Ionic parameters identification of an inverse problem of strongly coupled PDE's system in cardiac electrophysiology using Carleman estimates

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IONIC PARAMETERS IDENTIFICATION OF AN INVERSE PROBLEM OF STRONGLY COUPLED PDE'S SYSTEM IN CARDIAC ELECTROPHYSIOLOGY USING CARLEMAN ESTIMATES

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Abstract. In this paper, we consider an inverse problem of determining multiple ionic parameters of a 2×2 strongly coupled parabolic-elliptic reaction-diffusion system arising in cardiac electrophysiology modelling. We use the bidomain model coupled to an ODE system and we consider a general formalism of physiologicaly-detailed cellular membrane models to describe the ionic exchanges at the microscopic level. Our main result is the uniqueness and a Lipschitz stability estimate of the ion channels conductance parameters of the model using subboundary observations over an interval of time. The key ingredients are a global Carleman-type estimate with a suitable observations acting on a part of the boundary.

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1. Introduction

The electric wave in the heart is governed by a system of reaction-diffusion partial differential equations called the bidomain model. This system is coupled nonlinearly to an ordinary differential equations (ODEs) modeling the cellular membrane dynamics. The cellular membrane electrical activity model is based on the Hodgkin and Huxley (HH) formalism [25] which has been adapted to cardiac Purkinje cells by Denis Nobel [39]. After that, many other model have been introduced to describe the electrical activity of the cell membrane in the myocardium. In 1977, Beeler and Reuter [5] introduced a ventricular cells model. Di Francesco and Noble proposed in 1985 a model that takes into account ion pumps, which allows different chemical species such as the sodium potassium and calcium to regain their stable states [22]. Rudy and his collaborators proposed series of models based on the HH formalism which are chronologically more and more complex [34, 36, 37, 40, 45] and take into account more and more the physiological behaviors of the ion channels. Other models like [12, 16, 46] have been also extensively used in the computational electrophysiology community. In all these models, the ion channels maximal conductance parameter plays an important role in generating the action potential but

also to consider some pathological conditions or when taking into account the effect of drugs. In [38], authors studied the sensitivity of the strength and duration of the action potential in the parameters describing the sodium channel. In [54], authors demonstrate the ability of computational models to simulate the effect of drug action on the electrical activity of the heart, at the level of the ion-channel, cell, heart and ECG body surface potential. In [41, 42], authors showed how, with few changes in the maximal conductances of the ion currents, they reproduced different control action potentials. In [1], the authors propose a mathematical approach for the analysis of drugs effects on the electrical activity of hiPSC-CMs based on multi-electrode array experiments where the drug acts directly on the maximal conductance of the targeted ion channel. All these examples demonstrate the importance of identifying or estimating the maximal conductance parameters when dealing with numerical simulations in multi-scale models. Despite their importance, ion channel maximal conductances have not been subject of abondant theoretical studies. The only theoretical work that we know is [2], which proves under certain conditions the stability of the ionic conductance parameters identification problem in case of the monodomain approximation. Two other works has been dedicated to the parameters of phenomenological ionic models still in the case of the monodomain approximation. In [10], authors showed Lipschitz stability inequalities for the identification of some parameters of the FitzHugh-Nagumo model from measurements on the cardiac potential and the ionic variable. The paper [33] shows the stability of the identification a reaction parameter in the Mitchell-Schaeffer model for the monodomain system. To the best of our knowledge no work proves the stability of the ion channels conductances in the case of the bidomain model. This would be the subject of our paper.

In the framework of the bidomain model, there some works that have been dedicated to study the stability of the cardiac tissue conductivities identifiability problem. The paper by Ainseba et al. [4] obtains the stability results for the conductivities diffusion coefficients to a strongly reaction-diffusion system modeling electrical activity in the heart using Carleman estimate. But their method is based on an approximation of the monodomain model and establish a Carleman estimate for a family of parabolic equations. Recently, Wu and Yu [52] convert the strongly coupled terms to the derivatives of the state variables components. The authors establish a Hölder stability result for the inverse conductivities problem for a linearized reaction term in the bidomain model in electrophysiology where the conductivities are scalar functions. However, considering a linear reaction term significantly reduces the complexity of the problem. Authors also consider a linear and simple approximation of the dynamic system governing the cell membrane activity at the microscopic level. Both simplification are non-realistic but also non phenomenologically based models in the sense that one could not generate the shape of an action potential with these models. However, the trick that they proposed to weaken the coupling in the bidomain system is very interesting and gives a good way to deal with a strongly coupled problem.

