess sup}_{x \in \Omega_i} \sigma_i(x)$. It follows that the bilinear form $a(\cdot, \cdot)$ is continuous on $W \times W$. In particular, $a(\cdot, \cdot)$ is continuous on $W_h \times W_h$.

Let us prove the coercivity of $a(\cdot, \cdot)$. Let $w \in W$. Using (78), we have

$$\begin{aligned} a(w, w) &= \int_{\Omega_i} \sigma_i |\nabla w_i|^2 + \int_{\Omega_e} \sigma_e |\nabla w_e|^2 + \int_{\Gamma} (w_i - w_e)^2 \\ &\geq \min(1, \beta) \left(\|\nabla w_e\|_{L^2(\Omega_e)}^2 + \|\nabla w_i\|_{L^2(\Omega_i)}^2 + \|w_i - w_e\|_{L^2(\Gamma)}^2 \right) \geq \nu \|w\|_W^2, \end{aligned}$$

where $\nu = \alpha \min(1, \beta) > 0$ and $\beta = \min(\text{ess inf}_{x \in \Omega_i} \sigma_i, \text{ess inf}_{x \in \Omega_e} \sigma_e) > 0$. It follows that the bilinear form $a(\cdot, \cdot)$ is coercive on W .

- (ii) Let $\varphi = (\varphi_i, \varphi_e) \in W$ be arbitrary and fix $u = (u_i, u_e) \in W$. Using the continuity of the bilinear form $a(\cdot, \cdot)$, we have

$$|l(\varphi)| \leq C \|u\|_W \|\varphi\|_W.$$

Therefore, the variational formulation problem (77) has a unique solution thanks to the Lax-Milgram theorem.

□

4.4. Error estimates in space

The following lemma due to Céa will be useful in the sequel.

Lemma 4.4. *Let $u \in W$. Let $\nu > 0$ and $M > 0$ be the coercivity and continuity constants of the bilinear form $a(\cdot, \cdot)$ defined in (77), respectively. Then*

$$\|u - P_h u\|_W \leq \sqrt{\frac{M}{\nu}} \inf_{\chi_h \in W_h} \|u - \chi_h\|_W. \tag{80}$$

For the proof of this lemma, see ([13], Lemma 2.28).

Let us write the error as in (74) and set

$$\theta = \begin{cases} \theta_i = u_{ih} - P_h u_i, & \text{in } \Omega_i, \\ \theta_e = u_{eh} - P_h u_e, & \text{in } \Omega_e, \end{cases} \tag{81}$$

$$\rho = \begin{cases} \rho_i = P_h u_i - u_i, & \text{in } \Omega_i, \\ \rho_e = P_h u_e - u_e, & \text{in } \Omega_e, \end{cases} \tag{82}$$

$$\begin{cases} \theta^\Gamma = \theta_i - \theta_e = v_h - (P_h u_i - P_h u_e), & \text{on } \Gamma, \\ \rho^\Gamma = P_h u_i - P_h u_e - v, & \text{on } \Gamma, \end{cases} \tag{83}$$

where $v_h = u_{ih} - u_{eh}$ and $v = u_i - u_e$. The following error estimates hold:

Proposition 4.5. *Let $u \in W$. We assume that $u_i \in H^{l+1}(\Omega_i)$ and $u_e \in H^{l+1}(\Omega_e)$ for $1 \leq l \leq d$. Then,*

$$\|\rho_e\|_{H^1(\Omega_e)} \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \tag{84}$$

$$\|\rho_i\|_{H^1(\Omega_i)} \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \tag{85}$$

$$\|\rho^\Gamma\|_{L^2(\Gamma)} \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \tag{86}$$

where $|\cdot|_{H^l(\Omega)}$ is the usual $H^l(\Omega)$ -seminorm and C is some constant independent of the mesh size.

Proof. Let $\chi_h = (\chi_{ih}, \chi_{eh}) \in W_h$ be arbitrary. We have

$$\|u - \chi_h\|_W^2 = \|u_e - \chi_{eh}\|_{H^1(\Omega_e)}^2 + \|u_i - \chi_{ih}\|_{H^1(\Omega_i)}^2 + \|(u_i - u_e) - (\chi_{ih} - \chi_{eh})\|_{L^2(\Gamma)}^2.$$

Taking $\chi_{jh} = \Pi_h^j u_j$, $j = i, e$, where Π_h^j , $j = i, e$, is the Lagrange interpolation operator defined in (41), see e.g. [8, 13]. It follows that

$$\begin{aligned} \inf_{\chi_h \in W_h} \left\{ \|u - \chi_h\|_W^2 \right\} &\leq \|u_e - \Pi_h^e u_e\|_{H^1(\Omega_e)}^2 + \|u_i - \Pi_h^i u_i\|_{H^1(\Omega_i)}^2 + 2\|u_i - \Pi_h^i u_i\|_{L^2(\Gamma)}^2 + 2\|u_e - \Pi_h^e u_e\|_{L^2(\Gamma)}^2 \\ &\leq C \left(\|u_e - \Pi_h^e u_e\|_{H^1(\Omega_e)}^2 + \|u_i - \Pi_h^i u_i\|_{H^1(\Omega_i)}^2 \right) \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \end{aligned}$$

for some constant $C > 0$, thanks to the inequalities (41) and (42). On account of the inequality (80), the following error estimate holds

$$\|\rho\|_W \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \tag{87}$$

for some constant $C > 0$. From (87), we deduce the error estimates (84)–(86). □

In what follows, we fix $]0, T[$ as the evolution time interval, and we define the following space-time domains

$$\begin{aligned} \mathcal{Q}_i &= \Omega_i \times]0, T[, \\ \mathcal{Q}_e &= \Omega_e \times]0, T[, \\ \Sigma &= \Gamma \times]0, T[. \end{aligned}$$

It is worth remembering that there are isometric isomorphisms from $L^2(0, T; L^2(\Omega_i))$ and $L^2(0, T; L^2(\Omega_e))$ to $L^2(\mathcal{Q}_i)$ and $L^2(\mathcal{Q}_e)$, respectively.

