# Reaction-Diffusion systems for the microscopic cellular model of the cardiac electric field*

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**Abstract.** The paper deals with a mathematical model for the electric activity of the heart at microscopic level. The membrane model used to describe the ionic currents is a generalization of the phase-I Luo-Rudy, a model widely used in 2-D and 3-D simulations of the action potential propagation. From the mathematical viewpoint the model is made up of a parabolic reaction diffusion system coupled with an ODE system. We derive existence and some regularity results.

**Key words:** Reaction-diffusion equations, modelization of the cardiac electric field, degenerate evolution equations.

**AMS Subject Classification:** 35K57 (93A30, 35K65, 92C30)

## 1 Introduction and main result

The aim of this paper is to study the reaction-diffusion systems arising from the mathematical models of the electric activity of cardiac ventricular cells, at microscopic level. The models we analyze are widely used in medical and bioengineering works, in numerical simulations, and they constitute the bases for present research and more and more accurate and complex modelizations. Nevertheless, up to now, a rigorous mathematical analysis regarding the well posedness of these models is still lacking. In this paper we prove the existence for a solution of a wide class of models, including the classical Hodgkin-Huxley model [16], the first membrane model for ionic currents in an axon, and the Phase-I Luo-Rudy (LR1) model [28], which is one of the most widely used models in two-dimensional and three-dimensional simulations of the cardiac action potential propagation, and laid the basis for the modern dynamical models.

The contraction of the heart muscle is initiated by an electric signal starting in the sinoatrial node, see e.g. [22, ch. 11], [23]. The electrical signal then travels along a special type of cells known as Purkinje fibres, through the atria and the ventricula. When the muscle cells are stimulated electrically, they rapidly depolarize, *i.e.,* the electrical potential inside the cell is changed. The depolarization causes the contraction of the cells and the electrical signal is also passed on to the neighbouring cells. This reaction causes an electric field to be created in the heart and the body. The measurement of this field on the body surface is called the electrocardiogram (ECG). In order to achieve

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realistic simulations of these measurements, it is important to study how the electric signal is created in the heart and how it is conducted through the heart and body tissue. The conduction in the body tissue and, more generally, in biological systems, is a vast field of present research, see e.g. [22, 13, 19, 2, 3, 5, 4].

The dynamics inside the heart are much complex, mainly, due to the different anisotropy of the intracellular and the extracellular tissue, to the excitability of the heart muscle cells and to the great variety of different cell and ionic channels types. The electric behaviour of the membrane of excitable cells has been widely investigated in the last fifty years, and the modeling of the ionic currents in the ventricular myocardium, in particular, has undergone a continuous development from the paper by Beeler and Reuter [7], in 1977, to nowadays: [28, 27, 12], for example, study guinea pigs, [38, 14, 17] focus on canine cells, [37, 32] concentrate on the human myocardium, while [30] is a review of the development of cardiac ventricular models (we cite only a few examples, but we remark that the literature concerning the modelization of the cardiac action potential, in different species and with different pathologies, is impressively rich).

Moreover, recent theoretical and computational advanced studies in electrocardiology investigating the electrical behaviour of the anisotropic cardiac tissue are based on the macroscopic *bidomain model* [33, 15, 8, 9, 23]. A rigorous mathematical derivation of the *bidomain model* can be obtained [31] directly from the microscopic properties of the tissue. We defer the treatment of the well posedness problem in the macroscopic bidomain model to a forthcoming paper.

From the mathematical viewpoint, the problem consists of a Poisson equation on two adjoining domains, coupled with a dynamic condition, involving a system of ODEs, on the intersection of the boundaries. We remark that standard techniques and results on reaction diffusion systems (see e.g. [36, 1]), cannot be directly exploited in the case of microscopic models of the cardiac electric field, due to their degenerate structure, to the unusual coupling of PDEs and ODEs on the boundary and to the lack of a maximum principle. We will give more details about the mathematical difficulties after the description of the model.

***The microscopic structure of the cardiac tissue.*** At a microscopic level the cardiac structure is composed of a collection of elongated cardiac cells, endowed with special electric (mainly end-to-end) connections, named *gap junctions*, embedded in the extracellular fluid. The *gap junctions* form the long fiber structure of the cardiac muscle, whereas the presence of lateral junctions establishes a connection between the elongated fibers. Since the interconnection between cells has resistance comparable to that of the intra-cellular volume, we can consider the cardiac tissue as a single isotropic intramural connected domain $\Omega_i$ separated from the extra-cellular fluid $\Omega_e$ by a membrane surface $\Gamma$.

***The geometry and the main physical quantities and variables.*** We call

$\Omega_i$ the intra-cellular domain,

$\Omega_e$ the extra-cellular domain,

$\overline{\Gamma} = \partial\Omega_i \cap \partial\Omega_e$ the cellular membrane,

$\Omega := \Omega_i \cup \Omega_e \cup \Gamma \in \mathbb{R}^3$ the physical region occupied by the heart.

We denote by

$u_{i,e} : \overline{\Omega}_{i,e} \to \mathbb{R}$, the intra- and extra-cellular electric potentials,
$v := u_i - u_e : \Gamma \to \mathbb{R}$, the transmembrane potential,
$\mathbf{w} : \Gamma \to \mathbb{R}^k$, the vector of the gating variables,
$\mathbf{z} : \Gamma \to \mathbb{R}^m$, the vector of the intracellular ionic concentrations,
$\sigma_{i,e} : \overline{\Omega}_{i,e} \to \mathbb{M}^{3\times 3}$, the intra- and extra-cellular conductivities,
which are *symmetric, positive definite, continuous* tensors, and satisfy the uniform ellipticity condition:

$$\exists\, \underline{\sigma}, \overline{\sigma} > 0 : \quad \underline{\sigma}|\xi|^2 \le \sigma_{i,e}(x)\xi \cdot \xi \le \overline{\sigma}|\xi|^2, \qquad \forall\, \xi \in \mathbb{R}^3,\ \forall\, x \in \Omega_{i,e}. \tag{1.1}$$

***Basic equations.*** (See e.g. [22, ch. 11.3], [20, 21]) Imposing the conservation of currents, we have that the normal current flux through the membrane is continuous: if $\nu_i, \nu_e$ denote the unit exterior normals to the boundary of $\Omega_i$ and $\Omega_e$ respectively, satisfying $\nu_i = -\nu_e$ on $\Gamma$, we have

$$\sigma_i \nabla u_i \cdot \nu_i + \sigma_e \nabla u_e \cdot \nu_e = 0, \qquad \text{on } \Gamma. \tag{1.2}$$

Denoting by $I_i^s, I_e^s$ the (given) stimulation currents applied to the intra- and extra-cellular space, we have

$$-\mathrm{div}(\sigma_i \nabla u_i) = I_i^s, \quad \text{in } \Omega_i, \qquad -\mathrm{div}(\sigma_e \nabla u_e) = I_e^s, \quad \text{in } \Omega_e. \tag{1.3}$$

On the other hand, since the only active source elements lie on the membrane $\Gamma$, each flux equals the membrane current per unit area $I_m$, which consists of a capacitive and a ionic term (see [22, ch. 2],[18])

$$\sigma_e \nabla u_e \cdot \nu_e + I_m = -\sigma_i \nabla u_i \cdot \nu_i + I_m = 0, \tag{1.4}$$

where $I_m$, modeling the membrane as an RC circuit, may be expressed as

$$\boxed{I_m := C_m \partial_t v + I_{ion}(v,t),} \qquad \text{on } \Gamma, \tag{1.5}$$

where $C_m$ is the surface capacitance of the membrane and $I_{ion}$ is the ionic current. We remark that $\Gamma$ is a discontinuity surface for the potential. In order to complete the model, we need a description of the ionic current $I_{ion}$ which appears in (1.5). We defer to the end of this section an explanation of the structure of the ionic current and the consequent motivation of the following mathematical hypothesis upon $I_{ion}$.

***The ionic current.*** In this work we assume that the ionic current

$$\begin{aligned} I_{ion} : \mathbb{R} \times \mathbb{R}^k \times (0,+\infty)^m &\to \mathbb{R}, \\ (v, \mathbf{w}, \mathbf{z}) &\to I_{ion}(v, \mathbf{w}, \mathbf{z}) \end{aligned}$$

has the general form:

$$I_{ion}(v, \mathbf{w}, \mathbf{z}) := \sum_{i=1}^{m} \left(J_i(v, \mathbf{w}, \log z_i)\right) + \tilde{H}(v, \mathbf{w}, \mathbf{z}), \tag{1.6}$$

where, $\forall\, i = 1, \dots, m$,

$$J_i \in C^1\left(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}\right), \tag{1.7a}$$

$$0 < \underline{G}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} J_i(v, \mathbf{w}, \zeta) \leq \overline{G}(\mathbf{w}), \tag{1.7b}$$

$$\left| \frac{\partial}{\partial v} J_i(v, \mathbf{w}, 0) \right| \leq L_v(\mathbf{w}), \tag{1.7c}$$

$\underline{G}, \overline{G}, L_v$ belong to $C^0(\mathbb{R}^k, \mathbb{R}_+)$, and

$$\tilde{H} \in C^0(\mathbb{R} \times \mathbb{R}^k \times (0, +\infty)^m) \cap \text{ Lip}(\mathbb{R} \times [0,1]^k \times (0, +\infty)^m). \tag{1.8}$$

***The dynamics of the gating variables*** are described by the system of ODE's

$$\frac{\partial w_j}{\partial t} = F_j(v, w_j), \qquad j = 1, \dots, k. \tag{1.9}$$

We assume that

$$F_j : \mathbb{R}^2 \to \mathbb{R} \text{ is locally Lipschitz continuous;} \tag{1.10a}$$

$$F_j(v, 0) \geq 0, \quad \forall\, v \in \mathbb{R}; \tag{1.10b}$$

$$F_j(v, 1) \leq 0, \quad \forall\, v \in \mathbb{R}, \tag{1.10c}$$

$\forall\, j = 1, \dots, k$.

In the models considered $F_j$ has the particular form

$$F_j(v, w_j) := \alpha_j(v)(1 - w_j) - \beta_j(v) w_j, \qquad j = 1, \dots, k,$$

where $\alpha_j$ and $\beta_j$ are positive rational functions of exponentials in $v$. A general expression for both $\alpha_j$ and $\beta_j$ is given by

$$\frac{C_1 e^{\frac{v - v_n}{C_2}} + C_3(v - v_n)}{1 + C_4 e^{\frac{v - v_n}{C_5}}},$$

where $C_1, C_3, C_4, v_n$ are non-negative constants and $C_2, C_5$ are positive constants.

***The dynamics of the ionic concentrations*** are described by the system of ODE's

$$\frac{\partial z_i}{\partial t} = G_i(v, \mathbf{w}, \mathbf{z}) := -J_i(v, \mathbf{w}, \log z_i) + H_i(v, \mathbf{w}, \mathbf{z}), \qquad i = 1, \dots, m, \tag{1.11}$$

where $J_i$ is the function described in (1.7a, 1.7b, 1.7c) and

$$H_i \in C^0(\mathbb{R} \times \mathbb{R}^k \times (0, +\infty)^m) \cap \text{ Lip}(\mathbb{R} \times [0,1]^k \times (0, +\infty)^m), \qquad i = 1, \dots, m. \tag{1.12}$$

We refer to (1.2)-(1.6), (1.9), (1.11) as the equations of the *microscopic model*, together with Neumann boundary conditions imposed on $u_i, u_e$ on the remaining part of the boundaries $\Gamma_{i,e} := \partial\Omega_{i,e}\setminus\Gamma$

$$\sigma_i \nabla u_i \cdot \nu_i = g_i, \quad \text{on } \Gamma_i, \qquad \sigma_e \nabla u_e \cdot \nu_e = g_e, \quad \text{on } \Gamma_e,$$

or with Dirichlet boundary conditions

$$u_i = 0 \quad \text{on } \Gamma_i, \qquad u_e = 0 \quad \text{on } \Gamma_e,$$

and with the (degenerate with respect to $v$) initial Cauchy condition

$$v(x,0) = v_0(x), \qquad \mathbf{w}(x,0) = \mathbf{w}_0(x), \qquad \mathbf{z}(x,0) = \mathbf{z}_0(x), \qquad \text{on } \Gamma.$$

Thus our problem is made up of two adjoining open domains with their boundaries partly intersecting, of a Poisson equation in each of them and, on the common boundary, of a system of equations connecting the fluxes and the difference of potentials. In contrast to classical problems for the Poisson equation with a jump discontinuity for normal derivatives across some surface, here $\Gamma$ is a discontinuity surface for the potential and the related conditions are dynamic and involve the assistant variables $w_j$, $z_i$ in a nonlinear way.