Strongly coupled systems are notoriously difficult to treat. Many of the standard results are not valid for a strongly coupled system. For example, there is no maximum principle nor DeGiorgi-Nash-Moser type estimates nor Carleman type estimates unless the system has special structures. In literature, it has been mostly assumed that the systems are regular elliptic and bounndedness of solutions are known in the study of the direct problem. Many inverse problems for the parameter identification use Carleman's estimates which are quite difficult to deal with, because the equations are coupled in the highest derivatives terms. Until now, only partial results were available in the literature concerning the Carleman estimates for strongly coupled systems. Different from the existing methods dealing with weakly or strongly coupled system, such as Fan and Chen [20] and Bellassoued & Yamamoto [8]. Carleman estimates for a weakly coupled parabolic system could be derived by adding up all Carleman estimates corresponding to each equation. The weakly coupled terms are absorbed by the terms on the left-hand side of the obtained inequality in this process, see Benabdallah et al. [9], Cristofol et al. [17]. As for a strongly coupled parabolic or hyperbolic system, the method above does not work, because the strongly coupled terms could not be simultaneously absorbed by adding up each Carleman estimate. However, to our best knowledge, if the matrix $(a_{i,j})_{1 \leq i,j \leq 2}$ formed by the parameters $a_{1,1}, a_{2,2}$ describing the self diffusion of the state variables and $a_{1,2}, a_{2,1}$ describing the influence of each component on another, is diagonalizable then the transformed system satisfies a weakly coupled system. In this case, Carleman estimate is obtained similarly to that of the weakly coupled system, see [8, 21, 50]. But due to the fact that the anisotropy in the bidomain

equations depends on the fiber directions, and the fact that the fiber direction are space dependent, one cannot diagonalize the problem as in [8, 50].

In this paper, we study the stability of the inverse problem of identification of these conductances parameters for a bidomain model: the reconstruction of these conductances from the measurement of electrical potentials over a part of the space boundary during the time and the state variables at a suitable time t_0. The stability results is based on a global Carleman estimate for a non-linear coupled system with one observation. Our inverse stability results are new because the bidomain system contains a strong coupling term. The technics we shall discuss are similar to the framework using Carleman estimates for inverse problems but the obtained estimates differs from those of [17, 44, 53] because of the strongly coupled terms. We use the same strategy introduced by Wu and Yu in [51] to convert the strongly coupled terms to the gradient of the extra-cellular potential u_e. Then, we consider the new version of the bidomain model as a whole to establish Carleman estimate under a weaker coupled equations. The paper is organized as follows: In Section 2, we briefly recall the general structure of cardiac cellular membrane models describing the transmembrane potential and the ionic exchange at the cell membrane. Then, we present the bidomain model describing the electrical wave propagation and recall some existence and uniqueness results that have been shown in [49] and we deal with a regularity results of the bidomain solution which will be useful in stability analysis. In section 3, we announce the main stability result including the conditions we need for the identification of multiple parameters. The proof of the main result is divided into two sections. In Section 4, we prove the global Carleman inequality for the reaction-diffusion system. Most of the non-classical parts of the proof of the main result are presented in Section 5 where we prove the stability estimate of conductances parameters.

2. Mathematical Model

Let $\Omega \subset \mathbb{R}^n$ $(n \geq 1)$ be a bounded connected open set whose boundary $\Gamma = \partial \Omega$ is regular enough, $(\Omega \subset \mathbb{R}^3$ being the natural domain of the hearth). Let $T > 0$ and $\Gamma_0 \subset \Gamma$ be a relatively open subset of Γ. We will use the notation $Q = \Omega \times (0, T)$, $\Sigma = \Gamma \times (0, T)$ and $\Sigma_0 = \Gamma_0 \times (0, T)$.

We introduce a two reaction-diffusion parabolic PDEs system called *bidomain model*, coupled to a system of ODEs. This model was proposed in the late 1970s by Tung [47] and is now the generally accepted model of electrical behaviour of cardiac tissue (see Henriquez [24], Keener and Sneyd [31]), can be written as:

$$
\begin{cases}
c_m \partial_t v + I_{ion}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) = div(\boldsymbol{\sigma}_i \nabla u_i) + I_i^s & \text{in } Q, \\
c_m \partial_t v + I_{ion}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) = -div(\boldsymbol{\sigma}_e \nabla u_e) - I_e^s & \text{in } Q, \\
\partial_t \mathbf{w} = \boldsymbol{F}(v, \mathbf{w}) & \text{in } Q, \\
\partial_t \mathbf{z} = \boldsymbol{G}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) & \text{in } Q, \\
\boldsymbol{\sigma}_i \nabla u_i . \nu = \boldsymbol{\sigma}_e \nabla u_e . \nu = 0 & \text{on } \Sigma,
\end{cases}
\tag{2.1}
$$

where $u_i = u_i(x, t)$ and $u_e = u_e(x, t)$ represent, respectively, the intracellular and extracellular electric potentials, whose difference $v := u_i - u_e$ is the transmembrane potential. $\mathbf{w} := \mathbf{w}(x, t) = (w_1, \ldots, w_k)(x, t)$ and $\mathbf{z} := \mathbf{z}(x, t) = (z_1, \ldots, z_m)(x, t)$ are the gating variables and the ionic intracellular concentration variables, respectively. The surface capacitance of the membrane is represented by the constant $c_m > 0$. For simplicity, we shall suppose $c_m = 1$. Here, $I_i^s := I_i^s(x, t)$ and $I_e^s := I_e^s(x, t)$ are respectively the internal and the external applied current sources.

In an isolated heart, no current flows out of the heart, as expressed by the Neumann conditions. We complete this model with initial data:

$$
v(\cdot, 0) = v_0, \quad \mathbf{w}(\cdot, 0) = \mathbf{w}_0, \quad \mathbf{z}(\cdot, 0) = \mathbf{z}_0, \quad x \in \Omega.
\tag{2.2}
$$

The ionic current $I_{ion} := I_{ion}(x, t)$ and the functions $\boldsymbol{F}$ and $\boldsymbol{G}$ depends of the considering ionic model.