Theorem 4.6. *Let u and u_h be the solutions of (12) and (46). Let us assume that $u_{i,e} \in H^1(0, T; H^{l+1}(\Omega_{i,e}))$ for $1 \leq l \leq d$. There exist positive constants C depending only on T , and the Lipschitz constant L_f , such that*

$$\|\nabla(u_i - u_{ih})\|_{L^2(\mathcal{Q}_i)}^2 + \|\nabla(u_e - u_{eh})\|_{L^2(\mathcal{Q}_e)}^2 \leq Ch^{2l} \int_0^T \left(|u_e|_{H^{l+1}(\Omega_e)}^2 + |u_i|_{H^{l+1}(\Omega_i)}^2 \right) dt$$

$$+ Ch^{2l} \int_0^T \left(\left| \frac{\partial u_e}{\partial t} \right|_{\mathbf{H}^{l+1}(\Omega_e)}^2 + \left| \frac{\partial u_i}{\partial t} \right|_{\mathbf{H}^{l+1}(\Omega_i)}^2 \right) dt. \tag{88}$$

$$\|v - v_h\|_{L^2(\Gamma)}^2 \leq Ch^{2l} \int_0^T \left(|u_e|_{\mathbf{H}^{l+1}(\Omega_e)}^2 + |u_i|_{\mathbf{H}^{l+1}(\Omega_i)}^2 + \left| \frac{\partial u_e}{\partial t} \right|_{\mathbf{H}^{l+1}(\Omega_e)}^2 + \left| \frac{\partial u_i}{\partial t} \right|_{\mathbf{H}^{l+1}(\Omega_i)}^2 \right). \tag{89}$$

Proof. With the error written as in (74) it suffices, in view of Proposition 4.5, to bound $\theta = u_h - P_h u$.

Let $\chi_h \in W_h$. Since u and u_h satisfy (12) and (46), respectively, using the projection operator in (75) we have

$$\begin{aligned} (\partial_t(\theta_i - \theta_e), \chi_{ih} - \chi_{eh})_\Gamma + a(\theta, \chi) &= \int_\Gamma \partial_t v (\chi_{ih} - \chi_{eh}) + \int_\Gamma (f(v) - f(v_h)) (\chi_{ih} - \chi_{eh}) \\ &\quad + \int_\Gamma (v_h - v) (\chi_{ih} - \chi_{eh}) - \int_\Gamma \partial_t (P_h u_i - P_h u_e) (\chi_{ih} - \chi_{eh}). \end{aligned}$$

We have for all $\chi_h \in W_h$,

$$\begin{aligned} (\partial_t(\theta_i - \theta_e), \chi_{ih} - \chi_{eh})_\Gamma + a(\theta, \chi) &= -(\partial_t \rho^\Gamma, \chi_{ih} - \chi_{eh})_\Gamma + (v_h - v, \chi_{ih} - \chi_{eh})_\Gamma \\ &\quad + (f(v) - f(v_h), \chi_{ih} - \chi_{eh})_\Gamma, \end{aligned} \tag{90}$$

where $\rho^\Gamma = P_h u_i - P_h u_e - v$. Setting $\chi_h = \theta$ in (90) and using Young inequality yield

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \|\theta^\Gamma\|_{L^2(\Gamma)}^2 + \beta \left(\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2 \right) + \|\theta^\Gamma\|_{L^2(\Gamma)}^2 &\leq \|\partial_t \rho^\Gamma\| \|\theta^\Gamma\|_{L^2(\Gamma)} + (1 + L_f) \|v_h - v\|_{L^2(\Gamma)} \|\theta^\Gamma\|_{L^2(\Gamma)} \\ &\leq \frac{5}{4} (1 + L_f) \|\theta^\Gamma\|_{L^2(\Gamma)}^2 + 2(1 + L_f) \|\rho^\Gamma\|_{L^2(\Gamma)}^2 + \frac{2}{(1 + L_f)} \|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2. \end{aligned}$$

It follows that

$$\frac{1}{2} \frac{d}{dt} \|\theta^\Gamma\|_{L^2(\Gamma)}^2 + \beta \left(\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2 \right) \leq \frac{1}{4} (1 + L_f) \|\theta^\Gamma\|_{L^2(\Gamma)}^2 + C_1 \|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2 + C_2 \|\rho^\Gamma\|_{L^2(\Gamma)}^2, \tag{91}$$

for some constants $C_1, C_2 > 0$. From the previous inequality, we deduce that

$$\frac{d}{dt} \|\theta^\Gamma\|_{L^2(\Gamma)}^2 \leq \frac{(1 + L_f)}{2} \|\theta^\Gamma\|_{L^2(\Gamma)}^2 + C_1 \|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2 + C_2 \|\rho^\Gamma\|_{L^2(\Gamma)}^2. \tag{92}$$

Then,

$$\frac{d}{dt} \left(e^{-0.5(1+L_f)t} \|\theta^\Gamma\|_{L^2(\Gamma)}^2 \right) \leq C e^{-0.5(1+L_f)t} \left[\|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2 + \|\rho^\Gamma\|_{L^2(\Gamma)}^2 \right] \tag{93}$$

By integrating (93) with respect to time, we obtain that

$$\|\theta^\Gamma(t)\|_{L^2(\Gamma)}^2 \leq C \left[\|\theta^\Gamma(0)\|_{L^2(\Gamma)}^2 + \|\partial_t \rho^\Gamma\|_{L^2(0,T;L^2(\Gamma))}^2 + \|\rho^\Gamma\|_{L^2(0,T;L^2(\Gamma))}^2 \right], \tag{94}$$

for a.e. $t \in (0, T)$ and for some constant $C > 0$ depending on L_f and T . From (91), we have

$$\begin{aligned} 2\beta \int_0^T \left(\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2 \right) dt &\leq \|\theta^\Gamma(0)\|_{L^2(\Gamma)}^2 + \frac{(1 + L_f)}{2} \int_0^T \|\theta^\Gamma\|_{L^2(\Gamma)}^2 dt \\ &\quad + C_1 \int_0^T \|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2 dt + C_2 \int_0^T \|\rho^\Gamma\|_{L^2(\Gamma)}^2 dt. \end{aligned}$$