***The complete formulation.*** In order to give a complete formulation of the problem, let us suppose that $\Omega_{i,e}$ are bounded, Lipschitz domains, that $\Omega_i$ is connected (since we are going to put Neumann boundary conditions on $\Omega_i$), that $\Gamma$ is a Lipschitz surface and that $\sigma_i, \sigma_e$ are measurable. We fix $]0,T[$ as the evolution time interval, and we define the associated space-time domains following the usual notation of [26]

$$Q_{i,e} := \Omega_{i,e}\times]0,T[, \qquad \Sigma := \Gamma\times]0,T[, \qquad \Sigma_{i,e} := \Gamma_{i,e}\times]0,T[.$$

We denote the vectors by boldface letters (so that $\mathbf{F} = (F_1,\dots,F_k)$, $\mathbf{G} = (G_1,\dots,G_m)$, and so on). Moreover, for sake of simplicity, we choose Neumann boundary conditions on $\Gamma_i$ and homogeneous Dirichlet boundary conditions on $\Gamma_e$. We also define the space

$$H^1_{\Gamma_e^0}(\Omega_e) := \left\{ u \in H^1(\Omega_e) : u(x)_{|\Gamma_e} = 0, \text{ a.e.} \right\}.$$

*Remark* 1. The result stated in Theorem 1.1 would be identical if we made the widely used choice of Neumann conditions on both boundaries $\Gamma_i$ and $\Gamma_e$. In this case, we should ask for both domains to be connected and the potentials $u_i, u_e$ would result defined up to an additive constant.

The formal statement of the microscopic model is then:

**Problem (m).** Given

$$I^s_{i,e} : Q_{i,e} \to \mathbb{R}, \qquad g_i : \Sigma_i \to \mathbb{R},$$
$$v_0 : \Gamma \to \mathbb{R}, \qquad \mathbf{w}_0 : \Gamma \to \mathbb{R}^k, \qquad \mathbf{z}_0 : \Gamma \to (0,+\infty)^m,$$

we seek

$$u_{i,e} : Q_{i,e} \to \mathbb{R}, \qquad \mathbf{w} = (w_1, \dots, w_k) : \Sigma \to \mathbb{R}^k,$$

$$v := u_i - u_e : \Sigma \to \mathbb{R}, \qquad \mathbf{z} = (z_1, \dots, z_m) : \Sigma \to (0, +\infty)^m,$$

satisfying the equations on $Q_{i,e}$ and $\Sigma_{i,e}$

$$\begin{aligned} -\mathrm{div}(\sigma_{i,e}\nabla u_{i,e}) &= I^s_{i,e} && \text{on } Q_{i,e}, \\ \sigma_i \nabla u_i \cdot \nu_i &= g_i && \text{on } \Sigma_i, \\ u_e &= 0 && \text{on } \Sigma_e, \end{aligned} \tag{1.13}$$

and the evolution system on the surface $\Sigma$

$$C_m \partial_t v + I_{ion}(v, \mathbf{w}, \mathbf{z}) = -\sigma_i \nabla u_i \cdot \nu_i \qquad \text{on } \Sigma, \tag{1.14a}$$

$$C_m \partial_t v + I_{ion}(v, \mathbf{w}, \mathbf{z}) = \sigma_e \nabla u_e \cdot \nu_e \qquad \text{on } \Sigma, \tag{1.14b}$$

$$\partial_t \mathbf{w} = \mathbf{F}(v, \mathbf{w}) \qquad \text{on } \Sigma, \tag{1.14c}$$

$$\partial_t \mathbf{z} = \mathbf{G}(v, \mathbf{w}, \mathbf{z}) \qquad \text{on } \Sigma, \tag{1.14d}$$

with initial data

$$v(x, 0) = v_0(x) \qquad \text{on } \Gamma, \tag{1.15a}$$

$$\mathbf{w}(x, 0) = \mathbf{w}_0(x) \qquad \text{on } \Gamma, \tag{1.15b}$$

$$\mathbf{z}(x, 0) = \mathbf{z}_0(x) \qquad \text{on } \Gamma. \tag{1.15c}$$

In the following part, the expression ‘ $\mathbf{log\,z}$’ stands for the vector $(\log z_1, \dots, \log z_m)$ and ‘$\mathbf{z\,log\,z}$’ is not a scalar product, but represents the vector $(z_1 \log z_1, \dots, z_m \log z_m)$. We can now state our main result concerning the existence of a variational solution of Problem **m**.

**Theorem 1.1.** *Let be given the data*

$$v_0 \in H^{1/2}(\Gamma), \qquad \mathbf{w}_0 : \Gamma \to [0,1]^k \quad \textit{measurable},$$

$$\mathbf{z}_0 \in (L^2(\Gamma))^m, \quad \textit{with} \quad \mathbf{log\,z}_0 \in (L^2(\Gamma))^m,$$

$$I^s_{i,e} \in H^1(0, T; L^2(\Omega_{i,e})), \qquad g_i \in H^1(0, T; H^{-1/2}(\Gamma_i)),$$

*the ionic currents $I_{ion}(v, \mathbf{w}, \mathbf{z})$, satisfying (1.6–1.8), the dynamics of the gating variables $\mathbf{F}(v, \mathbf{w})$, satisfying (1.9–1.10c), the dynamics of the ionic concentrations $\mathbf{G}(v, \mathbf{w}, \mathbf{z})$, satisfying (1.11), (1.12).*

*Then, there exist $k + m + 2$ functions $w_1, \dots, w_k,\ z_1, \dots, z_m,\ u_i,\ u_e$,*

$$u_i \in L^2(0, T; H^1(\Omega_i)), \qquad u_e \in L^2(0, T; H^1_{\Gamma^0_e}(\Omega_e)),$$

$$v := u_{i|\Gamma} - u_{e|\Gamma} \ \in H^1(0, T; L^2(\Gamma)) \cap L^2(0, T; H^{1/2}(\Gamma)),$$

$$\mathbf{w} : \Sigma \to [0,1]^k \ \textit{measurable}, \qquad \mathbf{z} : \Sigma \to (0, +\infty)^m \ \textit{measurable},$$

$$w_j(x,\cdot) \in C^1(0,T) \cap C^0([0,T]) \quad \textit{for a.e. } x \in \Gamma, \qquad j = 1,\dots,k,$$
$$z_i(x,\cdot) \in C^1(0,T) \cap C^0([0,T]) \quad \textit{for a.e. } x \in \Gamma, \qquad i = 1,\dots,m,$$
$$\mathbf{w} \in L^2(\Gamma; C^0([0,T]))^k, \quad \mathbf{z} \in H^1(0,T; L^2(\Gamma))^m, \quad \mathbf{log}(\mathbf{z}) \in L^2(\Gamma; C^0([0,T])^m,$$

*which solve* Problem $\mathbf{m}$.

***Steps of the proof and plan of the paper.*** The proof of the existence is divided into three parts. In a first step we consider $v$ as an assigned function on $\Sigma$ and we solve the ODE system of the gating variables (1.14c) and the ODE system of the concentration variables (1.14d), obtaining suitable a priori estimates and qualitative properties of the solution (Section 2).

In the second step we write a variational formulation for the remaining part of the model, which leads to a reaction-diffusion equation of degenerate parabolic type in a classical Hilbert triple, and we solve the parabolic equation considering $I_{ion}(v, \mathbf{w}, \mathbf{z})$ as a known function (Section 3).

Then, by choosing the correct functional spaces for $\mathbf{w}, \mathbf{z}$ and $v$, it is possible to find existence for a solution $(v, \mathbf{w}, \mathbf{z})$ using Schauder Fixed Point Theorem (Section 4). Continuity of the fixed point operator is obtained by means of a classical interpolation inequality combined with an infinite dimensional version of a theorem on the continuity of Nemitski operators.

The main difficulties in the parabolic equation reside in its degenerate structure, which reflects the differences in the anisotropy of the intra- and extra-cellular tissues, and in the lack of a maximum principle. The latter, in addition, forbids a distributional formulation for the gating variables ODEs, because $v$ appears as argument for exponential functions in $F_j$ (equation 1.14c) and since $v \notin L^\infty$, we do not know if $F_j(v) \in L^1_{loc}$ and the equation cannot be taken in the sense of distributions. Moreover, the concentration variables $z_i$ appear as argument of a logarithm, both in the dynamics of the concentrations and in the ionic currents, and therefore it is necessary to bound $\mathbf{z}$ far from zero. Again, the task of finding an estimate for $\log z$ in $L^\infty$, is complicated by the absence of an estimate for $v$ in $L^\infty$, due to the lack of a maximum principle in the degenerate parabolic equation.

We conclude this section with a description of the structure of the ionic currents.

***Membrane models and ionic currents.*** The first membrane model for ionic currents was given in the celebrated work on nerve action potential by Alan Hodgkin and Andrew Huxley [16], work that earned them the Nobel prize in Medicine in 1963. Models of Hodgkin-Huxley type have been later developed for the cardiac action potential. In these models, (see, for example, [29, 7, 28, 27, 38, 37]) the ionic current through channels of the membrane depends on

- the transmembrane potential $v$;
- $k$ gating variables (introduced by Hodgkin and Huxley), $(w_1, \dots, w_k) =: \mathbf{w}$;
- $m$ intracellular ionic concentrations, $(z_1, \dots, z_m) =: \mathbf{z}$.

In general, $I_{ion}$ may be expressed as the sum of several contributions. The simplest expression for the ionic current that satisfies the Nernst principle (see e.g. [22, ch. 2.6]), is a linear model, giving the current as

$$I_{ion} = \sum_S I_S, \qquad I_S = I_S(v) = \bar{G}_S(v - E_S),$$

where $S = Na^+, K^+, Ca^{2+}, \ldots$ are the different ionic species and $\bar{G}_S$ is the constant membrane conductivity of the specific channel. $E_S$ is the related equilibrium (Nernst) potential and is given by

$$E_S = \bar{C}_S \log \frac{[S]_e}{[S]_i}, \tag{1.16}$$

where $\bar{C}_S$ is a constant and $[S]_{i,e}$ are the intracellular and extracellular concentrations for the ion S.

In the original model for nerve cells by Hodgkin and Huxley, the conductivities are not constant anymore, but depend on the gating variables $\mathbf{w}$. Each contribution has the form

$$I_S^{(1)} = I_S^{(1)}(v, \mathbf{w}) = G_S(\mathbf{w})(v - E_S),$$

$$G_S(\mathbf{w}) := \bar{G}_S \prod_{j=1}^{k} w_j^{p_{j,S}}$$

where $\bar{G}_S$ is the (constant) maximum membrane conductivity, $S = Na^+, K^+, L$ ($L$ is a non-specified leakage current) and the exponents $p_{j,S}$ are nonnegative integers.

In some models, the variation of $[Ca^{2+}]_i$ is considered [7, 28], while other more recent descriptions consider the variation of the internal concentration of all the ionic species [27, 38, 37], so that $[S]_i$ becomes an unknown in the model, which we denote by $z_S$, and its dynamics are described by the system of ordinary differential equations:

$$\frac{d}{dt} z_S = -\gamma_S \sum_j I_{S_j}, \tag{1.17}$$

where $\gamma_S$ is a constant depending on the geometry of the cell, and $I_{S_j}$ are the currents which carry the ion $S$. In these models, the contribution by the ion $S$ to the $\mathbf{w}$-gated, time-dependent current, becomes

$$I_S^{(2)} = I_S^{(2)}(v, \mathbf{w}, z_S) = G_S(\mathbf{w})(v - E_S(z_S)),$$

where $E_S$ is given by (1.16). To be precise, there are also currents like the $Ca^{2+}$ and $Na^+$ background currents [27, 38, 37], the ($K^+$) background current [28] or the ATP-sensitive $K^+$ current [34], which are not gated by $\mathbf{w}$, so that

$$I_S^{(3)} = I_S^{(3)}(v, \mathbf{w}, z_S) = G_S(\mathbf{w})(v - E_S(z_S)) + \underline{G}_S(v - E_S(z_S)), \tag{1.18}$$

$\underline{G}_S$ constant.

*Remark* 2. The presence of these background currents, which may not be quantitatively relevant in itself, prevents the term $I_S$ from disappearing when $\mathbf{w}$ becomes zero, and henceforward protects equation (1.17) from the flaw of degeneracy.

*Remark* 3. In the particular case of the phase–I Luo–Rudy model [28], the simple background current $I_b$ does not take into account the variation in the internal Calcium concentration. We remark that any of the subsequent models involving Calcium dynamics does include a Calcium background current with the needed shape ($I_{bCa} = \underline{G}\,(v - E(z))$), and that the LR1 model, with this addition, satisfies all our assumptions.