In the membrane model, the ionic current I_{ion} has the following general structure [43]:

$$I_{ion}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) = \sum_{i=1}^{N} \bar{\varrho}_i y_i(v) \prod_{j=1}^{k} w_j^{p_{j,i}} (v - E_i(\mathbf{z})), \tag{2.3}$$

where N is the number of ionic currents, $\bar{\varrho}_i := \bar{\varrho}_i(x)$ is the maximal conductance associated with the ith current, y_i is a gating function depending only on the membrane potentiel v, $p_{j,i}$ are positive integers exponents and E_i is the reversal potential for the ith current I_i, which is the related equilibrium (Nernst) potential and is given by

$$E_i(\mathbf{z}) = \overline{\gamma}_i \log\left(\frac{z_e}{z_i}\right), \quad \mathbf{z} = (z_1, \dots, z_m), \tag{2.4}$$

where $\overline{\gamma}_i$ is a constant and z_i, $i = 1, \dots, m$, are the intracellular concentrations. The constant z_e denotes an extracellular concentration. The anisotropic properties of the two media are modeled by an intracellular and extracellular conductivity tensors $\boldsymbol{\sigma}_i(x)$ and $\boldsymbol{\sigma}_e(x)$. Generally, the conductivities $\boldsymbol{\sigma}_i$ and $\boldsymbol{\sigma}_e$ are two matrices given by

$$\boldsymbol{\sigma}_j(x) = \sigma_j^t(x)\boldsymbol{I} + (\sigma_j^l(x) - \sigma_j^t(x))\boldsymbol{a}_l(x)\boldsymbol{a}_l^T(x),$$

where σ_j^l and σ_j^t, $j \in \{i, e\}$ are the intra- and extracellular conductivities along and transversal to the direction of the fiber (parallel to $\boldsymbol{a}_l(x)$), respectively. In the case of equal anisotropy, i.e the so-called anisotropy ratios $\sigma_i^t/\sigma_i^l = \sigma_e^t/\sigma_e^l = 1$, the $\boldsymbol{\sigma}_i$ and $\boldsymbol{\sigma}_e$ are simplified as $\boldsymbol{\sigma}_i(x) = \sigma_i(x)\boldsymbol{I}$ and $\boldsymbol{\sigma}_e(x) = \sigma_e(x)\boldsymbol{I}$ with $\sigma_i(x) = \sigma_i^t(x)$, $\sigma_e(x) = \sigma_e^t(x)$, which is the case we discussed.

For the ODEs, the dynamics of the gating variable $\mathbf{w}$ is described in the Hodgkin-Huxley formalism by a system of ordinary differential equations which when w_j is a gating variable ($0 \leq w_j \leq 1$) are governed by the following equation,

$$\partial_t w_j = F_j(v, w_j) := \alpha_j(v)(1 - w_j) - \beta_j(v)w_j, \quad j = 1, \dots, k, \tag{2.5}$$

where α_j and β_j are positive rational functions of exponentials in v. A general expression for both α_j and β_j is given by

$$\frac{\mu_1 e^{\mu_2(v - v_n)} + \mu_3(v - v_n)}{1 + \mu_4 e^{\mu_5(v - v_n)}}, \tag{2.6}$$

where μ_1, μ_3, μ_4, v_n are non-negative constants and μ_2, μ_5 are positive constants.

The dynamics of the ionic concentration variables $\mathbf{z}$ is described by the additional system of ODEs:

$$\partial_t z_i = G_i(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) := -J_i(\bar{\varrho}, v, \mathbf{w}, \log z_i) + H_i(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}), \quad i = 1, \dots, m. \tag{2.7}$$

Assumptions 2.1. *We assume that:*

1) *The conductivities of the intracellular and extracellular $\sigma_i, \sigma_e \in \mathcal{C}^2(\bar{\Omega})$, such that $0 < \underline{\sigma_j} < \sigma_j(x) < \overline{\sigma_j}$, $j \in \{i, e\}$, in $\bar{\Omega}$.*

2) *We use the regularized form of the variable $y_i(v)$ in hyperbolic functions introduced in [19]. In this case, $y_i(v)$ is a $\mathcal{C}^\infty$ function with respect to the variable v for $i = 1, \dots, N$, and then is locally Lipschitz since v is bounded, similarly for the function $y_i(v)v$.*

3) *J_i and H_i are locally Lipschitz continuous functions where:*

$$J_i \in \mathcal{C}^2(\mathbb{R}_+^* \times \mathbb{R} \times \mathbb{R}^k \times \mathbb{R}), \quad 0 < g_*(\mathbf{w}) \leq \frac{\partial J_i}{\partial \tau}(\bar{\varrho}, v, \mathbf{w}, \tau) \leq g^*(\mathbf{w}), \quad \left|\frac{\partial J_i}{\partial v}(\bar{\varrho}, v, \mathbf{w}, 0)\right| \leq L_v(\mathbf{w}), \tag{2.8}$$

g_*, g^*, L_v *belong to $\mathcal{C}^1(\mathbb{R}^k, \mathbb{R}_+)$, and*

$$H_i \in \mathcal{C}^2(\mathbb{R}_+^* \times \mathbb{R} \times \mathbb{R}^k \times (0, +\infty)^m) \cap \mathrm{Lip}(\mathbb{R}_+^* \times \mathbb{R} \times [0, 1]^k \times (0, +\infty)^m). \tag{2.9}$$