Thus,

$$\int_0^T \left(\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2 \right) dt \leq C \left[\|\theta^\Gamma(0)\|_{L^2(\Gamma)}^2 + \|\partial_t \rho^\Gamma\|_{L^2(0,T;L^2(\Gamma))}^2 \right] + C \|\rho^\Gamma\|_{L^2(0,T;L^2(\Gamma))}^2, \tag{95}$$

where $C > 0$ is a constant that depends on T, β and L_f . In addition,

$$\begin{aligned} \|\theta^\Gamma(0)\|_{L^2(\Gamma)} &\leq \|v_h(0) - v(0)\|_{L^2(\Gamma)} + \|v(0) - (P_h u_i(0) - P_h u_e(0))\|_{L^2(\Gamma)} \\ &= \|v_h(0) - v(0)\|_{L^2(\Gamma)} + \|\rho^\Gamma(0)\|_{L^2(\Gamma)} \leq Ch^l (|u_e|_{H^{l+1}(\Omega_e)} + |u_i|_{H^{l+1}(\Omega_i)}), \end{aligned} \tag{96}$$

using (86) together with the continuity of the trace operator and the interpolation error estimates (41). From (86), we deduce that

$$\|\partial_t \rho^\Gamma\|_{L^2(\Gamma)}^2 \leq Ch^{2l} \left(\left| \frac{\partial u_e}{\partial t} \right|_{H^{l+1}(\Omega_e)}^2 + \left| \frac{\partial u_i}{\partial t} \right|_{H^{l+1}(\Omega_i)}^2 \right) \tag{97}$$

Plugging (86), (96) and (97) in (94) and (95) yields, respectively,

$$\begin{aligned} \|\theta^\Gamma(t)\|_{L^2(\Gamma)}^2 &\leq Ch^{2l} \int_0^T \left(|u_e|_{H^{l+1}(\Omega_e)}^2 + |u_i|_{H^{l+1}(\Omega_i)}^2 + \left| \frac{\partial u_e}{\partial t} \right|_{H^{l+1}(\Omega_e)}^2 \right. \\ &\quad \left. + \left| \frac{\partial u_i}{\partial t} \right|_{H^{l+1}(\Omega_i)}^2 \right) dt. \end{aligned} \tag{98}$$

$$\begin{aligned} \int_0^T (\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2) dt &\leq Ch^{2l} \int_0^T (|u_e|_{H^{l+1}(\Omega_e)}^2 + |u_i|_{H^{l+1}(\Omega_i)}^2) dt \\ &\quad + Ch^{2l} \int_0^T \left(\left| \frac{\partial u_e}{\partial t} \right|_{H^{l+1}(\Omega_e)}^2 + \left| \frac{\partial u_i}{\partial t} \right|_{H^{l+1}(\Omega_i)}^2 \right) dt. \end{aligned} \tag{99}$$

Further, we have

$$\|v - v_h\|_{L^2(\Gamma)}^2 \leq C \left(\|\theta^\Gamma(t)\|_{L^2(\Gamma)}^2 + \|\rho^\Gamma(t)\|_{L^2(\Gamma)}^2 \right). \tag{100}$$

The error estimate (89) is obtained by plugging (98) and (86) in (100).

We are now in position to prove the error estimate (88). We have

$$\begin{aligned} \|\nabla(u_i - u_{ih})\|_{L^2(Q_i)}^2 + \|\nabla(u_e - u_{eh})\|_{L^2(Q_e)}^2 &\leq \int_0^T (\|\nabla \theta_i\|_{L^2(\Omega_i)} + \|\nabla \rho_i\|_{L^2(\Omega_i)})^2 \\ &\quad + \int_0^T (\|\nabla \theta_e\|_{L^2(\Omega_e)} + \|\nabla \rho_e\|_{L^2(\Omega_e)})^2 \\ &\leq C \int_0^T (\|\nabla \theta_i\|_{L^2(\Omega_i)}^2 + \|\nabla \rho_i\|_{L^2(\Omega_i)}^2 + \|\nabla \theta_e\|_{L^2(\Omega_e)}^2 + \|\nabla \rho_e\|_{L^2(\Omega_e)}^2). \end{aligned}$$

The error estimate (88) is derived by substituting (84), (85) and (99) in the previous inequality. □

5. TIME DISCRETIZATION AND SOLUTION OF THE ALGEBRAIC SYSTEMS

In Section 4.1, we introduced a semi-discrete problem with unknowns standing only on the interface Γ for the sake of proving the existence of a solution for this problem. Combined with an appropriate time discretization, this approach can certainly lead to new and very efficient numerical methods, but this requires the non-trivial computation of a discrete Steklov–Poincaré operator. Instead, we opted for solving (46). We present details in this section.

In practice, we solve problem (1)–(8) using a fully discretized method in time and space. Using the notations from Sections 3.1 to 4.1, we set in (46) and the variational equation for (7)

$$u_{ih} = \sum_{j=1}^{N_{ih}} u_{i,j} \Phi_{i,j}, \quad u_{eh} = \sum_{j=1}^{N_{eh}} u_{e,j} \Phi_{e,j}, \quad w_h = \sum_{j=1}^{N_\Gamma} w_j \Phi_j^\Gamma, \quad v_h = (u_{ih} - u_{eh})|_\Gamma.$$

For instance, we use the second order semi-implicit backward differentiation formula (SBDF2) [3, 4, 40] for the time discretization. We set $v^n \approx v(t_n)$, $w^n \approx w(t_n)$, the discrete time $t_n = n\Delta t$ and time step $\Delta t = \frac{T}{N}$. The time derivatives $\frac{\partial v}{\partial t}$ and $\frac{\partial w}{\partial t}$ are then approximated as follows

$$\begin{aligned} \frac{\partial v}{\partial t} &\approx \frac{3v^n - 4v^{n-1} + v^{n-2}}{2\Delta t}, \\ \frac{\partial w}{\partial t} &\approx \frac{3w^n - 4w^{n-1} + w^{n-2}}{2\Delta t}. \end{aligned}$$