In some cases, instead of the time-dependent gating $G_S(\mathbf{w})$, there is a gating function $K_S$ depending directly on the membrane potential $v$:

$$I_S^{(3bis)} = I_S^{(3bis)}(v, z_S) = K_S(v)(v - E_S(z_S)). \tag{1.19}$$

In the LR1 model, where the concentrations $[K^+]_i$ and $[Na^+]_i$ are constant, the time-dependent Potassium current has the particular form

$$I_K = I_K(v, \mathbf{w}) = X(\mathbf{w})X_i(v)(v - \bar{E}), \tag{1.20}$$

where $X$ is a continuous function of $\mathbf{w}$, $X_i(v)v$ is a Lipschitz function and $\bar{E} = E_K$ is a constant. Owing to (1.18), (1.19) and (1.20) we will consider a current with the form

$$I_S^{(4)} = I_S^{(4)}(v, \mathbf{w}, z_S) = (G_S(\mathbf{w}) + \underline{G}_S + K_S(v))\,(v - E_S(z_S)) + X(\mathbf{w})X_i(v)(v - \bar{E}). \tag{1.21}$$

In the mathematical analysis, we describe $I_S^{(4)}$ by means of a general $C^1$ function $J_S = J_S(v, \mathbf{w}, \log z_S)$. The assumptions (1.7b,1.7c) on $J_S$ reflect

- the monotonicity of $I_S^{(4)}(v, \mathbf{w}, \log z_S)$, with respect to $\log z_S$,
- the linear growth of the term $(G_S(\mathbf{w}) + \underline{G}_S + K_S(v) + X(\mathbf{w})X_i(v))\,v$, with respect to $v$.

In fact, we remark that if $K_S, X_i$ are continuously differentiable, bounded, and their derivatives decrease fast enough as $|v| \to +\infty$, then $K_S(v)v, X_i(v)v$ are Lipschitz functions. This is, for example, the case of the $K^+$ Plateau function in [27, 38, 37] and of all the Potassium currents in [28].

Moreover, any model for the cardiac action potential takes into account (more or less explicitly) the ionic exchanges due to other non–Hodgkin–Huxley–type dynamics, such as: $Ca^{2+}$ current through the L-type channel, $Na^+$-$Ca^{2+}$ exchanger, $Na^+$-$K^+$ pump, currents through the sarcolemma, and other. We assume that the remaining part of the ionic current carrying the ion $S$ may be approximated by a Lipschitz function $H_S := H_S(v, \mathbf{w}, \mathbf{z})$, so that the structure of (1.21) becomes

$$I_S^{(5)}(v, \mathbf{w}, z_S) = J_S(v, \mathbf{w}, \log z_S) + H_S(v, \mathbf{w}, \mathbf{z}), \tag{1.22}$$

(this assumption is satisfied, for example, by the $Na^+$-$K^+$ pump and by the nonspecific $Ca$-activated currents, but not by the $Na^+$-$Ca^{2+}$ exchanger, see e.g. [27]). The variation of $z_S = [S]_i$ is then completely described by (1.22). But not all these contributions flow into the final $I_{ion}$, because a part of $H_S$ may take place inside the cell (through the sarcolemma) instead of between the intra- and extracellular medium [27, 37];

$$H_S \;=\; \underbrace{\tilde{H}_S}_{\text{intra-extracell. exchange}} \;+\; \underbrace{h_S.}_{\text{internal flow}}$$

In order to take into account this difference, we shall call $\tilde{H}_S$ the non-Hodgkin-Huxley-type current in $I_{ion}$ and we shall suppose that $\tilde{H}_S$ enjoys the same structural properties of $H_S$.

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## 2 The ODE systems

### 2.1 The gating variables

Our first step will be to show that, for every $v \in H^1(0,T;L^2(\Gamma))$, there exists a unique $\mathbf{w} = (w_1, \dots, w_k)$, measurable, which solves equations (1.14c), (1.15b)

$$\begin{cases} \dfrac{\partial \mathbf{w}}{\partial t} = \mathbf{F}(v, \mathbf{w}), & \text{on } \Sigma, \\ \mathbf{w}(x,0) = \mathbf{w}_0(x), & \text{on } \Gamma. \end{cases} \tag{2.1}$$

in a sense which we will make precise, moreover we will also show the universal bounds

$$\boxed{0 \le w_j \le 1, \quad \text{a.e. in } \Sigma, \quad \forall\, j = 1, \dots, k.}$$

*Remark* 4. In Section 3. we will show that $v \in H^1(0,T;L^2(\Gamma)) \cap L^2(0,T;H^{1/2}(\Gamma))$; since the dimension of $\Gamma$ is 2, we cannot deduce from this regularity and standard Sobolev embeddings that $v \in L^\infty(\Sigma)$, moreover, no maximum principle seems to apply to equations (1.13),(1.14a),(1.14b). So, we do not know if $F_j(v) \in L^1_{loc}(\Sigma)$ and therefore system (2.1) cannot be taken in the sense of distributions.

**Proposition 2.1.** *Let $v \in H^1(0,T;L^2(\Gamma))$, $\mathbf{w}_0(x) : \Gamma \to [0,1]^k$, measurable. Then $\exists!\ \mathbf{w} : \Gamma \times [0,T] \to [0,1]^k$, measurable, such that for a.e. $x \in \Gamma$, $\mathbf{w}(x,\cdot) \in (C^1(0,T))^k$, and*

$$\begin{cases} \dfrac{\partial \mathbf{w}}{\partial t}(x,t) = \mathbf{F}(v(x,t), \mathbf{w}(x,t)), & \text{for a.e. } x \in \Gamma,\ \forall\, t \in (0,T], \\ \mathbf{w}(x,0) = \mathbf{w}_0(x), & \text{for a.e. } x \in \Gamma. \end{cases} \tag{2.2}$$

If we consider $v \in C^0([0,T])$, and therefore we drop the dependence on $x \in \Gamma$, then we can prove the continuous dependence on $v$, precisely:

**Lemma 2.1.** *The operator which maps a function $v \in C^0([0,T])$ into the solution $\mathbf{w}$ of the ODE system*

$$\begin{cases} \dfrac{d}{dt}\mathbf{w}(t) = \mathbf{F}(v(t), \mathbf{w}(t)), & \forall\, t \in (0,T], \\ \mathbf{w}(0) = \mathbf{w}_0 \in [0,1]^k, \end{cases} \tag{2.3}$$

*is continuous.*

*Proof of Proposition 2.1.* We denote by $\mathscr{H}^2$ the usual bidimensional Haussdorff measure. We will make use of the following standard lemma:

**Lemma 2.2.** *Let $v \in L^2(\Gamma\times(0,T))$; the map $t \mapsto v_t(\cdot) = v(\cdot,t)$ belongs to $H^1(0,T,L^2(\Gamma))$ if and only if for a.e. $x \in \Gamma$*

$$t \mapsto v_t(x) \in H^1(0,T) \quad \text{and} \quad \int_\Gamma \|v_t(x)\|^2_{H^1(0,T)} d\mathscr{H}^2 < +\infty.$$

Therefore, for a.e. $x \in \Gamma$, the map $t \mapsto v_t(\cdot) = v(\cdot,t)$ admits a unique representative in $C^0([0,T])$, and then, by continuity of $F_j$ (1.10a), the map $t \mapsto F_j(v_t(x), w)$ admits a representative in $C^0([0,T])$, for a.e. $x \in \Gamma$, $\forall\, w \in \mathbb{R}$. Owing to (1.10a), (1.10b), (1.10c) and standard results for ordinary differential equations, for a.e. $x \in \Gamma$ there exists a unique classical solution $\mathbf{w}_t(x) = \mathbf{w}(x,t)$ of the Cauchy problem (2.2) and

$$0 \le w_j(x,t) \le 1, \quad \text{for a.e. } (x,t) \in \Sigma, \quad \forall\, j = 1,\dots,k. \tag{2.4}$$

Moreover, $\mathbf{w}$ is measurable. In fact, the map

$$\begin{array}{rccc} \mathbf{F}\circ v: & \Gamma\times[0,T]\times[0,1]^k & \to & \mathbb{R}^k, \\ & (x,t,\mathbf{w}) & \mapsto & \mathbf{F}(v(x,t),\mathbf{w}), \end{array}$$

is a Carathéodory function (it is measurable in $x$ and continuous in $t$ and $\mathbf{w}$), therefore, by Scorza–Dragoni theorem (see e.g. [11]), $\forall\, \varepsilon > 0$ there exists a compact set $K_\varepsilon \subset \Gamma$, such that $\mathscr{H}^2(K_\varepsilon) \le \varepsilon$, and

$$(\mathbf{F}\circ v)|_{(\Gamma\setminus K_\varepsilon)\times[0,T]\times[0,1]^k} \quad \text{is continuous.}$$

Thus, we have that

$$\mathbf{w}|_{(\Gamma\setminus K_\varepsilon)\times[0,T]} \quad \text{is continuous,}$$

and therefore measurable. Since this is true $\forall\, \varepsilon > 0$, we conclude that $\mathbf{w}$ is measurable on $\Gamma\times[0,T]$. □

*Proof of Lemma 2.1.* For sake of simplicity we shall suppress index $j$ from calculations, and we carry on this part of the proof for the generic $w, F$, instead of $w_j, F_j$.

Let $v, v_n \in C^0([0,T])$, $w_0 \in [0,1]$. The correspondent solutions $w, w_n$ of system (2.3) satisfy

$$w(t) = w_0 + \int_0^t F(v(s), w(s))ds,$$

$$w_n(t) = w_0 + \int_0^t F(v_n(s), w_n(s))ds.$$

We make the difference and we sum and subtract $F(v(s), w_n(s))$

$$|w_n(t) - w(t)| = \left| \int_0^t F(v_n(s), w_n(s)) - F(v(s), w_n(s)) + F(v(s), w_n(s)) - F(v(s), w(s)) ds \right|.$$

Owing to the local Lipschitz continuity of $F$ (hypothesis (1.10a)), there exists a nonnegative function $\mu \in C^0(\mathbb{R}^2)$ such that

$$|F(\nu_1,\omega_1) - F(\nu_2,\omega_2)| \le \mu(\nu_1,\nu_2)(|\nu_1-\nu_2| + |\omega_1-\omega_2|), \quad \forall\, \nu_1,\nu_2 \in \mathbb{R},\ \forall\, \omega_1,\omega_2 \in [0,1].$$

Then, the map $s \mapsto \mu(v(s), v_n(s))$ is continuous in $[0,T]$, and we have that

$$\left| \int_0^T F(v_n(t), w_n(t)) - F(v(t), w_n(t))\, dt \right| \le \int_0^T \mu(v_n(t), v(t)) |v_n(t) - v(t)|\, dt =: M_n, \quad (2.5)$$

and

$$\left| \int_0^t F(v(s), w_n(s)) - F(v(s), w(s))\, ds \right| \le \int_0^t \mu(v(s), v(s)) |w_n(s) - w(s)|\, ds.$$

We define

$$L := \max_{s\in[0,T]} \mu(v(s), v(s)) < +\infty, \quad (2.6)$$

so that

$$|w_n(t) - w(t)| \le M_n + L \int_0^t |w_n(s) - w(s)|\, ds,$$

and owing to Gronwall Lemma, we conclude that

$$|w_n(t) - w(t)| \le M_n e^{LT}, \quad \forall\, t \in [0,T]. \quad (2.7)$$

Now let $\{v_n\}_{n\in\mathbb{N}}$, $v$ be such that $v_n \to v$ in $C^0([0,T])$. Then, there exists a compact set $K \subset \mathbb{R}^2$ such that

$$(v_n(t), v(t)) \in K, \quad \forall t \in [0,T], \quad \forall n \in \mathbb{N},$$

and by estimates (2.5), (2.6) and (2.7) we have

$$|w_n(t) - w(t)| \le e^{LT} \int_0^T \mu(v_n(s), v(s))\, |v_n(s) - v(s)|\, ds, \quad \forall t \in [0,T], \quad \forall n \in \mathbb{N}.$$

Let $\bar{\mu} := \max\{\mu(\nu_1, \nu_2) : (\nu_1, \nu_2) \in K\} < +\infty$. Hence

$$\max_{t\in[0,T]} |w_n(t) - w(t)| \le e^{LT} \bar{\mu} \int_0^T |v_n(s) - v(s)|\, ds, \quad \forall n \in \mathbb{N},$$

and

$$w_n \to w, \quad \text{strongly in } C^0([0,T]). \quad (2.8)$$

□

## 2.2 The concentration variables

Now we turn to the system of ODEs (1.14d), with initial data (1.15c), which describes the dynamics of the $m$ concentration variables. We follow the same idea as for the gating variables, that is, we show that for every $v \in H^1(0,T; L^2(\Gamma))$ and for every vector function $\mathbf{w}$ given by Proposition 2.1, we can solve an ordinary Cauchy Problem in time, for a.e. $x \in \Gamma$. The difficulty, now, lies in the lack of a priori conditions such as (1.10b) and (1.10c), which, in (2.1) guaranteed the boundedness for $\mathbf{w}$. We use instead the monotonicity of $J_i$ in the variable $z_i$, combined with the linear growth of $H_i$. Moreover, functions $J_i$ contain a logarithmic term, so we also need to bound $\mathbf{z}$ far from zero.