Remark 2.2. *One could find in the literature many refined models based on Hodgkin-Huxley formalism taking into account different quantities. For example, we recall here the following models: Beeler-Reuter ([5], $N = 4, k = 6, m = 1$), phase-I Luo-Rudy ([36], $N = 6, k = 6, m = 1$), phase-II Luo-Rudy ([37], $N = 10, k = 6, m = 5$).*

Now, we propose a new approach to the bidomain equations (2.1). Our idea is to use a reformulation of (2.1) as a parabolic PDE coupled to an elliptic one, by replacing $u_i = v + u_e$ in the first PDE. The boundary condition is also reformulated in terms of v and u_e. We have:

$$\begin{cases} \partial_t v - div(\sigma_i \nabla v) + I_{ion}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) = div(\sigma_i \nabla u_e) + I_i^s & \text{in } Q, \\ -div(\sigma_e \nabla u_e) - I_{ion}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) = \partial_t v + I_e^s & \text{in } Q, \\ \partial_t \mathbf{w} = \boldsymbol{F}(v, \mathbf{w}) & \text{in } Q, \\ \partial_t \mathbf{z} = \boldsymbol{G}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) & \text{in } Q, \\ \sigma_i \nabla v . \nu + \sigma_i \nabla u_e . \nu = 0 & \text{on } \Sigma, \\ \sigma_e \nabla u_e . \nu = 0 & \text{on } \Sigma, \end{cases} \tag{2.10}$$

By using the second equation in (2.10), we obtain

$$\begin{aligned} -div(\sigma_i \nabla u_e) &= -\nabla \cdot (\sigma_i \sigma_e^{-1} \sigma_e \nabla u_e) \\ &= -\nabla(\sigma_i \sigma_e^{-1}) \cdot \sigma_e \nabla u_e - \sigma_i \sigma_e^{-1} div(\sigma_e \nabla u_e) \\ &= \sigma_e^{-1}(\sigma_i \partial_t v + \sigma_i(I_{ion} + I_e^s)) + \boldsymbol{A}(x) \cdot \nabla u_e, \end{aligned} \tag{2.11}$$

with

$$\boldsymbol{A}(x) := -\nabla(\sigma_e^{-1} \sigma_i)\sigma_e = \sigma_e^{-1}(\sigma_i \nabla \sigma_e - \sigma_e \nabla \sigma_i). \tag{2.12}$$

Substituting (2.11) into (2.10) yields

$$\begin{cases} (1 + \sigma_i \sigma_e^{-1})\partial_t v - div(\sigma_i \nabla v) = -(1 + \sigma_i \sigma_e^{-1})I_{ion}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) - \boldsymbol{A}(x) \cdot \nabla u_e + I_i^s - \sigma_i \sigma_e^{-1} I_e^s & \text{in } Q, \\ -div(\sigma_e \nabla u_e) = \partial_t v + I_{ion}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) + I_e^s & \text{in } Q, \\ \partial_t \mathbf{w} = \boldsymbol{F}(v, \mathbf{w}) & \text{in } Q, \\ \partial_t \mathbf{z} = \boldsymbol{G}(\bar\varrho, v, \mathbf{w}, \mathbf{z}) & \text{in } Q, \\ \sigma_i \nabla v . \nu + \sigma_i \nabla u_e . \nu = 0 & \text{on } \Sigma, \\ \sigma_e \nabla u_e . \nu = 0 & \text{on } \Sigma, \end{cases} \tag{2.13}$$

Hence we consider the problem of finding unknown functions v, u_e, $\mathbf{w}$ and $\mathbf{z}$ verifying (2.13). Since $v = u_i - u_e$, it is natural decompose the initial condition v_0 as $v_0 = u_{i,0} - u_{e,0}$.

Now, we state some regularity and estimate results proved in [48, 49] of a strong solution to problem (2.1).

Lemma 2.3. *Assume that $(v_0, \mathbf{w}_0, \mathbf{z}_0) \in H^2(\Omega) \times L^2(\Omega)^k \times L^2(\Omega)^m$, with $\log \mathbf{z}_0 := (\log z_{0,1}, \ldots, \log z_{0,m}) \in L^2(\Omega)^m$, and*

$$I_{i,e}^s \in L^p(0, T; L^2(\Omega)) \cap H^2(0, T; H^2(\Omega)), \, p > 4, \tag{2.14}$$

then we have
    1)

$$u_{i,e} \in L^p(0, T; H^2(\Omega)),$$

$$v \in W^{1,p}(0,T;L^2(\Omega)) \cap L^2(0,T;H^2(\Omega)) \cap \mathcal{C}^0([0,T],\mathcal{C}^0(\Omega)), \quad \text{for } p > 4,$$
$$\mathbf{w} : Q \to [0,1]^k \quad measurable, \quad \mathbf{z} : Q \to (0,+\infty)^m \quad measurable,$$
$$w_j(x,.) \in \mathcal{C}^1(0,T) \cap \mathcal{C}^0([0,T]), \quad for \quad a.e., \quad x \in \Omega, \quad j = 1,\dots,k,$$
$$z_i(x,.) \in \mathcal{C}^1(0,T) \cap \mathcal{C}^0([0,T]), \quad for \quad a.e., \quad x \in \Omega, \quad i = 1,\dots,m,$$
$$\mathbf{z} \in H^1(0,T;L^2(\Omega))^m \cap L^\infty(Q)^m, \quad \mathbf{\log z} := (\log z_1,\dots,\log z_m) \in L^\infty(Q)^m.$$