The nonlinear terms f , g , $I_{i,\text{stim,ex}}$ and $I_{e,\text{stim,ex}}$ are extrapolated at $t = t^n$ as follows

$$\begin{aligned} f(v^n, w^n) &\approx 2f(v^{n-1}, w^{n-1}) - f(v^{n-2}, w^{n-2}) \\ g(v^n, w^n) &\approx 2g(v^{n-1}, w^{n-1}) - g(v^{n-2}, w^{n-2}) \\ I_{i,\text{stim,ex}}^n &\approx 2I_{i,\text{ex}}^{n-1} - I_{i,\text{ex}}^{n-2}, \\ I_{e,\text{stim,ex}}^n &\approx 2I_{e,\text{ex}}^{n-1} - I_{e,\text{ex}}^{n-2}, \end{aligned}$$

where $I_{e,\text{stim,ex}}^n = I_{e,\text{stim,ex}}(t_n)$ and $I_{i,\text{stim,ex}}^n = I_{i,\text{stim,ex}}(t_n)$. We can rewrite the equations (1)–(6) under the following matrix form:

$$\begin{aligned} AU^n &= F^{n-2,n-1}, \\ A &= \begin{pmatrix} A_i & M_{ie} \\ M_{ei} & A_e \end{pmatrix}, \quad U^n = \begin{pmatrix} U_i^n \\ U_e^n \end{pmatrix}, \quad F^{n-2,n-1} = \begin{pmatrix} F_i^{n-2,n-1} \\ F_e^{n-2,n-1} \end{pmatrix}, \quad n \in \{2, \dots, N\} \end{aligned}$$

where

$$\begin{aligned} (A_i)_{lj} &= \int_{\Omega_i} \sigma_i \nabla \Phi_{i,j} \cdot \nabla \Phi_{i,l} + \frac{3}{2\Delta t} \int_{\Gamma} \Phi_{i,j} \Phi_{i,l}, & 1 \leq j, l \leq N_{ih}, \\ (M_{ie})_{lj} &= -\frac{3}{2\Delta t} \int_{\Gamma} \Phi_{e,j} \Phi_{i,l}, & 1 \leq j \leq N_{eh}, 1 \leq l \leq N_{ih}, \\ U_i^n &= (u_{i,1}^n, \dots, u_{i,N_{ih}}^n)^\top, \quad U_e^n = (u_{e,1}^n, \dots, u_{e,N_{eh}}^n)^\top, \\ (F_i^{n-2,n-1})_l &= \int_{\Omega_i} (2I_{i,\text{stim}}^{n-1} - I_{i,\text{stim}}^{n-2}) \Phi_{i,l} + \int_{\Gamma} (f(v_h^{n-2}, w_h^{n-2}) - 2f(v_h^{n-1}, w_h^{n-1})) \Phi_{i,l} \\ &\quad + \frac{1}{2\Delta t} \int_{\Gamma} (4w_h^{n-1} - w_h^{n-2}) \Phi_{i,l}, & 1 \leq l \leq N_{ih}. \end{aligned}$$

Similarly, $(A_e)_{lj}$, $(M_{ei})_{lj}$ and $F_e^{n-2,n-1}$ are obtained by replacing $\Phi_{i,j}$, $\Phi_{i,l}$, $\Phi_{e,j}$ and Ω_i by $\Phi_{e,j}$, $\Phi_{e,l}$, $\Phi_{i,j}$ and Ω_e , respectively. The variable w^n is updated by solving the system of ODEs (7), which in matrix form reads:

$$M_\Gamma W^n = G^{n-2,n-1}, \tag{101}$$

where

$$\begin{aligned} (M_\Gamma)_{lj} &= \frac{3}{2\Delta t} \int_{\Gamma} \Phi_j^\Gamma \Phi_l^\Gamma, \quad 1 \leq j, l \leq N_\Gamma \\ (G^{n-2,n-1})_l &= \int_{\Gamma} (2g(v_h^{n-1}, w_h^{n-1}) - g(v_h^{n-2}, w_h^{n-2})) \Phi_l^\Gamma + \frac{1}{2\Delta t} \int_{\Gamma} (4w_h^{n-1} - w_h^{n-2}) \Phi_l^\Gamma, \quad 1 \leq l \leq N_\Gamma, \\ W^n &= (w_1^n, \dots, w_{N_\Gamma}^n)^\top, \quad n \in \{2, \dots, N\}. \end{aligned}$$

A startup procedure is needed for the first time step, e.g., a semi-implicit Euler method.

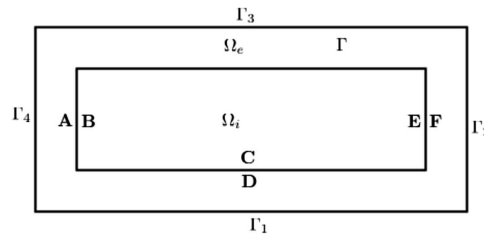


FIGURE 3. Sketch of $\Omega = \Omega_i \cup \Omega_e \cup \Gamma$, $\Gamma = \overline{\Omega}_i \cap \overline{\Omega}_e$, with points A&B, C&D, and E&F.

6. NUMERICAL EXPERIMENTS

We present numerical tests to compare the practical order of convergence of the method with the theoretical error estimates.

6.1. Ionic model

Our choice for the ionic model falls on a variant of the Mitchell–Schaeffer (MS) model [29] introduced by Djabella *et al.* [11].

$$\frac{\partial v}{\partial t} = f(v, w) + I_{stim}(t), \quad \text{with } f(v, w) = \frac{1}{\tau_{in}} w v^2 (1 - v) - \frac{1}{\tau_{out}} v, \tag{102}$$

$$\frac{\partial w}{\partial t} = g(v, w), \quad \text{with } g(v, w) = \frac{1}{\tau_k} [(1 - w_k)(1 - w) - w_k w], \tag{103}$$

$$\begin{aligned} \tau_k(v, v_{gate}) &= \tau_{open} + (\tau_{close} - \tau_{open}) w_k(v, v_{gate}) \\ w_k(v, v_{gate}) &= \frac{1}{2} (1 + \tanh(k(v - v_{gate}))), \end{aligned}$$

where k is a given parameter. In our calculation, we choose $k = 5, \tau_{open} = 120$ ms, $\tau_{close} = 150$ ms, $\tau_{in} = 0.3$ ms, $\tau_{out} = 6$ ms and $v_{gate} = 0.13$. These values provide a solution that is close to the solution of the standard MS model [29].