**Proposition 2.2.** *Let* $v \in H^1(0,T;L^2(\Gamma))$, $\mathbf{w}$ *as in Proposition 2.1, and* $\mathbf{z}_0 : \Gamma \to (0,+\infty)^m$*, such that*

$$\mathbf{z}_0 \in (L^2(\Gamma))^m, \qquad \mathbf{log}\, \mathbf{z}_0 \in (L^2(\Gamma))^m.$$

*Then* $\exists!\ \mathbf{z} : \Gamma \times [0,T] \to (0,+\infty)^m$*, measurable, such that for a.e.* $x \in \Gamma$: $\mathbf{z}(x,\cdot) \in (C^1(0,T))^k$*, and*

$$\begin{cases} \dfrac{\partial \mathbf{z}}{\partial t}(x,t) = \mathbf{G}(v(x,t), \mathbf{w}(x,t), \mathbf{z}(x,t)), & \text{for a.e. } x \in \Gamma,\ \forall\ t \in (0,T], \\ \mathbf{z}(x,0) = \mathbf{z}_0(x), & \text{for a.e. } x \in \Gamma. \end{cases} \tag{2.9}$$

*Moreover,* $\mathbf{z}$, $\mathbf{log}\,\mathbf{z}$, $\partial\mathbf{z}/\partial t$ *belong to* $(L^2(\Sigma))^m$ *and there exists a constant* $C > 0$*, independent of* $v, \mathbf{w}, \mathbf{z}_0$*, such that*

$$|\mathbf{z}(x,t)| \le C \left(1 + |\mathbf{z}_0(x)| + \|v(x)\|_{L^2(0,t)}\right), \tag{2.10}$$

$$|\,\mathbf{log}\,\mathbf{z}(x,t)| + \left|\frac{\partial \mathbf{z}}{\partial t}(x,t)\right| \le C \left(1 + |\mathbf{z}_0(x)| + \|v(x)\|_{C^0(0,t)}\right), \tag{2.11}$$

$$\int_0^t |\,\mathbf{log}\,\mathbf{z}(x,s)|^2 + \left|\frac{\partial \mathbf{z}}{\partial s}(x,s)\right|^2 ds \le C \left(1 + |\mathbf{z}_0(x)\,\mathbf{log}\,\mathbf{z}_0(x)| + |\mathbf{z}_0(x)|^2 + \|v(x)\|^2_{L^2(0,t)}\right), \tag{2.12}$$

$\forall\ t \in [0,T]$*, for a.e.* $x \in \Gamma$*.*

Like in Lemma 2.1, we let $v \in C^0([0,T])$, that is, we suppress the dependence on $x \in \Gamma$, and we state the continuous dependence on $v, \mathbf{w}$ of the correspondent solution.

**Lemma 2.3.** *The operator which maps the functions* $(v, \mathbf{w}) \in C^0([0,T]) \times C^0([0,T])^k$ *into the solution* $\mathbf{z}$ *of the ODE system*

$$\begin{cases} \dfrac{d}{dt}\mathbf{z}(t) = \mathbf{G}(v(t), \mathbf{w}(t), \mathbf{z}(t)), & \forall\ t \in (0,T], \\ \mathbf{z}(0) = \mathbf{z}_0 \in (0,+\infty)^m, \end{cases} \tag{2.13}$$

*is continuous.*

*Proof of Proposition 2.2.* We note that, for $i = 1, \dots, m$, we can write

$$J_i(v, \mathbf{w}, \log z_i) = J_i(v, \mathbf{w}, 0) + \frac{J_i(v, \mathbf{w}, \log z_i) - J(v, \mathbf{w}, 0)}{\log z_i} \log z_i. \tag{2.14}$$

Owing to (1.7c), there exists a constant $\bar{L} > 0$, depending on $L_v$, such that

$$|J_i(v, \mathbf{w}, 0)| \le \left| \frac{J_i(v, \mathbf{w}, 0) - J_i(0, \mathbf{w}, 0)}{v} v \right| + |J_i(0, \mathbf{w}, 0)| \le \bar{L}(1 + |v|),\ \forall (v, \mathbf{w}) \in \mathbb{R} \times [0,1]^k; \tag{2.15}$$

by (1.7b) there exist constants $\underline{G}, \overline{G} > 0$ such that

$$\underline{G} \le \frac{J_i(v, \mathbf{w}, \log z_i) - J(v, \mathbf{w}, 0)}{\log z_i} \le \overline{G}, \quad \forall\ (v, \mathbf{w}, z_i) \in \mathbb{R} \times [0,1]^k \times (0,+\infty), \tag{2.16}$$

and by hypothesis (1.12) there exists a constant $\Lambda > 0$ such that

$$|\mathbf{H}(v, \mathbf{w}, \mathbf{z})| \leq \Lambda(1 + |v| + |\mathbf{z}|), \quad \forall\ (v, \mathbf{w}, \mathbf{z}) \in \mathbb{R} \times [0,1]^k \times (0, +\infty)^m. \tag{2.17}$$

By Lemma 2.2, there exists $\mathcal{N} \subset \Gamma$ such that $\mathscr{H}^2(\mathcal{N}) = 0$, and $\forall x \in \Gamma \backslash \mathcal{N},\ v(x, \cdot)$, $\mathbf{w}(x, \cdot)$ have a representative in $C^0([0, T])$. Thus, we can simplify the following calculations, considering $x$ fixed in $\Gamma \backslash \mathcal{N}$. Our estimates will then hold only for a.e. $x \in \Gamma$. Since $\mathbf{G}$ is locally Lipschitz continuous in $(0, +\infty)$, local existence and uniqueness for the maximal solution are straightforward. In order to get existence and uniqueness on the whole interval $[0, T]$, we must find an estimate for $\log z_i$ in $L^\infty(0, T)$ (estimate II). The measurability of $\mathbf{z}$ follows from the Carathéodory property of $\mathbf{G}$, like in the previous subsection. The proof of Proposition 2.2 relies on four estimates.

**Estimate I**. We now prove:

$$|\mathbf{z}(t)| \leq C\left(1 + |\mathbf{z}_0| + \|v\|_{L^2(0,t)}\right).$$

We get a first a priori estimate by multiplying equation (2.9) (scalarly in $\mathbb{R}^m$) by $\mathbf{z}(t)$:

$$\frac{d\mathbf{z}}{dt}(t) \cdot \mathbf{z}(t) = -\mathbf{J}(v, \mathbf{w},\ \mathbf{log}\ \mathbf{z})(t) \cdot \mathbf{z}(t) + \mathbf{H}(v, \mathbf{w}, \mathbf{z})(t) \cdot \mathbf{z}(t),$$

and using (2.17), we get

$$\frac{1}{2}\frac{d}{dt}|\mathbf{z}(t)|^2 \leq -\sum_{i=1}^m J_i(v(t), \mathbf{w}(t), \log z_i(t)) z_i(t) + \Lambda(1 + |v(t)| + |\mathbf{z}(t)|)|\mathbf{z}(t)|,$$

using decomposition (2.14) and the following estimates (2.15), (2.16), (2.17), we find

$$\frac{1}{2}\frac{d}{dt}|\mathbf{z}(t)|^2 \leq \sum_{i=1}^m \left(\bar{L}(1 + |v(t)|)|z_i(t)| + \overline{G}[\log z_i(t) z_i(t)]^-\right) + \Lambda(1 + |v(t)| + |\mathbf{z}(t)|)|\mathbf{z}(t)|,$$

Since $z \log z \geq -e^{-1}$, $\forall\ z > 0$, by Cauchy's inequality we get

$$\frac{1}{2}\frac{d}{dt}|\mathbf{z}(t)|^2 \leq \frac{m\overline{G}}{e} + \frac{1}{2}\bar{L}^2(1 + |v(t)|)^2 + \frac{1}{2}|\mathbf{z}(t)|^2 +$$
$$+ \frac{\Lambda^2}{2}(1 + |v(t)|)^2 + \frac{1}{2}|\mathbf{z}(t)|^2 + \Lambda|\mathbf{z}(t)|^2.$$

By Gronwall's Lemma we obtain

$$|\mathbf{z}(t)|^2 \leq e^{C_1 t}\left[|\mathbf{z}(0)|^2 + C_2 \int_0^t (1 + |v(s)|)^2 ds\right], \quad \forall\ t \in [0, T],$$

where $C_1 := 2(\Lambda + 1)$, and $C_2$ depends on $m, \bar{L}, \overline{G}, \Lambda$. We conclude that there exists a constant $C_3 > 0$, dependent on $m, \bar{L}, \overline{G}, \Lambda$, and $T$ such that

$$|\mathbf{z}(t)| \leq C_3\left(1 + |\mathbf{z}_0| + \|v\|_{L^2(0,t)}\right), \quad \forall\ t \in [0, T]. \tag{2.18}$$

**Estimate II**. Now we can show that each $z_i$ is far from zero, or, more precisely, that

$$z(t) \geq \exp\left[-C(1+|\mathbf{z}_0|+\|v\|_{C^0(0,t)})\right] > 0, \quad \forall\, t \in [0,T]. \tag{2.19}$$

For sake of simplicity we shall suppress index $i$ from calculations and carry on this part of the proof for the generic $z$ instead of $z_i$, moreover, since we now want to show (2.19) and $\exp[-C(1+|\mathbf{z}_0|+\|v\|_{C^0(0,t)})] < 1$, we can limit the study to $z < 1$.

We consider the equation

$$\frac{dz}{dt} = -J(v,\mathbf{w},\log z) + H(v,\mathbf{w},\mathbf{z}),$$

Again, by (2.14, …, 2.17) we find

$$\frac{dz}{dt} \geq -\bar{L}(1+|v|) - \underline{G}\log z - \Lambda(1+|v|+|\mathbf{z}|). \tag{2.20}$$

Owing to estimate (2.18), if

$$\underline{G}\log z(t) \leq -\bar{L}\left(1+\|v\|_{C^0(0,t)}\right) - \Lambda\left(1+\|v\|_{C^0(0,t)} + C_3(1+|\mathbf{z}_0|+\|v\|_{L^2(0,t)})\right)$$

then

$$\frac{dz}{dt}(t) \geq 0.$$

Since

$$\|v\|_{L^2(0,t)} \leq \sqrt{T}\|v\|_{C^0(0,t)}, \qquad \forall t \in [0,T]$$

there exist a constant $C_4 > 0$, depending on $m, \bar{L}, \underline{G}, \overline{G}, \Lambda, T$ such that

$$z(t) \geq \exp\left[-C_4\left(1+|\mathbf{z}_0|+\|v\|_{C^0(0,t)}\right)\right] > 0, \qquad \forall t \in [0,T].$$

We need two more estimates.

**Estimate III**. We are going to show that

$$\left\|\frac{dz}{dt}\right\|_{L^2(0,t)} \leq C\left(1+C(z_0)+\|v\|_{L^2(0,t)}\right), \qquad \forall t \in [0,T].$$

We multiply the $i$-th equation of (2.9) by $dz_i/dt$, (and we suppress index $i$), obtaining

$$\left(\frac{dz}{dt}(t)\right)^2 = -J(v(t),\mathbf{w}(t),\log z(t))\frac{dz}{dt}(t) + H(v(t),\mathbf{w}(t),\mathbf{z}(t))\frac{dz}{dt}(t) =$$

$$= -\left[\frac{J(v(t),\mathbf{w}(t),\log z(t)) - J(v(t),\mathbf{w}(t),0)}{\log z(t)}\right]\log z(t)\frac{dz}{dt}(t) +$$

$$+[J(v(t),\mathbf{w}(t),0) + H(v(t),\mathbf{w}(t),\mathbf{z}(t))]\frac{dz}{dt}(t). \tag{2.21}$$

Let

$$\Phi(t) := \left[\frac{J(v(t),\mathbf{w}(t),\log z(t)) - J(v(t),\mathbf{w}(t),0)}{\log z(t)}\right],$$

by (2.16), we have that

$$\underline{G} \leq \Phi(t) \leq \overline{G}, \qquad \forall\, t \in [0,T]. \tag{2.22}$$

We note that

$$\frac{d}{dt}[z(t)\log z(t) - z(t)] = \frac{dz}{dt}(t)\log z(t).$$

We divide equation (2.21) by $\Phi(t)$ and we integrate between 0 and $t$

$$\int_0^t \frac{1}{\Phi(s)}\left(\frac{dz}{ds}(s)\right)^2\ ds = -[z(t)\log z(t) - z(t) - z(0)\log z(0) + z(0)]+$$

$$+\int_0^t \left(\frac{J(v(s),\mathbf{w}(s),0) + H(v(s),\mathbf{w}(s),\mathbf{z}(s))}{\Phi(s)}\right)\frac{dz}{ds}(s)\ ds.$$

Since $z\log z - z \geq -1,\ \forall\ z > 0$, using (2.22), we get

$$\frac{1}{\overline{G}}\int_0^t \left(\frac{dz}{ds}(s)\right)^2 ds \leq z(0)\log z(0) - z(0) + 1+$$

$$+\int_0^t \underline{G}^{-1}(|J(v(s),\mathbf{w}(s),0)| + |H(v(s),\mathbf{w}(s),\mathbf{z}(s))|)\left|\frac{dz}{ds}(s)\right| ds.$$

By (2.15) and (2.17) we get

$$\frac{1}{\overline{G}}\int_0^t \left(\frac{dz}{ds}(s)\right)^2 ds \leq z(0)\log z(0) - z(0) + 1 + \frac{\bar{L}+\Lambda}{\underline{G}}\int_0^t (1 + |v(s)| + |\mathbf{z}(s)|)\left|\frac{dz}{ds}(s)\right| ds,$$

and by Cauchy inequality and estimate I (2.18) we find

$$\int_0^t \left(\frac{dz}{ds}(s)\right)^2 ds \leq C_5\left(1 + z(0)\log z(0) - z(0) + \int_0^t \left(1 + |v(s)| + |\mathbf{z}_0| + \|v\|_{L^2(0,t)}\right)^2 ds,\right)$$

and we conclude that there exists $C_6 > 0$ such that

$$\int_0^t \left(\frac{dz}{ds}(s)\right)^2 ds \leq C_6\left(1 + |z(0)\log z(0) - z(0)| + |\mathbf{z}_0|^2 + \|v\|^2_{L^2(0,t)}\right), \qquad \forall\, t \in [0,T]. \tag{2.23}$$

This estimate can be immediately used to get an equivalent estimate for $\log z(t)$.