2) *There exists a constant $C > 0$, independant of $v, \mathbf{w}, \mathbf{z}$, such that*

$$|\mathbf{z}(x,t)| \le C(1 + |\mathbf{z}_0(x)| + \|v(x)\|_{L^2(0,t)}), \quad a.e., \ x \in \Omega, \tag{2.15}$$

and

$$|\mathbf{\log z}(x,t)| + |\partial_t \mathbf{z}(x,t)| \le C(1 + |\mathbf{z}_0(x)| + \|v(x)\|_{\mathcal{C}^0(0,t)}), \quad a.e., \ x \in \Omega, \tag{2.16}$$
$\forall t \in [0,T]$, *for a.e.* $x \in \Omega$.

3) *There exists a constant $C > 0$, depending on m, T such that, $\forall i = 1,\dots,m$,*

$$z_i(x,t) \ge \exp[-C(1 + \|\mathbf{z}_0\|_{L^\infty} + \|v\|_{\mathcal{C}^0([0,T],\mathcal{C}^0(\Omega))})] > 0, \quad \forall t \in [0,T], a.e., x \in \Omega. \tag{2.17}$$

4) *There exists $M_\infty > 0$, depending on the data of the problem, such that:*

$$\sup\{|v(x,t)| : (x,t) \in Q\} \le M_\infty. \tag{2.18}$$

Now, we will establish regularity results for the solution of the bidomain system (2.13). The aim is to improve the regularity results given in Lemma 2.3 in order to satisfy some assumptions useful for the stability result.

Proposition 2.4. *Let $(v, u_e, \mathbf{w}, \mathbf{z})$ be the solution of bidomain system (2.1), with initial conditions $(v_0, u_{e,0}, \mathbf{w}_0, \mathbf{z}_0)$.* ∎

- *If $v_0, u_{e,0} \in H^2(\Omega)$, $\mathbf{w}_0 \in L^2(\Omega)^k$, $\mathbf{z}_0 \in L^2(\Omega)^m$, and $I_{i,e}^s$ verify the regularity (2.14), then*

$$v, u_e \in W^{1,\infty}(0,T;H^1(\Omega)) \cap L^2(0,T;H^2(\Omega)) \cap H^1(0,T;H^1(\Omega)),$$
$$\mathbf{w} \in W^{1,\infty}(0,T;L^2(\Omega))^k, \quad and \quad \mathbf{z} \in W^{1,\infty}(0,T;L^2(\Omega))^m. \tag{2.19}$$

Moreover if

$$\mathbf{w}_0 \in H^1(\Omega)^k, \quad and \quad \mathbf{z}_0 \in H^1(\Omega)^m, \tag{2.20}$$

then

$$\mathbf{w} \in W^{1,\infty}(0,T;H^1(\Omega))^k, \quad and \quad \mathbf{z} \in W^{1,\infty}(0,T;H^1(\Omega))^m. \tag{2.21}$$

- *If $v_0, u_{e,0} \in H^4(\Omega)$, $\mathbf{w}_0 \in H^2(\Omega)^k$, $\mathbf{z}_0 \in H^2(\Omega)^m$, and $I_{i,e}^s$ verify the regularity (2.14). Then the solution of (2.1) satisfies*

$$v, u_e \in H^1(0,T;H^3(\Omega)) \cap H^2(0,T;H^1(\Omega)),$$
$$\mathbf{w} \in W^{1,\infty}(0,T;H^2(\Omega))^k \cap H^2(0,T;L^2(\Omega))^k, \tag{2.22}$$
$$\mathbf{z} \in W^{1,\infty}(0,T;H^2(\Omega))^m \cap H^2(0,T;L^2(\Omega))^m.$$

Moreover if

$$\mathbf{w}_0 \in H^3(\Omega)^k, \quad and \quad \mathbf{z}_0 \in H^3(\Omega)^m, \tag{2.23}$$

then

$$\mathbf{w} \in W^{1,\infty}(0,T;H^3(\Omega))^k \hookrightarrow H^1(0,T;H^3(\Omega))^k,$$
$$\mathbf{z} \in W^{1,\infty}(0,T;H^3(\Omega))^m \hookrightarrow H^1(0,T;H^3(\Omega))^m. \tag{2.24}$$

The proof of proposition 2.4 is provided in the Appendix 7.

3. Inverse problem: Main result

Our inverse problem is related to determination of multiple ionic parameter $\bar{\varrho}_i$, $1 \leq i \leq N$, of a non linear parabolic reaction diffusion system coupled with an ordinary differential equations from a set of boundary observations $(u_{e,\ell}, \mathbf{w}_\ell, \mathbf{z}_\ell)_{|\Gamma_0 \times (0,T)}$ and $(u_{e,\ell}(x, t_0), \mathbf{w}_\ell(x, t_0), \mathbf{z}_\ell(x, t_0))$, $x \in \Omega$, $1 \leq \ell \leq N$.