6.2. Numerical tests with a manufactured solution

To evaluate the convergence of the numerical method applied to the problem (1)–(6), we use the method of manufactured solutions, see *e.g.* [38]. We investigate the accuracy of the numerical method using mesh refinement. We consider a 2D domain consisting of the single cell Ω_i surrounded by the extracellular domain Ω_e , see (3):

$$\begin{aligned} \Omega_i &= (10, 110) \times (10, 30), \\ \Omega_e &= [(0, 120) \times (0, 40)] \setminus \overline{\Omega}_i. \end{aligned}$$

We assume that the conductivities σ_i and σ_e are scalar and we let $\sigma_i = \sigma_e = 1$. We implement our methods using the software Freefem++ and UMFPACK for solving linear systems. Our computations are carried on a desktop computer with a 4 core Intel(R) i7-3770 3.40GHz processor.

We consider the following activation function

$$\gamma(t) = \frac{1}{1 + e^{-at}},$$

for some real number a , and we let

$$u_{i,ex}(x, y, t) = 2\gamma(t) + \varepsilon[(x - x_0)^p + (y - y_0)^p], \tag{104}$$

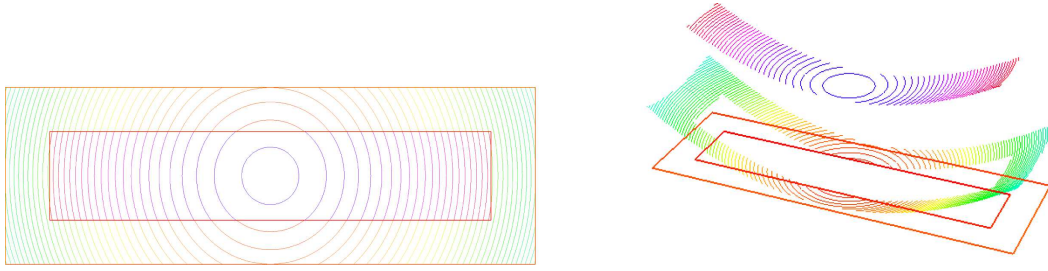


FIGURE 4. Contour plot and 3D graph of the manufactured solution for $p = 2$.

$$u_{e,\text{ex}}(x, y, t) = \gamma(t) + \varepsilon[(x - x_0)^p + (y - y_0)^p], \tag{105}$$

$$v_{\text{ex}}(x, y, t) = \gamma(t), \tag{106}$$

$$w_{\text{ex}}(x, y, t) = 2\gamma(-t), \tag{107}$$

where $p \geq 2$ is a given integer, (x_0, y_0) are the coordinates of the center of Ω_i , $\varepsilon = \varepsilon(t)$ is a given function that controls the magnitude of $z = (x - x_0)^p + (y - y_0)^p$. Figure 4 shows contour and 3D plots of the manufactured solution for $p = 2$. The stimulation currents $I_{i,\text{stim}}$ and $I_{e,\text{stim}}$ become:

$$I_{i,\text{stim,ex}} = \varepsilon p(p - 1)[(x - x_0)^{p-2} + (y - y_0)^{p-2}] \tag{108}$$

$$I_{e,\text{stim,ex}} = \varepsilon p(p - 1)[(x - x_0)^{p-2} + (y - y_0)^{p-2}]. \tag{109}$$

The problem (1)–(6) is then modified with source terms

$$-\nabla \cdot (\sigma_i \nabla u_i) = I_{i,\text{stim,ex}} \quad \text{in } \Omega_i, \tag{110}$$

$$-\nabla \cdot (\sigma_e \nabla u_e) = I_{e,\text{stim,ex}} \quad \text{in } \Omega_e, \tag{111}$$

$$s(x, y, t) := \frac{\partial v}{\partial t} + f(v, w) - I_m \quad \text{on } \Gamma, \tag{112}$$

$$\sigma_e \nabla u_e \cdot n_e = -\sigma_i \nabla u_i \cdot n_i = I_m \quad \text{on } \Gamma, \tag{113}$$

$$v = u_i - u_e \quad \text{on } \Gamma, \tag{114}$$

$$\sigma_e \nabla u_e \cdot n_e = g_e \quad \text{on } \Gamma_e, \tag{115}$$

where $p \geq 2$. It follows that

$$\begin{aligned} s(x, y, t) &= a\gamma(t)(1 - \gamma(t)) + f(v_{\text{ex}}, w_{\text{ex}}) - \sigma_e \nabla u_{e,\text{ex}} \cdot n_e, \\ g_{e,\text{ex}}(x, y, t) &= \sigma_e \nabla u_{e,\text{ex}} \cdot n_e, \end{aligned}$$

where the function $f(v, w)$ is defined in (102). The variational formulations (110)–(115) reads

$$\int_{\Omega_e} \sigma_e \nabla u_e(t) \cdot \nabla \varphi_e - \int_{\Gamma} \left(\frac{\partial v(t)}{\partial t} + f(v(t), w(t)) \right) \varphi_e = \int_{\Omega_e} I_{e,\text{stim,ex}} \varphi_e + \int_{\partial\Omega_e \setminus \Gamma} g_{e,\text{ex}} \varphi_e - \int_{\Gamma} s(x, y, t) \varphi_e, \tag{116}$$

$$\int_{\Omega_i} \sigma_i \nabla u_i(t) \cdot \nabla \varphi_i + \int_{\Gamma} \left(\frac{\partial v(t)}{\partial t} + f(v(t), w(t)) \right) \varphi_i = \int_{\Omega_i} I_{i,\text{stim,ex}} \varphi_i + \int_{\Gamma} s(x, y, t) \varphi_i, \tag{117}$$

$$\int_{\Gamma} \frac{\partial w(t)}{\partial t} \varphi - \int_{\Gamma} g(v(t), w(t)) \varphi = \int_{\Gamma} \frac{\partial w_{\text{ex}}(t)}{\partial t} \varphi - \int_{\Gamma} g(v_{\text{ex}}(t), w_{\text{ex}}(t)) \varphi, \tag{118}$$

for a.e. $t \in [0, T]$.