**Estimate IV**.
We have

$$J(v,\mathbf{w},\log z) = H(v,\mathbf{w},\mathbf{z}) - \frac{dz}{dt},$$

$$\left(\frac{J(v,\mathbf{w},\log z) - J(v,\mathbf{w},0)}{\log z}\right)\log z = H(v,\mathbf{w},\mathbf{z}) - \frac{dz}{dt} - J(v,\mathbf{w},0),$$

$$\left(\frac{J(v,\mathbf{w},\log z) - J(v,\mathbf{w},0)}{\log z}\right)^2 (\log z)^2 \leq 3\left(H^2(v,\mathbf{w},\mathbf{z}) + \left(\frac{dz}{dt}\right)^2 + J(v,\mathbf{w},0)^2\right),$$

$$\underline{G}^2(\log z)^2 \leq 3\left(H^2(v,\mathbf{w},\mathbf{z}) + \left(\frac{dz}{dt}\right)^2 + J(v,\mathbf{w},0)^2\right),$$

$$\int_0^t \underline{G}^2(\log z)^2 \ ds \leq 3\int_0^t \left( H^2(v,\mathbf{w},\mathbf{z}) + \left(\frac{dz}{dt}\right)^2 + J(v,\mathbf{w},0)^2 \right) \ ds,$$

therefore, by (2.17) and (2.18), (2.23), (2.15), we find

$$\int_0^t (\log z(s))^2 \ ds \leq C\left(1 + |z(0)\log z(0) - z(0)| + |\mathbf{z}_0|^2 + \|v\|^2_{L^2(0,t)}\right).$$

□

*Proof of Lemma 2.3.* Let $v, v_n \in C^0([0,T])$, $\mathbf{w}, \mathbf{w}_n \in C^0([0,T])^k$. We denote by $z, z_n$ the corresponding solutions of system (2.13). We take the difference between the two equations

$$\frac{dz_n}{dt} - \frac{dz}{dt} = -[J(v_n,\mathbf{w}_n,\log z_n) - J(v,\mathbf{w},\log z)] + H(v_n,\mathbf{w}_n,\mathbf{z}_n) - H(v,\mathbf{w},\mathbf{z}),$$

we sum and subtract $J(v_n,\mathbf{w}_n,\log z)$

$$\begin{aligned} \frac{dz_n}{dt} - \frac{dz}{dt} &= -[J(v_n,\mathbf{w}_n,\log z_n) - J(v_n,\mathbf{w}_n,\log z)] + && \text{(2.24a)} \\ &\quad -[J(v_n,\mathbf{w}_n,\log z) - J(v,\mathbf{w},\log z)] + && \text{(2.24b)} \\ &\quad +H(v_n,\mathbf{w}_n,\mathbf{z}_n) - H(v,\mathbf{w},\mathbf{z}), && \text{(2.24c)} \end{aligned}$$

we multiply by $z_n - z$ and, since *log* is monotone increasing and the incremental quotient is positive by (1.7b), for the term (2.24a) we have

$$\frac{J(v_n,\mathbf{w}_n,\log z_n) - J(v_n,\mathbf{w}_n,\log z)}{\log z_n - \log z}(\log z_n - \log z)(z_n - z) \geq 0. \tag{2.25}$$

In order to deal with (2.24b), we remark that since $J$ is locally Lipschitz continuous (1.7a), there exists a nonnegative function
$\eta \in C^0(\mathbb{R}^2 \times (0,+\infty))$ such that

$$|J(\nu_2,\boldsymbol{\omega}_2,\zeta) - J(\nu_1,\boldsymbol{\omega}_1,\zeta)| \leq \eta(\nu_1,\nu_2,\zeta)(|\nu_2-\nu_1| + |\boldsymbol{\omega}_2 - \boldsymbol{\omega}_1|),$$

$\forall\, \nu_1,\nu_2 \in \mathbb{R}$, $\forall\, \boldsymbol{\omega}_1,\boldsymbol{\omega}_2 \in [0,1]^k$, $\forall\, \zeta \in \mathbb{R}$. Hence, using (2.25) and (2.17), we obtain

$$\frac{1}{2}\frac{d}{dt}|z_n - z|^2 \leq \eta(v,v_n,\log z)(|v_n - v| + |\mathbf{w}_n - \mathbf{w}|)|z_n - z| +$$

$$+\Lambda\Big(|v_n - v| + |\mathbf{w}_n - \mathbf{w}| + |\mathbf{z}_n - \mathbf{z}|\Big)|z_n - z|.$$

Summing up the contributions of the $m$ components of $\mathbf{z}$ and integrating between 0 and $t$ we obtain

$$\frac{1}{2}|\mathbf{z}_n(t) - \mathbf{z}(t)|^2 \leq \int_0^t |\boldsymbol{\eta}(v,v_n,\ \mathbf{log\, z})|(|v_n - v| + |\mathbf{w}_n - \mathbf{w}|)|\mathbf{z}_n - \mathbf{z}| \ ds +$$

$$+\sqrt{m}\Lambda\int_0^t \Big(|v_n - v| + |\mathbf{w}_n - \mathbf{w}| + |\mathbf{z}_n - \mathbf{z}|\Big)|\mathbf{z}_n - \mathbf{z}| \ ds,$$

where $\boldsymbol{\eta}(v, v_n, \ \mathbf{log}\,\mathbf{z})$ denotes the vector of components $\eta_i(v, v_n, \log z_i)$, and by Cauchy's inequality

$$|\mathbf{z}_n(t) - \mathbf{z}(t)|^2 \leq M + L \int_0^t |\mathbf{z}_n(s) - \mathbf{z}(s)|^2 \ ds, \tag{2.26}$$

where

$$M := \int_0^T \left(|\boldsymbol{\eta}(v, v_n, \ \mathbf{log}\,\mathbf{z})|^2 + m\Lambda^2\right) (|v_n - v| + |\mathbf{w}_n - \mathbf{w}|)^2 ds, \tag{2.27}$$

and $L = 2(\sqrt{m}\Lambda + 1)$.

Therefore, applying Gronwall Lemma to equation (2.26), we get

$$|\mathbf{z}_n(t) - \mathbf{z}(t)|^2 \leq M e^{LT}, \quad \forall\, t \in [0, T]. \tag{2.28}$$

Now let $\{v_n\}_{n\in\mathbb{N}}, \ v, \ \{\mathbf{w}_n\}_{n\in\mathbb{N}}, \ \mathbf{w}$, be such that

$$v_n \to v \quad \text{in } C^0([0, T]), \qquad \mathbf{w}_n \to \mathbf{w} \quad \text{in } C^0([0, T])^m.$$

We remark that $\mathbf{z}$ is continuous by Proposition 2.2, and $\mathbf{log}(\mathbf{z})$ is continuous and bounded owing to estimate (2.11), moreover, since $v_n \to v$ in $C^0([0, T])$, there exists a compact set $K \subset \mathbb{R}^{2+m}$ such that

$$(v(t), v_n(t), \ \mathbf{log}\,\mathbf{z}(t)) \in K, \quad \forall\, t \in [0, T], \ \forall\, n \in \mathbb{N}.$$

Let

$$\bar{\eta} := \max_{(\nu_1, \nu_2, \zeta) \in K} |\boldsymbol{\eta}(\nu_1, \nu_2, \zeta)|^2 < +\infty.$$

By estimates (2.27), (2.28), we obtain

$$\max_{t\in[0,T]} |\mathbf{z}_n(t) - \mathbf{z}(t)|^2 \leq (\bar{\eta} + m\Lambda^2) \int_0^T (|v_n(s) - v(s)| + |\mathbf{w}_n(s) - \mathbf{w}(s)|)^2 ds, \quad \forall\, n \in \mathbb{N},$$

and therefore

$$\mathbf{z}_n \to \mathbf{z} \quad \text{in } C^0([0, T])^m.$$

□

# 3 The Parabolic equation

Our next step will be to write a variational formulation for system (1.13) and equations (1.14a), (1.14b), (1.15a), considering the ionic current $\bar{I}_{ion}$ as a known function. In order to choose the correct assumptions on $\bar{I}_{ion}$, we look at the estimates just obtained: let $\mathbf{w}$, $\mathbf{z}$, be known functions, satisfying the thesis of Propositions 2.1 and 2.2, let $\bar{v} \in H^1(0, T; L^2(\Gamma))$ given, and set

$$\bar{I}_{ion}(x, t) := I_{ion}(\bar{v}(x, t), \mathbf{w}(x, t), \mathbf{z}(x, t)). \tag{3.1}$$

Then, by the definition of $I_{ion}$ (1.6), using estimates (1.7b), (1.7c) and (2.4) we obtain

$$|J(v, \mathbf{w}, \log z)| \leq |J(0, \mathbf{w}, 0)| + L_v|v| + \overline{G}|\log z| \leq C(1 + |v| + |\log z|),$$

and thus, owing to (2.12), we have that $\bar{I}_{ion} \in L^2(\Sigma)$, and

$$\|\bar{I}_{ion}\|^2_{L^2(0,t;L^2(\Gamma))} \le C\left(1 + \|\bar{v}\|^2_{L^2(0,t;L^2(\Gamma))}\right), \qquad \forall\, t \in [0,T], \tag{3.2}$$

where $C$ is a constant, independent of $\bar{v}, \mathbf{w}, \mathbf{z}$.

In the following section we will find a unique solution $(u_i, u_e)$ for (1.13), (1.14a), (1.14b), (1.15a), which we recall and renumber

$$\begin{cases} -\text{div}(\sigma_{i,e}\nabla u_{i,e}) &= I^s_{i,e} \qquad \text{on } Q_{i,e}, \\ \sigma_i \nabla u_i \cdot \nu_i &= g_i \qquad \text{on } \Sigma_i, \\ u_e &= 0 \qquad \text{on } \Sigma_e, \end{cases} \tag{3.3}$$

$$C_m \partial_t v + \bar{I}_{ion} = -\sigma_i \nabla u_i \cdot \nu_i \qquad \text{on } \Sigma, \tag{3.4a}$$

$$C_m \partial_t v + \bar{I}_{ion} = \sigma_e \nabla u_e \cdot \nu_e \qquad \text{on } \Sigma, \tag{3.4b}$$

$$v(x,0) = v_0(x) \qquad \text{on } \Gamma, \tag{3.4c}$$

**Variational formulation**

The variational formulation and the well posedness for the resulting problem follow directly from [10, Theorem 1]. In particular, here, we have that the ionic current $\bar{I}_{ion}$ is a given function in $L^2(\Sigma)$, so that it does not depend on $v$ and $\mathbf{w}$ as in [10]. In order to provide the reader with a handier explanation, we report the complete variational formulation and we collect the adapted results in Proposition 3.1, while we refer to [10] for the proof and the derivation of the main estimates.