In order to formulate our results, we need to introduce the following notations: For a sequence functions $(\widetilde{v}_\ell, \widetilde{\mathbf{w}}_\ell, \widetilde{\mathbf{z}}_\ell) \in H^3(\Omega) \times \mathcal{C}^1(\Omega)^k \times \mathcal{C}^1(\Omega)^m$, we define the $N \times N$ matrix Λ as follows

$$\Lambda(\widetilde{v}_\ell(x), \widetilde{\mathbf{w}}_\ell(x), \widetilde{\mathbf{z}}_\ell(x)) = \begin{pmatrix} S_{1,1}(x) & S_{2,1}(x) & \ldots & S_{N,1}(x) \\ S_{1,2}(x) & S_{2,2}(x) & \ldots & S_{N,2}(x) \\ \vdots & \vdots & \ddots & \vdots \\ S_{1,N}(x) & S_{2,N}(x) & \ldots & S_{N,N}(x) \end{pmatrix}, \tag{3.1}$$

where

$$S_{i,\ell}(x) = y_i(\widetilde{v}_\ell(x)) \, (\widetilde{v}_\ell(x) - E_i(\widetilde{\mathbf{z}}_\ell(x))) \prod_{j=1}^k (\widetilde{\mathbf{w}}_\ell)_j^{p_{j,i}}(x), \quad 1 \leq \ell, i \leq N.$$

Let us fix constant $M_0 > 0$. We introduce an admissible set of unknown coefficients vector $\bar{\varrho}$ by

$$\mathcal{A} = \left\{ \bar{\varrho} \in H^3(\Omega)^N, \ \|\bar{\varrho}\|_{l^2(H^3(\Omega)^N)} \leq M_0 \right\}. \tag{3.2}$$

We obtain the following stability result.

Theorem 3.1. *Let $t_0 \in (0, T)$, Γ_0 be a subdomain of $\partial\Omega$ and let $\bar{\varrho}^{(2)} \in \mathcal{A}$ be arbitrary fixed. We assume that $I_{i,e}^{s,\ell} \in L^p(0, T; L^2(\Omega)) \cap H^1(0, T; H^2(\Omega))$, $p > 4$, $1 \leq \ell \leq N$, satisfy*

$$\det \left(\Lambda \left(v_\ell^{(2)}(x, t_0), \mathbf{w}_\ell^{(2)}(x, t_0), \mathbf{z}_\ell^{(2)}(x, t_0) \right) \right) \neq 0, \quad \forall x \in \Omega. \tag{3.3}$$

Here $v_\ell^{(2)}, \mathbf{w}_\ell^{(2)}$ and $\mathbf{z}_\ell^{(2)}$ are the state variables of (2.13) with $\bar{\varrho} = \bar{\varrho}^{(2)}$ and $I_{i,e}^s = I_{i,e}^{s,\ell}$. Furthermore, we assume that

$$\|v_\ell^{(2)}\|_{\mathcal{C}^0([0,T];\mathcal{C}^1(\overline{\Omega}))} + \|\mathbf{w}_\ell^{(2)}\|_{\mathcal{C}^0([0,T];\mathcal{C}^1(\overline{\Omega}))^k} + \|\mathbf{z}_\ell^{(2)}\|_{\mathcal{C}^0([0,T];\mathcal{C}^1(\overline{\Omega}))^m} \leq M, \tag{3.4}$$

for some positive M. Then there exists a constant $C > 0$ such that we have:

$$\|\bar{\varrho}^{(1)} - \bar{\varrho}^{(2)}\|_{l^2(L^2(\Omega))^N} \leq C \sum_{\ell=1}^N \Big(\|(u_{e,\ell}^{(1)} - u_{e,\ell}^{(2)})\|_{H^2(0,T;H^1(\Gamma_0))}$$

$$+ \|(u_{e,\ell}^{(1)} - u_{e,\ell}^{(2)})(\cdot, t_0)\|_{H^2(\Omega)} + \|(\mathbf{w}_\ell^{(1)} - \mathbf{w}_\ell^{(2)})(\cdot, t_0)\|_{L^2(\Omega)^k} + \|(\mathbf{z}_\ell^{(1)} - \mathbf{z}_\ell^{(2)})(\cdot, t_0)\|_{L^2(\Omega)^m} \Big), \tag{3.5}$$

for all $\bar{\varrho}^{(1)} \in \mathcal{A}$.

Remark 3.2. *The condition (3.4) is a straightforward consequence of the Proposition 2.4 and a Sobolev embedding theorem (e.g., Thm. 5.4 in [3]).*

$$H^1(0, T; H^3(\Omega)) \hookrightarrow \mathcal{C}^0([0, T]; \mathcal{C}^1(\overline{\Omega})), \tag{3.6}$$

if the initial conditions verify

$$v_\ell^{(2)}(t = 0) \in H^4(\Omega), \quad u_{e,\ell}^{(2)}(t = 0) \in H^4(\Omega), \quad \mathbf{w}_\ell^{(2)}(t = 0) \in H^3(\Omega)^k, \quad \text{and} \quad \mathbf{z}_\ell^{(2)}(t = 0) \in H^3(\Omega)^m. \tag{3.7}$$

We introduced the condition (3.4), because it may be obtained with a less regularities on the initial conditions.