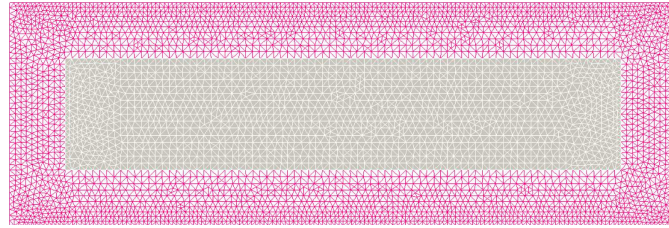


FIGURE 5. A 2D mesh of the domains Ω_e and Ω_i for $n = 10$.

TABLE 1. L^2 -norm errors with fixed $n = 10$, at the final time $T = N \times \Delta t = 0.8$ ms.

n	Δt	$\ u_{e,h}^N - u_{e,ex}\ _{L^2(\Omega_e)}$	$\ u_{i,h}^N - u_{i,ex}\ _{L^2(\Omega_i)}$	$\ v_h^N - v_{ex}\ _{L^2(\Gamma)}$	$\ w_h^N - w_{ex}\ _{L^2(\Gamma)}$
10	1.0e-03	5.25545e-04	6.47831e-04	2.25664e-04	1.91362e-06
10	5.0e-04	5.25544e-04	6.24351e-04	2.25007e-04	4.78142e-07
10	2.5e-04	5.25545e-04	6.18681e-04	2.24936e-04	1.19556e-07
10	1.25e-04	5.25543e-04	6.17272e-04	2.24917e-04	3.01018e-08

We estimate the errors between the fully discretized solutions $u_{i,h}^N, u_{e,h}^N, v_h^N$, and w_h^N and the exact solutions $u_{i,ex}, u_{e,ex}, v_{ex}$, and w_{ex} , respectively. We compute the L^2 -norms, $\|u_{i,h}^N - u_{i,ex}\|_{0,\Omega_i}, \|u_{e,h}^N - u_{e,ex}\|_{0,\Omega_e}, \|v_h^N - v_{ex}\|_{0,\Gamma}$ and $\|w_h^N - w_{ex}\|_{0,\Gamma}$, as well as the H^1 -norms $\|\nabla u_{e,h}^N - \nabla u_{e,ex}\|_{0,\Omega_e}$ and $\|\nabla u_{i,h}^N - \nabla u_{i,ex}\|_{0,\Omega_i}$, at the final time $T = N \times \Delta t = 0.8$ ms. In our computations, we take $\varepsilon = 0.0001$ and we let $a = 8$ to achieve a faster transient with an upstroke duration of about 1 ms. The manufactured solution corresponds to the second half of the upstroke. The domains Ω_e and Ω_i consist of $(16n) \times (4n)$ and $(8n) \times (2n)$ nodes on the sides of the subdomains, respectively, where n is a given integer. The mesh is fixed, unstructured and conformal on the interface Γ , see Figure 5.

The computation is performed for different spatial resolutions and time steps. Since we are interested in semidiscretization error in space, we shall determine a time step Δt for which the time error is significantly smaller than the space error. We fix $n = 10$. Starting with $\Delta t = 0.001$, we decrease the time-step Δt till the error in time is negligible compared to the error in space. Table 1 shows that Δt should be selected smaller than 0.0001 for the variables u_i, u_e and v . To study the convergence in space, we increase n . To ensure that the error in space remains dominant, we decrease Δt simultaneously. We assume that the error in space is proportional to h^p , where p is the convergence rate that can be estimated thanks to the formula

$$p \approx \frac{\log(|E_{2h}/E_h|)}{\log(2)}, \tag{119}$$

where E_h is the error associated to the step size h . Table 2 reports the results of the convergence tests on the variables u_e, u_i, v and w . We observe that the convergence rate is two for the error in the L^2 -norm for both $u_{e,h}$ and $u_{i,h}$, while it is between 1 and 2 on the variables v and w . Therefore, the rate of convergence obtained from our numerical test is better than what is shown in the theoretical estimate (89) for the L^2 -norm of the error on v . From Table 3, we observe that a first order convergence is achieved in the H^1 -norm for the variables $u_{e,h}$ and $u_{i,h}$, which is in agreement with the theoretical estimates (88).

7. CONCLUSION

The unusual coupling of PDEs and ODEs on the boundary makes the EMI model challenging to solve numerically. To get around this difficulty, we have reformulated the model on the interface using a Steklov–

TABLE 2. L^2 -norm errors with convergence rates in parentheses, at the final time $T = N \times \Delta t = 0.8$ ms.

n	Δt	$\ u_{e,h}^N - u_{e,ex}\ _{L^2(\Omega_e)}$	$\ u_{i,h}^N - u_{i,ex}\ _{L^2(\Omega_i)}$	$\ v_h^N - v_{ex}\ _{L^2(\Gamma)}$	$\ w_h^N - w_{ex}\ _{L^2(\Gamma)}$
10	1.0e-04	5.25543e-04	6.17104e-04	2.24914e-04	1.94744e-08
20	5.0e-5	1.30516e-04 (2.00)	1.49744e-04 (2.04)	6.04427e-05 (1.89)	4.93266e-09 (1.89)
40	2.5e-05	3.16817e-05 (2.04)	4.01872e-05 (1.89)	2.35998e-05 (1.36)	1.32895e-09 (1.89)
80	1.25e-05	7.15588e-06 (2.15)	8.87071e-06 (2.18)	8.41393e-06 (1.48)	3.81054e-10 (1.80)

TABLE 3. H^1 -seminorm errors with convergence rates in parentheses.