Now we need to choose the functional spaces in which we will set the equations and seek a solution. For simplicity, we set constant $C_m = 1$. Let us assume that for a.e. $t \in ]0,T[$

$$I^s_{i,e}(\cdot,t) \in L^2(\Omega_{i,e}), \qquad g_i(\cdot,t) \in H^{-1/2}(\Gamma_i), \tag{3.5}$$

$$u_e(\cdot,t) \in H^1_{\Gamma^0_e}(\Omega_e), \qquad u_i(\cdot,t) \in H^1(\Omega_i), \qquad \partial_t u_{i,e}(\cdot,t) \in H^1(\Omega_{i,e}),$$

so that the trace operator $u_{i,e} \mapsto u_{i,e|\Gamma}$ is well defined and continuous from $H^1(\Omega_{i,e})$ in $H^{1/2}(\Gamma)$ (see e.g. [26]). The space

$$H^1_{\Gamma^0_e}(\Omega_e) := \left\{ u \in H^1(\Omega_e) : \ u(x)_{|\Gamma_e} = 0, \text{ a.e.} \right\}$$

includes the Dirichlet boundary condition. From now on we shall use the simplified notation $v := u_i - u_e$ instead of $u_{i|\Gamma} - u_{e|\Gamma}$. We choose the test functions

$$\hat{u}_e \in H^1_{\Gamma^0_e}(\Omega_e), \quad \hat{u}_i \in H^1(\Omega_i), \quad \text{denote} \quad \hat{v} := \hat{u}_i - \hat{u}_e \in H^{1/2}(\Gamma),$$

and multiply equations (3.4a), (3.4b) by the trace of $\hat{u}_i$ and $-\hat{u}_e$ respectively. We denote by $\mathscr{H}^2$ the usual bidimensional Haussdorff measure. Integrating on $\Gamma$ and adding the two equations we get

$$\int_\Gamma (\partial_t v)\hat{v}\; d\mathscr{H}^2 + \int_\Gamma (\sigma_i \nabla u_i \cdot \nu_i)\hat{u}_i\; d\mathscr{H}^2 + \int_\Gamma (\sigma_e \nabla u_e \cdot \nu_e)\hat{u}_e\; d\mathscr{H}^2 + \int_\Gamma \bar{I}_{ion}\hat{v}\; d\mathscr{H}^2 = 0. \tag{3.6}$$

The third integral can be written as

$$\int_\Gamma (\sigma_i \nabla u_i \cdot \nu_i)\hat{u}_i \; d\mathscr{H}^2 = {}_{H^{-1/2}(\Gamma)}\langle \sigma_i \nabla u_i \cdot \nu_i \; , \; \hat{u}_i \rangle_{H^{1/2}(\Gamma)} \, .$$

Using the Green formula we get

$$\int_\Gamma (\sigma_i \nabla u_i \cdot \nu_i)\hat{u}_i \; d\mathscr{H}^2 = \int_{\Omega_i} (\sigma_i \nabla u_i \cdot \nabla \hat{u}_i + \mathrm{div}(\sigma_i \nabla u_i)\hat{u}_i) dx -$$

$$- \; {}_{H^{-1/2}(\Gamma_i)}\langle \sigma_i \nabla u_i \cdot \nu_i \; , \; \hat{u}_i \rangle_{H^{1/2}(\Gamma_i)} \, ,$$

and, using $\hat{u}_e \in H^1_{\Gamma_e^0}(\Omega_e)$,

$$\int_\Gamma (\sigma_e \nabla u_e \cdot \nu_e)\hat{u}_e \; d\mathscr{H}^2 = \int_{\Omega_e} (\sigma_e \nabla u_e \cdot \nabla \hat{u}_e + \mathrm{div}(\sigma_e \nabla u_e)\hat{u}_e) dx,$$

which are justified by the usual arguments of [26]. We now write (3.6) using the previous calculations and (3.3)

$$\begin{aligned} \int_\Gamma (\partial_t v)\hat{v} \; d\mathscr{H}^2 + \sum_{i,e} \int_{\Omega_{i,e}} \sigma_{i,e} \nabla u_{i,e} \cdot \nabla \hat{u}_{i,e} dx + \int_\Gamma \bar{I}_{ion} \hat{v} \; d\mathscr{H}^2 = \\ = \sum_{i,e} \int_{\Omega_{i,e}} I^s_{i,e} \hat{u}_{i,e} \, dx + {}_{H^{-1/2}(\Gamma_i)}\langle g_i \; , \; \hat{u}_i \rangle_{H^{1/2}(\Gamma_i)} . \end{aligned} \tag{3.7}$$

Let us analyze the particular structure of equation (3.7).
We denote by boldface letters $\mathbf{u}$ and $\hat{\mathbf{u}}$ the couples of functions $(u_i, u_e)$, $(\hat{u}_i, \hat{u}_e)$ and we introduce the product space

$$\mathbf{V} := H^1(\Omega_i) \times H^1_{\Gamma_e^0}(\Omega_e),$$

endowed with the norm

$$\|\mathbf{u}\|_{\mathbf{V}} = (\|u_i\|^2_{H^1(\Omega_i)} + \|u_e\|^2_{H^1(\Omega_e)})^{\frac{1}{2}},$$

and the bilinear forms

$$b(\mathbf{u}, \hat{\mathbf{u}}) := \int_\Gamma (u_i - u_e)(\hat{u}_i - \hat{u}_e) \; d\mathscr{H}^2,$$

$$a(\mathbf{u}, \hat{\mathbf{u}}) := \sum_{i,e} \int_{\Omega_{i,e}} \sigma_{i,e} \nabla u_{i,e} \cdot \nabla \hat{u}_{i,e} \; dx,$$

defined $\forall \; \mathbf{u}, \hat{\mathbf{u}} \in \mathbf{V}$. Denoting by $\mathbf{V}'$ the dual space of $\mathbf{V}$, we can associate to the bilinear forms $a, b$ the linear continuous operators $A, B : \mathbf{V} \to \mathbf{V}'$ defined by

$$\langle A\mathbf{u}, \hat{\mathbf{u}} \rangle := a(\mathbf{u}, \hat{\mathbf{u}}), \qquad \langle B\mathbf{u}, \hat{\mathbf{u}} \rangle := b(\mathbf{u}, \hat{\mathbf{u}}), \qquad \forall \; \mathbf{u}, \hat{\mathbf{u}} \in \mathbf{V}. \tag{3.8}$$

We introduce the family of linear functionals $\{\mathcal{I}_{ion}(t)\}_{t \in ]0,T[} \in \mathbf{V}'$

$$\langle \mathcal{I}_{ion}(t), \hat{\mathbf{u}} \rangle := \int_\Gamma \bar{I}_{ion}(x,t)(\hat{u}_i(x) - \hat{u}_e(x)) \; d\mathscr{H}^2, \tag{3.9}$$

Assuming (3.5) and $v_0 \in H^{1/2}(\Gamma)$ we can associate to the remaining part of the right side member in (3.7) the family of linear functionals $\{\mathbf{L}(t)\}_{t\in]0,T[} \in \mathbf{V}'$, and to the initial data the linear functional $\ell^0 \in \mathbf{V}'$ defined by

$$\begin{aligned} \langle \mathbf{L}(t), \hat{\mathbf{u}} \rangle &:= \sum_{i,e} \int_{\Omega_{i,e}} I^s_{i,e} \hat{u}_{i,e} dx + {}_{H^{-1/2}(\Gamma_i)}\langle g_i \ , \ \hat{u}_i \rangle_{H^{1/2}(\Gamma_i)} \,, && (3.10) \\ \langle \ell^0, \hat{\mathbf{u}} \rangle &:= \int_\Gamma v_0 (\hat{u}_i - \hat{u}_e) \, d\mathscr{H}^2. && (3.11) \end{aligned}$$

Now we have all the elements to give a precise statement of the problem.

**Problem (m2).** Given

$$I^s_{i,e} \in L^2(0,T; L^2(\Omega_{i,e})), \qquad g_i \in L^2(0,T; H^{-1/2}(\Gamma_i)),$$

$A, B, \mathcal{I}_{ion}(t), \mathbf{L}(t), \ell^0$, defined in (3.8),...,(3.11), we look for

$$\mathbf{u} \in L^2(0,T;\mathbf{V}), \text{ with } B\mathbf{u} \in H^1(0,T;\mathbf{V}'),$$

which solves the evolution system

$$\begin{cases} (B\mathbf{u}(t))' + A\mathbf{u}(t) = -\mathcal{I}_{ion}(t) + \mathbf{L}(t), & \text{in } \mathbf{V}' \quad \text{a.e. in } ]0,T[, \\ B\mathbf{u}(0) = \ell^0 & \text{in } \mathbf{V}'. \end{cases} \tag{3.12}$$

We can now state the result concerning this section

**Proposition 3.1.** *If*

$$I^s_{i,e} \in H^1(0,T; L^2(\Omega_{i,e})), \qquad g_i \in H^1(0,T; H^{-1/2}(\Gamma_i)),$$

$$\bar{I}_{ion} \in L^2(\Sigma), \qquad v_0 \in H^{1/2}(\Gamma),$$

*there exists a unique solution* $\mathbf{u}$ *of* ***Problem (m2)***,

$$\begin{aligned} &\mathbf{u} \in L^2(0,T;\mathbf{V}), \\ &B\mathbf{u} = v \in H^1(0,T;L^2(\Gamma)) \cap L^2(0,T;H^{1/2}(\Gamma)), \end{aligned}$$

*we have the a priori estimates*

$$\|\mathbf{u}\|_{L^2(0,T;\mathbf{V})} \le C\Big(\|v_0\|_{L^2(\Gamma)} + \|\bar{I}_{ion}\|_{L^2(\Sigma)} + \|I^s_{i,e}\|_{L^2(Q_{i,e})} + \|g_i\|_{L^2(0,T;H^{-1/2}(\Gamma_i))}\Big)\,, \tag{3.13}$$

$$\|v\|_{L^\infty(0,T;L^2(\Gamma))} \le C\Big(\|v_0\|_{L^2(\Gamma)} + \|\bar{I}_{ion}\|_{L^2(\Sigma)} + \|I^s_{i,e}\|_{L^2(Q_{i,e})} + \|g_i\|_{L^2(0,T;H^{-1/2}(\Gamma_i))}\Big)\,, \tag{3.14}$$

$$\|\partial_t v\|_{L^2(0,T;L^2(\Gamma))} \le C\Big(\|v_0\|_{H^{1/2}(\Gamma)} + \|\bar{I}_{ion}\|_{L^2(\Sigma)} + \|I^s_{i,e}\|_{H^1(0,T;L^2(\Omega_{i,e})} + \|g_i\|_{H^1(0,T;H^{-1/2}(\Gamma_i))}\Big) \tag{3.15}$$

*and, if* $v^{(1)}, v^{(2)}$ *are the solutions corresponding to data* $\bar{I}^{(1)}_{ion}, \bar{I}^{(2)}_{ion}$, *it holds:*

$$\|v^{(2)}(t) - v^{(1)}(t)\|^2_{L^2(\Gamma)} \le C \|\bar{I}^{(1)}_{ion} - \bar{I}^{(2)}_{ion}\|^2_{L^2(0,t;L^2(\Gamma))}. \tag{3.16}$$

*Remark* 5. These estimates may be derived by means of standard techniques for monotone, coercive operators (see e.g. [25]), paying attention to the particular structure shared by $B$ and $\mathcal{I}_{ion}(t)$ (see [10, 31]).

Up to now we have found an estimate on $v$, which depends, through $\bar{I}_{ion}$ (see (3.2)), upon the choice of $\bar{v} \in H^1(0,T;L^2(\Gamma))$. Now, let $H$ be a Hilbert space, for every $\lambda > 0$, we can define a new norm on $L^2(0,T;H)$ as

$$|||v|||_{\lambda,H} := \left( \int_0^T e^{-\lambda t} \|v(t)\|_H^2 \, dt \right)^{1/2}, \tag{3.17}$$

and we have that $|||\cdot|||_{\lambda,H}$ and $\|\cdot\|$ are equivalent norms on $L^2(0,T;H)$.

**Corollary 1.** *Let $\bar{v} \in H^1(0,T;L^2(\Gamma))$, let $\mathbf{w}, \mathbf{z}$ be the unique solutions of systems (2.2) and (2.9), given as in Propositions 2.1 and 2.2, and let $\bar{I}_{ion}$ be given as in (3.1), thus satisfying (3.2). Then there exists $\lambda > 0$ such that the solution $v$ of Problem* (***m2***) *satisfies*

$$|||v|||^2_{\lambda,L^2(\Gamma)} \leq \max\left\{1, |||\bar{v}|||^2_{\lambda,L^2(\Gamma)}\right\}, \quad \forall\, \bar{v} \in H^1(0,T;L^2(\Gamma)).$$

*Proof.* By estimate (3.14) we have

$$\|v(t)\|^2_{L^2(\Gamma)} \leq C_2\Big(\|v_0\|^2_{L^2(\Gamma)} + \|I^s_{i,e}\|^2_{L^2(Q_{i,e})} + \|g_i\|^2_{L^2(0,T;H^{-1/2}(\Gamma_i))} + \|\bar{I}_{ion}\|^2_{L^2(0,t;L^2(\Gamma))}\Big). \tag{3.18}$$

Let $\varphi(t) := \|v(t)\|^2_{L^2(\Gamma)}$, and $\bar{\varphi}(t) := \|\bar{v}(t)\|^2_{L^2(\Gamma)}$; owing to estimates (3.2) and (3.18) we find

$$\varphi(t) \leq C_3 + C_4 \int_0^t \bar{\varphi}(s)\, ds, \tag{3.19}$$

where $C_3$ may depend on $T$, $\|v_0\|^2_{L^2(\Gamma)}$, $\|I^s_{i,e}\|_{L^2(Q_{i,e})}$, $\|g_i\|_{L^2(0,T;H^{-1/2}(\Gamma_i))}$, $\|\mathbf{z}_0\|^2_{L^2(\Gamma)}$, $\|\mathbf{z}_0 \log \mathbf{z}_0\|_{L^2(\Gamma)}$, $\mathscr{H}^2(\Gamma)$, and

$$C_4 = C_4\left(T,\ \mathscr{H}^2(\Gamma)\right).$$

Now we multiply (3.19) by $e^{-\lambda t}$, ($\lambda > 0$), and we integrate between 0 and $T$:

$$\int_0^T e^{-\lambda t} \varphi(t)\, dt \leq C_3 \int_0^T e^{-\lambda t}\, dt + C_4 \int_0^T e^{-\lambda t} \left( \int_0^t \bar{\varphi}(s)\, ds \right) dt,$$

and integrating by parts

$$\begin{aligned}\int_0^T e^{-\lambda t} \varphi(t)\, dt &\leq \frac{1}{\lambda}\left[ C_3\left(1 - e^{-\lambda T}\right) + C_4 \int_0^T e^{-\lambda t} \bar{\varphi}(t)\, dt - C_4 e^{-\lambda T} \int_0^T \bar{\varphi}(t)\, dt \right] \\ &\leq \frac{1}{\lambda}\left[ C_3 + C_4 \int_0^T e^{-\lambda t} \bar{\varphi}(t)\, dt \right].\end{aligned}$$