By Theorem 3.1, we can readily derive the uniqueness in the inverse problem.

Corollary 3.3. *Under the same assumptions as in Theorem 3.1 and if*

$$(u_{e,\ell}^{(1)}(x,t_0), \mathbf{w}_\ell^{(1)}(x,t_0), \mathbf{z}_\ell^{(1)}(x,t_0)) = (u_{e,\ell}^{(2)}(x,t_0), \mathbf{w}_\ell^{(2)}(x,t_0), \mathbf{z}_\ell^{(2)}(x,t_0)), \quad in \ x \in \Omega, \tag{3.8}$$

$$u_{e,\ell}^{(1)}(x,t) = u_{e,\ell}^{(2)}(x,t), \quad in \ \Gamma_0 \times (0,T), \tag{3.9}$$

for $\ell = 1, \ldots, N$, *then* $\bar\varrho^{(1)} = \bar\varrho^{(2)}$ *in* Ω.

Since the number of the unknown coefficients is N, it is natural to expect that N-times observations can yield the Lipschitz stability. Our tool are a weighted L^2-norm estimates of the solution of a PDE called *Carleman estimates*, where the weight takes an exponential form. They are an important tool in subjects in analysis of PDEs such as unique continuation [13, 26], control theory [15, 18] and coefficient inverse problems [4, 6, 7, 27–29, 32, 52].

4. Global Carleman inequality for reaction-diffusion system

In this section, we give Carleman estimate for the reaction-diffusion model with a finite observations acting on a subboundary Σ_0 of $\partial\Omega$ on the right-hand side of the estimate. This Carleman estimate would be used later for the stability and uniqueness of the solution of the parameter identification problem. We are interested in identifying the parameters $\bar\varrho_i$, $i = 1, \ldots, N$, where $\bar\varrho_i$ is the maximal conductance associated with the ith current.

In order to frame a Carleman type estimate, we shall first introduce a particular type of weight functions.

4.1. **Weight functions and Carleman estimate**

For our Carleman estimate, we need a weight function β with the following properties [18].

Lemma 4.1. *Let* $\Gamma_0 \neq \emptyset \subset \partial\Omega$ *be an arbitrary relatively open subset. Then there exists a function* $\beta \in \mathcal{C}^2(\overline\Omega)$ *such that*

$$\beta(x) > 0 \quad \forall x \in \Omega, \qquad |\nabla\beta(x)| > 0 \quad \forall x \in \overline\Omega, \quad and \quad \boldsymbol\sigma_{i,e}(x)\nabla\beta(x) \cdot \nu(x) \leq 0, \qquad x \in \partial\Omega \setminus \Gamma_0. \tag{4.1}$$

Proof 4.1. *The proof of the Lemma 4.1 is given in [27].*

We set

$$\varphi(x,t) = \frac{e^{\lambda\beta(x)}}{t(T-t)} \tag{4.2}$$

and

$$\eta(x,t) = \frac{e^{2\lambda\|\beta\|_\infty} - e^{\lambda\beta(x)}}{t(T-t)} \tag{4.3}$$

where $\lambda > 0$ and $t \in (0,T)$. Let us consider a boundary value problem for the parabolic operator:

$$\begin{cases} \mathfrak{L}u(x,t) \equiv \partial_t u - \sum_{i,j=1}^n \sigma_{ij}(x)\partial_i\partial_j u = \mathcal{F}, & \text{in Q}, \\ \nabla u.\nu = 0, & \text{on } \Sigma. \end{cases} \tag{4.4}$$

We recall that

$$H^{2,1}(Q) = \{u \in L^2(Q) | \ \partial_t u, \partial_i u, \partial_i\partial_j u \in L^2(Q), \ 1 \leq i,j \leq n\}, \tag{4.5}$$

Moreover, we set

$$\tilde{\gamma} = \sum_{i,j=1}^{n} \|\sigma_{ij}\|_{C^2(\bar{\Omega})}, \tag{4.6}$$

By β constructed in Lemma 4.1, we have the following Lemma:

Lemma 4.2. *Let $\sigma(x) \in C^2(\overline{\Omega})$ and the function φ, η be defined by (4.1)-(4.3). Then there exists a number $\lambda_0 > 0$ such that for an arbitrary $\lambda \geq \lambda_0$, we can choose a constant $s_0(\lambda) \geq 0$ satisfying: there exists a constant $C = C(s_0, \lambda_0) > 0$ such that:*

$$\int_Q \left\{ (s\varphi)^{p-1}(|\partial_t u|^2 + \sum_{i,j=1}^{n} |\partial_i \partial_j u|^2) + (s\varphi)^{p+1}\lambda^2 |\nabla u|^2 + (s\varphi)^{p+3}\lambda^4 |u|^2 \right\} e^{-2s\eta} dx dt$$

$$\leq C \int_Q (s\varphi)^p |\mathfrak{L}u|^2 e^{-2s\eta} dx\,dt + Ce^{C(\lambda)s} \int_{\Sigma_0} \left(|\partial_t u|^2 + |\nabla u|^2 + |u|^2 \right) dSdt, \tag{4.7}$$

for all $s > s_0$, $p = 0, 1, 2$, and all $u \in H^{2,1}(Q)$. Here the constant $C > 0$ depends continuously on λ_0 but is independent of s, and λ_0 depends continuously on $\tilde{\gamma}$.