n	Δt	$\ \nabla u_{e,h}^N - \nabla u_{e,ex}\ _{L^2(\Omega_e)}$	$\ \nabla u_{i,h}^N - \nabla u_{i,ex}\ _{L^2(\Omega_i)}$
10	1.0e-04	3.80101e-03	3.84055e-03
20	5.0e-5	1.901220e-03 (0.99)	1.93780e-03 (0.99)
40	2.5e-05	9.433090e-04 (1.01)	9.66920e-04 (1.00)
80	1.25e-05	4.74793 e-04 (0.99)	4.88733e-04 (0.98)

Poincaré operator. We discretized the model in space using FEM. We proved the existence of semi-discrete solution and we derived stability and error estimates for FEM. From the numerical tests, the convergence rate is two for the error in the L^2 -norm for the intracellular and extracellular potentials $u_{i,h}$ and $u_{e,h}$, while it is between one and two on the membrane potential v and gating variable w . The theoretical estimates guarantee a convergence rate of at least one for the error in the L^2 -norm on the membrane potential v . The theoretical analysis of the L^2 -norm errors on the variables $u_{i,h}$ and $u_{e,h}$ was not investigated. However, a first order convergence is achieved in the H^1 -norm for the variables $u_{e,h}$ and $u_{i,h}$, which is in agreement with the theoretical estimates.

Acknowledgements. This work was supported by the Natural Sciences and Engineering Research Council (NSERC) through a scholarship to the first author from the CREATE program in Simulation-based Engineering Science (SBES, grant N₀ 481695-2016) and a Discovery Grant (N₀ RGPIN-2019-06855) to the second author. This work was partly supported by the Canadian Queen Elizabeth II Diamond Jubilee Scholarship Program (QES II) in partnership with the African Institute of Mathematical Sciences (AIMS-NEI).

REFERENCES

- [1] R.A. Adams and J.J.F. Fournier. Sobolev spaces, in *Pure and Applied Mathematics*. Elsevier Science (2003).
- [2] A. Agudelo-Toro and A. Neef, Computationally efficient simulation of electrical activity at cell membranes interacting with self-generated and externally imposed electric fields. *J. Neural Eng.* **10** (2013) 026019.
- [3] G. Akrivis, Stability of implicit and implicit-explicit multistep methods for nonlinear parabolic equations. *IMA J. Numer. Anal.* **38** (2017) 1768–1796.
- [4] U.M. Ascher, S.J. Ruuth and B.T.R. Wetton, Implicit-explicit methods for time-dependent partial differential equations. *SIAM J. Numer. Anal.* **32** (1995) 797–823.
- [5] P.-E. Bécue, *Modélisation et Simulation de L'électrophysiologie Cardiaque à L'échelle Microscopique*. Ph.D. thesis, Université de Bordeaux, France (2018).
- [6] C. Bernardi, Y. Maday and A.T. Patera, Domain decomposition by the mortar element method, in *Asymptotic and Numerical Methods for Partial Differential Equations with Critical Parameters*, Springer Netherlands (1993) 269–286.
- [7] H. Brezis, *Functional Analysis, Sobolev Spaces and Partial Differential Equations*. Springer (2010).
- [8] P.G. Ciarlet, *The Finite Element Method for Elliptic Problems*. Society for Industrial and Applied Mathematics, USA (2002).
- [9] E.D. Copene and J.P. Keener, Ephaptic coupling of cardiac cells through the junctional electric potential. *J. Math. Biol.* **57** (2008) 265–284.
- [10] M. Crouzeix and A.L. Mignot, *Analyse numérique des équations différentielles*. Vol. 1. Masson, Paris (1984).