If $\displaystyle\int_0^T e^{-\lambda t} \bar{\varphi}(t)\, dt \geq 1$, we have that

$$\int_0^T e^{-\lambda t} \varphi(t)\, dt \leq \frac{C_3 + C_4}{\lambda} \int_0^T e^{-\lambda t} \bar{\varphi}(t)\, dt.$$

Hence, if $\lambda \geq C_3 + C_4$, then

$$|||v|||^2_{\lambda,L^2(\Gamma)} = \int_0^T e^{-\lambda t}\varphi(t)\ dt \leq \max\left\{1, \int_0^T e^{-\lambda t}\bar{\varphi}(t)\ dt\right\} = \max\left\{1, |||\bar{v}|||^2_{\lambda,L^2(\Gamma)}\right\}.$$

□

Using estimates (3.13) and (3.15), Corollary 1 and the continuity of the trace operator, we easily obtain:

**Corollary 2.** *Let $M_0 \geq 1$, let $\bar{v}, \mathbf{w}, \mathbf{z}$, be as in the statement of Corollary 1, such that*

$$|||\bar{v}|||_{\lambda,L^2(\Gamma)} \leq M_0,$$

*then there exist $M_1 > 0$, depending only on $M_0$ and the data of the problem, such that*

$$|||\mathbf{u}|||_{\lambda,\mathbf{V}} \leq M_1,$$

$$|||v|||_{\lambda,H^{1/2}(\Gamma)} \leq M_1,$$

$$|||\partial_t v|||_{\lambda,L^2(\Gamma)} \leq M_1.$$

## 4 The fixed point argument

Let us recall Schauder's fixed point theorem, (see e.g. [39, p. 56]).

**Schauder's Theorem** *Let $M$ be a nonempty, compact, convex subset of a Banach space $X$. Let $\mathcal{T} : M \to M$ be a continuous operator. Then $\mathcal{T}$ has a fixed point.*

We denote by $\mathcal{K}_\lambda$, $\mathcal{W}$ and $\mathcal{Z}$ the following sets

$$\mathcal{K}_\lambda := \Big\{\ v \in H^1(0,T;L^2(\Gamma)) \cap L^2(0,T;H^{1/2}(\Gamma)),\ \text{s.t.}\quad |||v|||_{\lambda,L^2(\Gamma)} \leq M_0, \\ |||\partial_t v|||_{\lambda,L^2(\Gamma)}, |||v|||_{\lambda,H^{1/2}(\Gamma)} \leq M_1,\ \text{and}\ v(x,0) = v_0(x)\ \text{a.e}\ \Big\},$$

endowed with the topology of $(L^2(0,T;L^2(\Gamma)), |||\cdot|||_{\lambda,L^2(\Gamma)})$, (the norm $|||\cdot|||_{\lambda,H}$ was defined in (3.17));

$$\mathcal{W} := \Big\{\ \mathbf{w} \in \left(L^2(\Sigma)\right)^k\ \text{s.t.}\quad \mathbf{w}(x,t) \in [0,1]^k,\quad \text{for a.e. } (x,t) \in \Sigma\Big\},$$

endowed with the topology of $\left(L^2(\Sigma)\right)^k$;

$$\mathcal{Z} := \Big\{\ \mathbf{z} \in \left(L^2(\Sigma)\right)^m\ \text{s.t.}\quad \mathbf{z}(x,t) \in (0,+\infty)^k,\quad \text{for a.e. } (x,t) \in \Sigma, \\ \log(\mathbf{z}) \in \left(L^2(\Sigma)\right)^m\ \text{and}\ \ \|\mathbf{z}\|_{(L^2(\Sigma))^m} + \|\log(\mathbf{z})\|_{(L^2(\Sigma))^m} \leq \overline{Z}\ \Big\},$$

endowed with the topology induced by the metric

$$d_{\mathcal{Z}}(\mathbf{z}_1, \mathbf{z}_2) := \|\mathbf{z}_1 - \mathbf{z}_2\|_{(L^2(\Sigma))^m} + \|\log(\mathbf{z}_1) - \log(\mathbf{z}_2)\|_{(L^2(\Sigma))^m},$$

where the constants $M_0, M_1$ were established in Section 3-Corollary 2, and the constant $\overline{Z}$ derives from estimates (2.10), (2.12) and $M_0$.
We define operators $\mathcal{F}_1,\ \mathcal{F}_2,\ \mathcal{T}$

$$\begin{array}{rccc} \mathcal{F}_1: & \mathcal{K}_\lambda & \longrightarrow & \mathcal{K}_\lambda \times \mathcal{W} \times \mathcal{Z} \\ & \bar{v} & \longmapsto & \bar{v}, \mathbf{w}, \mathbf{z} \end{array} \tag{4.1}$$

where $\mathbf{w}$ is the solution of (2.1), as in Proposition 2.1, and $\mathbf{z}$ is the solution of (2.9), as in Proposition 2.2, and

$$\begin{array}{rccc} \mathcal{F}_2: & \mathcal{K}_\lambda \times \mathcal{W} \times \mathcal{Z} & \longrightarrow & \mathcal{K}_\lambda \\ & \bar{v}, \mathbf{w}, \mathbf{z} & \longmapsto & v, \end{array}$$

where $v$ is the solution of Problem (**m2**), as in Proposition 3.1, and

$$\mathcal{T} := \mathcal{F}_2 \circ \mathcal{F}_1 : \ \mathcal{K}_\lambda \ \longrightarrow \ \mathcal{K}_\lambda.$$

In order to apply Schauder's Theorem to $\mathcal{K}_\lambda$ and $\mathcal{T}$, (being $\mathcal{K}_\lambda$ convex and nonempty), we need to check the compactness of $\mathcal{K}_\lambda$ and the continuity of $\mathcal{T}$ with respect to the strong topology of $(L^2(0,T;L^2(\Gamma)), |||\cdot|||_{\lambda,L^2(\Gamma)})$.

***Compactness for $\mathcal{K}_\lambda$.*** In order to obtain compactness for $\mathcal{K}_\lambda$ we apply Lions-Aubin Theorem (see e.g. [35, p. 106]).

**Lions–Aubin Theorem** *Let $B_0, B, B_1$ be Banach spaces with $B_0 \subset B \subset B_1$; assume $B_0 \hookrightarrow B$ is compact and $B \hookrightarrow B_1$ is continuous. Let $1 < p < \infty,\ 1 < q < \infty$, let $B_0$ and $B_1$ be reflexive, and define*

$$W \equiv \left\{ u \in L^p(0,T;B_0) : u' \in L^q(0,T;B_1) \right\}.$$

*Then the inclusion $W \hookrightarrow L^p(0,T;B)$ is compact.*

We choose $B_0 = H^{1/2}(\Gamma),\ B = B_1 = L^2(\Gamma),\ p = q = 2$. Owing to Rellich Theorem the inclusion $H^{1/2}(\Gamma) \hookrightarrow L^2(\Gamma)$ is compact. Then, by Lions-Aubin theorem we obtain that the inclusion

$$L^2(0,T;H^{1/2}(\Gamma)) \cap H^1\left(0,T;L^2(\Gamma)\right) \hookrightarrow L^2\left(0,T;L^2(\Gamma)\right)$$

is compact; since the norms $\|\cdot\|$ and $|||\cdot|||_\lambda$ are equivalent, in particular we have that

$$\mathcal{K}_\lambda \text{ is compact in } \left(L^2\left(0,T;L^2(\Gamma)\right), |||\cdot|||_{\lambda,L^2(\Gamma)}\right).$$

***Continuity of operator $\mathcal{T} = \mathcal{F}_2 \circ \mathcal{F}_1$***

**Theorem 4.1.** *The operator $\mathcal{T}$ is continuous with the topology of*

$$\left(L^2(0,T;L^2(\Gamma)), |||\cdot|||_{\lambda,L^2(\Gamma)}\right).$$

*Remark* 6. Since the norms $\|\cdot\|$ and $|||\cdot|||_\lambda$ are equivalent, in order to simplify the notation, we shall check instead the continuity of $\mathcal{T}$ in

$$\mathcal{K} := \Big\{ \ v \in H^1(0,T;L^2(\Gamma)) \cap L^2(0,T;H^{1/2}(\Gamma)), \text{ s.t. } \ \|v\|_{L^2(0,T;L^2(\Gamma))} \le M_0,$$
$$\|\partial_t v\|_{L^2(0,T;L^2(\Gamma))}, \|v\|_{L^2(0,T;H^{1/2}(\Gamma))} \le M_1, \text{ and } v(x,0) = v_0(x) \text{ a.e } \Big\}, \tag{4.2}$$

endowed with the topology of $\big(L^2(0,T;L^2(\Gamma)), \|\cdot\|\big)$.

The proof is divided into two steps: 1) the continuity of operator $\mathcal{F}_1$, which is divided into Propositions 4.1 and 4.2, and: 2) the continuity of operator $\mathcal{F}_2$.

***1) Continuity of operator*** $\mathcal{F}_1$. The proof is based on:

- the estimates on the ODE systems established in Propositions 2.1 and 2.2,
- Theorem 4.2, on the continuity of infinite dimentional Nemitski operators,
- a classical interpolation inequality (Lemma 4.1 and Lemma 4.2).

Let us recall the necessary tools.

**Theorem 4.2.** *Let $X$ be a measure space, let $B, C$ be separable Banach spaces and $\mathscr{A} : B \to C$ be a (nonlinear) continuous operator satisfying*

$$\|\mathscr{A} u\|_C \le c_1 + c_2 \|u\|_B, \quad \forall\, u \in B. \tag{4.3}$$

*Let $p \in [1, +\infty)$, then the operator*

$$\tilde{\mathscr{A}} : L^p(X;B) \to L^p(X;C),$$
$$(\tilde{\mathscr{A}} u)(x) := \mathscr{A} u(x), \quad \forall\, x \in X,$$

*is continuous.*

See [6] for a finite dimensional proof, which is almost identical in the case of continuous operators between Banach spaces.

We will make use of the following interpolation inequalities (see e.g. [26, 24]).

**Lemma 4.1.** *There exists $c > 0$ such that*

$$\|v\|_{C^0(0,T)} \le c \|v\|_{H^1(0,T)}^{1/2} \|v\|_{L^2(0,T)}^{1/2}, \quad \forall\, v \in H^1(0,T).$$

**Lemma 4.2.** *Let $X$ be a measure space, $A, B, C$ Banach spaces such that*

*(i)* $A \subset B \subset C$, *with continuous inclusions;*
*(ii)* $\|v\|_B \le c \|v\|_A^{1/2} \|v\|_C^{1/2}, \quad \forall\ v \in A.$

*Then*

$$\|v\|_{L^2(X,B)} \le c \|v\|_{L^2(X,A)}^{1/2} \|v\|_{L^2(X,C)}^{1/2}.$$

*In particular, let $M > 0$, $\{u_n\}_{n\in\mathbb{N}} \in L^2(X,A)$ such that $u_n \to u$ in $L^2(X,C)$ and $\|u_n\|_{L^2(X,A)} \le M$. Then $u_n \to u$ in $L^2(X,B)$.*

The following Propositions 4.1 and 4.2 are based on the same idea. We shall detail 4.1, while 4.2 follows likewise.

**Proposition 4.1.** *Let* $\{v_n\} \in \mathcal{K}$, $v$ *such that* $v_n \to v$ *in* $L^2(0,T;L^2(\Gamma))$ *(*$\mathcal{K}$ *is compact, so* $v \in \mathcal{K}$*). We denote by* $\mathbf{w}_n, \mathbf{w}$ *the solutions (for a.e.* $x$*,* $\forall\ t$*) of the Cauchy problems*

$$\begin{cases} \mathbf{w}_n' &= \mathbf{F}(v_n, \mathbf{w}_n), \qquad \textit{on}\ \ \Sigma, \\ \mathbf{w}_n(0) &= \mathbf{w}_0, \qquad \textit{on}\ \ \Gamma, \end{cases}$$

$$\begin{cases} \mathbf{w}' &= \mathbf{F}(v, \mathbf{w}), \qquad \textit{on}\ \ \Sigma, \\ \mathbf{w}(0) &= \mathbf{w}_0, \qquad \textit{on}\ \ \Gamma. \end{cases}$$

*Then*

$$\mathbf{w}_n \to \mathbf{w} \quad \textit{in}\ \ L^2(\Gamma; C^0([0,T])^k. \tag{4.4}$$

*Proof.* By Lemma 2.1 we know that the operator

$$\begin{array}{rccc} \mathscr{A}: & C^0([0,T]) & \to & C^0([0,T])^k, \\ & v & \mapsto & \mathbf{w}, \end{array}$$

which maps $v \in C^0([0,T])$ into the solution $\mathbf{w}$ of the system of ODE (2.3), is continuous. Moreover, estimate (2.4) ensures that $\mathscr{A}$ satisfies condition (4.3):

$$\|\mathscr{A} v\|_{C^0([0,T])^k} = \|\mathbf{w}\|_{C^0([0,T])^k} \le c_1.$$

Therefore we can apply Theorem 4.2 with $B = C = C^0([0,T])$, $X = \Gamma$, and we find that the operator

$$\tilde{\mathscr{A}} : L^2(\Gamma; C^0([0,T])) \to L^2(\Gamma; C^0([0,T])),$$
$$(\tilde{\mathscr{A}} v)(x) := \mathscr{A} v(x) = \mathbf{w}(x),$$

is continuous.