- [11] K. Djabella, M. Landau and M. Sorine, A two-variable model of cardiac action potential with controlled pacemaker activity and ionic current interpretation. *46th IEEE Conference on Decision and Control*, New Orleans, LA, USA (2007) 5186–5191.
- [12] S. Domínguez, J. Reimer, K.R. Green, R. Zolfaghari and R.J. Spiteri, A simulation-based method to study the LQT1 syndrome remotely using the EMI model. In *Emerging Technologies in Biomedical Engineering and Sustainable TeleMedicine*. Springer International Publishing (2021) 179–189.
- [13] A. Ern and J.L. Guermond, Theory and practice of finite elements, in *Applied Mathematical Sciences*. Springer New York (2004).
- [14] D. Fokoué, *Numerical methods for the microscopic cardiac electrophysiology model*, Ph.D. thesis, Université d'Ottawa, Canada (2022).
- [15] P.C. Franzone and G. Savaré, Degenerate evolution systems modeling the cardiac electric field at micro- and macroscopic level, in *Evolution Equations, Semi-Groups and Functional Analysis*. Birkhäuser Basel (2002) 49–78.
- [16] P.C. Franzone, L.F. Pavarino and S. Scacchi, *Mathematical Cardiac Electrophysiology*. Vol. 13. Springer International Publishing (2014).
- [17] D.E. Goldman, Electrodiffusion in membranes, in *Membrane Transport: People and Ideas*. Springer, New York (1989) 251–259.
- [18] A.L. Hodgkin and A.F. Huxley, A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* **117** (1952) 500–544.
- [19] K.H. Jæger and A. Tveito, Deriving the bidomain model of cardiac electrophysiology from a cell-based model; properties and comparisons. *Front. Physiol.* **12** (2022) 811029.
- [20] K.H. Jæger, A.G. Edwards, A. McCulloch and A. Tveito, Properties of cardiac conduction in a cell-based computational model. *PLOS Comput. Biol.* **15** (2019) 1–35.
- [21] K.H. Jæger, A.G. Edwards, W.R. Giles and A. Tveito, From millimeters to micrometers; re-introducing myocytes in models of cardiac electrophysiology. *Front. Physiol.* **12** (2021) 763584.
- [22] K.H. Jæger, K.G. Hustad, X. Cai and A. Tveito, Efficient numerical solution of the EMI model representing the extracellular space (E), cell membrane (M) and intracellular space (I) of a collection of cardiac cells. *Front. Phys.* **8** (2021) 579461.
- [23] J.P. Keener and J. Lin, Ephaptic coupling in cardiac myocytes. *IEEE Trans. Biomed. Eng.* **60** (2013) 576–582.
- [24] J. Lin and J.P. Keener, Modeling electrical activity of myocardial cells incorporating the effects of ephaptic coupling. *Proc. Natl. Acad. Sci.* **107** (2010) 20935–20940.
- [25] J. Lin and J.P. Keener, Microdomain effects on transverse cardiac propagation. *Biophys. J.* **106** (2014) 925–931.
- [26] J.-L. Lions, Quelques méthodes de résolution des problèmes aux limites non linéaires, in *Etudes Mathématiques*. Dunod (1969).
- [27] J.-L. Lions and E. Magenes, Problèmes aux limites non homogènes et applications, in *Travaux et recherches mathématiques*. Dunod (1968).
- [28] C.H. Luo and Y. Rudy, A model of the ventricular cardiac action potential: depolarization, repolarization, and their interaction. *Circ. Res.* **68** (1991) 1501–1526.
- [29] C.C. Mitchell and D.G. Schaeffer, A two-current model for the dynamics of cardiac membrane. *Bull. Math. Biol.* **65** (2003) 767–793.
- [30] Y. Mori and C.S. Peskin, A numerical method for cellular electrophysiology based on the electrodiffusion equations with internal boundary conditions at membranes. *Commun. Appl. Math. Comput. Sci.* **4** (2009) 85–134.
- [31] J.C. Neu and W. Krassowska, Homogenization of syncytial tissues. *Crit. Rev. Biomed. Eng.* **21** (1993) 137–199.
- [32] S. Niederer, L. Mitchell, N. Smith and G. Plank, Simulating human cardiac electrophysiology on clinical time-scales. *Front. Physiol.* **2** (2011) 14.
- [33] L. Perko, *Differential Equations and Dynamical Systems*. Springer-Verlag, Berlin, Heidelberg (1991).
- [34] J.B. Picone, N. Sperlakis and J.E. Mann, Expanded model of the electric field hypothesis for propagation in cardiac muscle. *Math. Comput. Model.* **15** (1991) 17–35.
- [35] A. Quarteroni and A. Valli, *Numerical Approximation of Partial Differential Equations*, 2nd edition. Springer, Berlin, New York (1997).
- [36] P.A. Raviart and J.M. Thomas, A mixed finite element method for second order elliptic problems. *Mathematical Aspects of Finite Element Methods*. Vol. 606. Springer, Berlin, Heidelberg (1977) 292–315.
- [37] P.-A. Raviart and J.-M. Thomas, *Introduction à l'analyse Numérique des Équations aux Dérivées Partielles*. Masson (1983).
- [38] P.J. Roache, *Verification and Validation in Computational Science and Engineering*. Hermosa Publishers (1998).
- [39] S.F. Roberts, J.G. Stinstra, and C.S. Henriquez, Effect of nonuniform interstitial space properties on impulse propagation: a discrete multidomain model. *Biophys. J.* **95** (2008) 3724–3737.
- [40] S.J. Ruuth, Implicit-explicit methods for reaction-diffusion problems in pattern formation. *J. Math. Biol.* **34** (1995) 148–176.
- [41] N. Sperlakis, An electric field mechanism for transmission of excitation between myocardial cells. *Circ. Res.* **91** (2002) 985–987.
- [42] N. Sperlakis and K. McConnell, Electric field interactions between closely abutting excitable cells. *IEEE Eng. Med. Biol. Mag.* **21** (2002) 77–89.
- [43] J.G. Stinstra, B. Hopenfeld and R.S. MacLeod, On the passive cardiac conductivity. *Ann. Biomed. Eng.* **33** (2005) 1743–1751.
- [44] J.G. Stinstra, S.F. Roberts, J.B. Pormann, R.S. MacLeod and C.S. Henriquez, A model of 3D propagation in discrete cardiac tissue. *Comput. Cardiol.* **33** (2006) 41–44.
- [45] J. Stinstra, R. MacLeod and C. Henriquez, Incorporating histology into a 3D microscopic computer model of myocardium to study propagation at a cellular level. *Ann. Biomed. Eng.* **38** (2010) 1399–1414.

- [46] J. Sundnes, G.T. Lines, X. Cai, B.F. Nielsen, K.A. Mardal and A. Tveito, *Computing the Electrical Activity in the Heart*. Vol. 1, 1st edition. Springer Berlin Heidelberg (2006).
- [47] V. Thomée, *Galerkin Finite Element Method for Parabolic Problems*. Vol. 1054. Springer-Verlag (2006).
- [48] L. Tung, *A Bi-domain Model for Describing Ischemic Myocardial D-C Potentials*, Ph.D. thesis, MIT, Cambridge, MA (1978).
- [49] A. Tveito, K.-A. Mardal and M.E. Rognes, *Modeling Excitable Tissue the EMI Framework*, Vol. 7. Springer International Publishing, Cham (2021).
- [50] A. Tveito, K.H. Jæger, M. Kuchta, K-A. Mardal and M.E. Rognes, A cell-based framework for numerical modeling of electrical conduction in cardiac tissue. *Front. Phys.* **5** (2017) 48.
- [51] A. Tveito, K.H. Jæger, G.T. Lines, L. Paszkowski, J. Sundnes, A.G. Edwards, T. Mäki-Marttunen, G. Halmes and G.T. Einevoll, An evaluation of the accuracy of classical models for computing the membrane potential and extracellular potential for neurons. *Front. Comput. Neurosci.* **11** (2017) 27.
- [52] M. Veneroni, Reaction diffusion systems for the microscopic cellular model of the cardiac electric field. *Math. Methods Appl. Sci.* **29** (2006) 1631–1661.



Please help to maintain this journal in open access!

This journal is currently published in open access under the Subscribe to Open model (S2O). We are thankful to our subscribers and supporters for making it possible to publish this journal in open access in the current year, free of charge for authors and readers.

Check with your library that it subscribes to the journal, or consider making a personal donation to the S2O programme by contacting subscribers@edpsciences.org.

More information, including a list of supporters and financial transparency reports, is available at <https://edpsciences.org/en/subscribe-to-open-s2o>.