Now, let $\{v_n\}_{n\in\mathbb{N}}$ and $v$ belong to $\mathcal{K}$, thus satisfying

$$\|v_n\|_{L^2(\Gamma;H^1(0,T))},\ \|v\|_{L^2(\Gamma;H^1(0,T))} \le \sqrt{M_0^2 + 4M_1^2},$$

(see the definition of $\mathcal{K}$ (4.2) and Lemma 2.2), and suppose that

$$v_n \to v, \qquad \text{in } L^2(0,T;L^2(\Gamma)) \cong L^2(\Gamma; L^2(0,T)).$$

Then, by Lemma 4.2,

$$v_n \to v \qquad \text{in}\ \ L^2(\Gamma; C^0([0,T])), \tag{4.5}$$

and finally, by continuity of $\tilde{\mathscr{A}}$, we obtain

$$\mathbf{w}_n \to \mathbf{w} \quad \text{in}\ \ L^2(\Gamma; C^0([0,T]))^k. \tag{4.6}$$

□

**Proposition 4.2.** *Let $\{v_n\}, v \in \mathcal{K}$, $\{\mathbf{w}_n\}, \mathbf{w} \in \mathcal{W}$, satisfy (4.5) and (4.6), that is*

$$\begin{array}{lll} i) & v_n \to v, & \text{in } L^2(\Gamma; C^0([0,T])), \\ ii) & \mathbf{w}_n, \to \mathbf{w} & \text{in } L^2(\Gamma, C^0([0,T]))^k, \end{array}$$

*We denote by $\mathbf{z}_n, \mathbf{z}$ the solutions of the Cauchy problems*

$$\begin{cases} \mathbf{z}_n' &= -\mathbf{J}(v_n, \mathbf{w}_n, \ \mathbf{log}\,(\mathbf{z}_n)) + \mathbf{H}(v_n, \mathbf{w}_n, \mathbf{z}_n), & \text{on } \Sigma, \\ \mathbf{z}_n(0) = \mathbf{z}_0, & & \text{on } \Gamma, \end{cases}$$

$$\begin{cases} \mathbf{z}' &= -\mathbf{J}(v, \mathbf{w}, \ \mathbf{log}\,(\mathbf{z})) + \mathbf{H}(v, \mathbf{w}, \mathbf{z}), & \text{on } \Sigma, \\ \mathbf{z}(0) &= \mathbf{z}_0, & \text{on } \Gamma. \end{cases}$$

*Then*

$$\mathbf{z}_n \to \mathbf{z}, \quad \mathbf{log}(\mathbf{z}_n) \to \mathbf{log}(\mathbf{z}), \quad \text{in } L^2(\Gamma; C^0([0,T]))^m.$$

*Proof.* Now we consider the operator

$$\begin{array}{llll} \mathscr{A}: & C^0([0,T]) \times C^0([0,T])^k & \to & (C^0([0,T]))^m \times (C^0([0,T]))^m, \\ & (v, \mathbf{w}) & \mapsto & (\mathbf{z}, \ \mathbf{log}(\mathbf{z})), \end{array}$$

where $\mathbf{z}$ is the solution of (2.9). Hence, let $\{v_n\}_{n\in\mathbb{N}}$, $v$, $\{\mathbf{w}_n\}_{n\in\mathbb{N}}$, $\mathbf{w}$ be as in the hypothesis of Proposition 4.2. Then, by Lemma 2.3

$$\mathscr{A}(v_n, \mathbf{w}_n) = \mathbf{z}_n \to \mathbf{z} = \mathscr{A}(v, \mathbf{w}) \quad \text{in } C^0([0,T])^m. \tag{4.7}$$

Moreover, convergence (4.7) and estimate (2.11) imply that there exists a compact set $K_2 \subset (0, +\infty)^m$ such that $\mathbf{z}_n(t) \in K$, $\forall\, t \in [0,T]$, $\forall\, n \in \mathbb{N}$, and therefore we obtain

$$\mathbf{log}(\mathbf{z}_n) \to \mathbf{log}(\mathbf{z}) \quad \text{in } C^0([0,T])^m, \tag{4.8}$$

so that $\mathscr{A}$ is continuous. Moreover, operator $\mathscr{A}$ satisfies condition (4.3), in fact, owing to estimate (2.10), there exist $c_1, c_2$ such that

$$\|\mathbf{z}\|_{C^0([0,T])^m} \leq c_1 + c_2 \|v\|_{L^2(0,T)}, \quad \forall\, v \in C^0([0,T]), \ \mathbf{w} \in C^0([0,T];[0,1])^k,$$

and estimate (2.11) guarantees that

$$\|\,\mathbf{log}(\mathbf{z})\|_{C^0([0,T])^m} \leq c_1 + c_2 \|v\|_{C^0([0,T])}, \quad \forall\, v \in C^0([0,T]), \ \mathbf{w} \in C^0([0,T];[0,1])^k.$$

Hence, by Theorem 4.2, the operator

$$\tilde{\mathscr{A}}: L^2(\Gamma; C^0([0,T])) \times L^2(\Gamma; C^0([0,T]))^k \to L^2(\Gamma; C^0([0,T]))^m \times L^2(\Gamma; C^0([0,T]))^m,$$

$$(\tilde{\mathscr{A}}(v, \mathbf{w}))(x) := \mathscr{A}(v(x), \mathbf{w}(x)) = (\mathbf{z}(x), \ \mathbf{log}\,\mathbf{z}(x))$$

is continuous.

Arguing as in the proof of Proposition 4.1, we conclude that if $\{v_n\}_{n\in\mathbb{N}}$ belong to $\mathcal{K}$ and $v_n \to v$ in $L^2(0,T; L^2(\Gamma))$, then

$$\mathbf{z}_n \to \mathbf{z}, \quad \mathbf{log}(\mathbf{z}_n) \to \mathbf{log}(\mathbf{z}) \quad \text{in } L^2(\Gamma; C^0([0,T]))^m. \tag{4.9}$$

□

***2) Continuity of operator*** $\mathcal{F}_2$. Now we are going to use the convergences (4.5), (4.6) and (4.9) in order to obtain continuity for $\mathcal{F}_2$.

*Remark* 7. Since $L^2(0,T;L^2(\Gamma)) \cong L^2(\Gamma;L^2(0,T))$, we remark that if

$$\{f_n\}, f \in L^2(\Gamma;C^0([0,T])), \quad f_n \to f \quad \text{in} \;\; L^2(\Gamma;C^0([0,T])),$$

then

$$f_n \to f \quad \text{in} \;\; L^2(0,T;L^2(\Gamma)).$$

**Proposition 4.3.** *Let* $\{\bar{v}_n\}, \;\bar{v} \in \mathcal{K}$, *such that*

$$\bar{v}_n \to \bar{v} \quad \text{in } L^2(0,T;L^2(\Gamma)).$$

*Let* $\{\mathbf{w}_n\}, \;\mathbf{w} \in \mathcal{W}$, *such that*

$$\mathbf{w}_n \to \mathbf{w} \quad \text{in } L^2(0,T;L^2(\Gamma))^k.$$

*Let* $\{\mathbf{z}_n\}, \;\mathbf{z} \in \mathcal{Z}$, *such that*

$$\mathbf{z}_n \to \mathbf{z}, \quad \mathbf{log}(\mathbf{z}_n) \to \mathbf{log}(\mathbf{z}) \quad \text{in } L^2(0,T;L^2(\Gamma))^m.$$

*We denote by* $\mathbf{u}, \mathbf{u}_n$ *the solutions of the systems*

$$\begin{cases} (B\mathbf{u}(t))' + A\mathbf{u}(t) = -\mathcal{I}_{ion}(t) + \mathbf{L}(t), & \text{in } \mathbf{V}' \quad \text{for a.e. } t \in ]0,T[, \\ B\mathbf{u}(0) = \ell^0 & \text{in } \mathbf{V}', \end{cases}$$

$$\begin{cases} (B\mathbf{u}_n(t))' + A\mathbf{u}_n(t) = -\mathcal{I}^n_{ion}(t) + \mathbf{L}(t), & \text{in } \mathbf{V}' \quad \text{for a.e. } t \in ]0,T[, \\ B\mathbf{u}_n(0) = \ell^0 & \text{in } \mathbf{V}', \end{cases}$$

*where* $\mathcal{I}_{ion} = \mathcal{I}_{ion}(\bar{v}, \mathbf{w}, \mathbf{z})$, $\mathcal{I}^n_{ion} = \mathcal{I}_{ion}(\bar{v}_n, \mathbf{w}_n, \mathbf{z}_n)$, $\mathbf{u} = (u_i, u_e)$, $\mathbf{u}_n = (u_{i,n}, u_{e,n})$, $v = u_i - u_e$, $v_n = u_{i,n} - u_{e,n}$.
*Then*

$$v_n \to v \quad \text{in} \;\; L^2(0,T;L^2(\Gamma)).$$

*Proof.* By estimate 3.16 we have that

$$\|v_n(t) - v(t)\|^2_{L^2(\Gamma)} \le C \int_0^t \|\bar{I}^n_{ion}(s) - \bar{I}_{ion}(s)\|^2_{L^2(\Gamma)} \, ds. \tag{4.10}$$

By definition (1.6), the right hand side is

$$\|\bar{I}^n_{ion} - \bar{I}_{ion}\|^2_{L^2(\Sigma)} = \int_0^T \int_\Gamma \left( \sum_{i=1}^m [J_i(\bar{v}_n, \mathbf{w}_n, \log z_{i,n}) - J_i(\bar{v}, \mathbf{w}, \log z_i)] + \right.$$

$$\left. + \tilde{H}(\bar{v}_n, \mathbf{w}_n, \mathbf{z}_n) - \tilde{H}(\bar{v}, \mathbf{w}, \mathbf{z}) \right)^2 d\mathscr{H}^2 dt,$$

so we need to show that

$$i) \quad J_i(\bar{v}_n, \mathbf{w}_n, \log z_{i,n}) \to J_i(\bar{v}, \mathbf{w}, \log z_i), \quad \text{in } L^2(\Sigma),$$

and

$$ii) \quad \tilde{H}(\bar{v}_n, \mathbf{w}_n, \mathbf{z}_n)) \to \tilde{H}(v, \mathbf{w}, \mathbf{z}), \quad \text{in } L^2(\Sigma),$$

$\forall\, i = 1, ..., m$. We see that $ii)$ comes immediately from the Lipschitz continuity of $\tilde{H}$ (see (1.8)), and the hypothesis on $\bar{v}_n$, $\mathbf{w}_n$ and $\mathbf{z}_n$. In order to prove $i)$ we make use of the finite–dimensional version of Theorem 4.2, with $X = \Sigma$, $B = \mathbb{R} \times \mathbb{R}^k \times \mathbb{R}^m$, $C = \mathbb{R}$.

For every $i = 1, \dots, m$, we can decompose $J_i$ into

$$J_i(v, \mathbf{w}, \log z_i) = J_i(v, \mathbf{w}, 0) + \frac{J_i(v, \mathbf{w}, \log z_i) - J_i(v, \mathbf{w}, 0)}{\log z_i} \log z_i =$$

$$= J_i(v, \mathbf{w}, 0) - J_i(0, \mathbf{w}, 0) + J_i(0, \mathbf{w}, 0) + \frac{J_i(v, \mathbf{w}, \log z_i) - J_i(v, \mathbf{w}, 0)}{\log z_i} \log z_i.$$

By hypothesis (1.7b) and (1.7c), since $\mathbf{w} \in [0,1]^k$ we obtain

$$|J_i(v, \mathbf{w}, \log z_i)| \le J_i(0, \mathbf{w}, 0) + L_v|v| + \overline{G}|\log z_i| \le C(1 + |v| + |\log z_i|).$$

Therefore, owing to Theorem 4.2 we conclude that

$$J_i(\bar{v}_n, \mathbf{w}_n, \log z_{i,n}) \to J_i(\bar{v}, \mathbf{w}, \log z_i) \quad \text{in} \quad L^2(0,T; L^2(\Gamma)), \quad \forall\, i = 1, \dots, m.$$

□

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