Proof 4.2. *The proof of this lemma is similar to the proof given in [14]. We can further refer to [23].*

4.2. **Global Carleman inequality for bidomain equations**

We consider the solutions $(v^{(n)}, u_e^{(n)}, \mathbf{w}^{(n)}, \mathbf{z}^{(n)})$, $n = 1, 2$, to the following systems

$$\begin{cases} (1 + \sigma_i \sigma_e^{-1})\partial_t v^{(n)} - div(\sigma_i \nabla v^{(n)}) + (1 + \sigma_i \sigma_e^{-1})I_{ion}(v^{(n)}, \mathbf{w}^{(n)}, \mathbf{z}^{(n)}) = \\ \boldsymbol{A}(x) \cdot \nabla u_e^{(n)} + I_i^s - \sigma_i \sigma_e^{-1}I_e^s & \text{in } Q, \\ -div(\sigma_e \nabla u_e^{(n)}) = I_{ion}(v^{(n)}, \mathbf{w}^{(n)}, \mathbf{z}^{(n)}) + \partial_t v^{(n)} + I_e^s & \text{in } Q, \\ \partial_t \mathbf{w}^{(n)} = \boldsymbol{F}(v^{(n)}, \mathbf{w}^{(n)}) & \text{in } Q, \\ \partial_t \mathbf{z}^{(n)} = \boldsymbol{G}(v^{(n)}, \mathbf{w}^{(n)}, \mathbf{z}^{(n)}) & \text{in } Q, \\ \sigma_i \nabla v^{(n)}.\nu + \sigma_i \nabla u_e^{(n)}.\nu = 0 & \text{on } \Sigma, \\ \sigma_e \nabla u_e^{(n)}.\nu = 0 & \text{on } \Sigma, \end{cases} \tag{4.8}$$

and we consider the difference

$$v = v^{(1)} - v^{(2)}, \quad u_e = u_e^{(1)} - u_e^{(2)}, \quad \mathbf{w} = \mathbf{w}^{(1)} - \mathbf{w}^{(2)}, \quad \mathbf{z} = \mathbf{z}^{(1)} - \mathbf{z}^{(2)}, \quad \bar{\varrho} = \bar{\varrho}^{(1)} - \bar{\varrho}^{(2)}. \tag{4.9}$$

Then, $(v, u_e, \mathbf{w}, \mathbf{z})$ is solution to the following problem

$$\begin{cases} (1 + \sigma_i \sigma_e^{-1})\partial_t v - div(\sigma_i \nabla v) = -(1 + \sigma_i \sigma_e^{-1})h - \boldsymbol{A}(x) \cdot \nabla u_e & \text{in } Q, \\ -div(\sigma_e \nabla u_e) = h + \partial_t v & \text{in } Q, \\ \partial_t \mathbf{w} = \Phi & \text{in } Q, \\ \partial_t \mathbf{z} = \Psi & \text{in } Q, \\ \sigma_i \nabla v.\nu + \sigma_i \nabla u_e.\nu = 0 & \text{on } \Sigma, \\ \sigma_e \nabla u_e.\nu = 0 & \text{on } \Sigma, \end{cases} \tag{4.10}$$

Here

$$
\begin{aligned}
h := \; & = \; I_{ion}(\bar{\varrho}^{(1)}, v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}) - I_{ion}(\bar{\varrho}^{(2)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}) \\
& = \; \mathbf{S}^{\top}(v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}) \cdot \bar{\varrho} + R(v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}),
\end{aligned}
\tag{4.11}
$$

where the vector $\mathbf{S} = (S_i)_{1 \leq i \leq N}$ is defined as follow:

$$
S_i(v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}) = y_i(v^{(2)})(v^{(2)} - E_i(\mathbf{z}^{(2)})) \prod_{j=1}^{k} (w_j^{(2)})^{p_{j,i}}, \quad i = 1, \dots, N,
\tag{4.12}
$$

and

$$
R(v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}) = I_{ion}(\bar{\varrho}^{(2)}, v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}) - I_{ion}(\bar{\varrho}^{(2)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}).
\tag{4.13}
$$

In (4.11), $^{\top}$ represent the transpose of any matrix and the expression $\mathbf{S}^{\top}(v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}) \cdot \bar{\varrho}$ is the Euclidian scalar products of the row vector $\mathbf{S}^{\top}$ and the colon vector $\bar{\varrho} := (\bar{\varrho}_i)_{1 \leq i \leq N}$ formed by the ionic parameters ϱ_i. Finally, the functions Φ and Ψ are respectively given by:

$$
\begin{aligned}
\Phi \; & = \; \boldsymbol{F}(v^{(1)}, \mathbf{w}^{(1)}) - \boldsymbol{F}(v^{(2)}, \mathbf{w}^{(2)}), & (4.14) \\
\Psi \; & = \; \boldsymbol{G}(\bar{\varrho}^{(1)}, v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}) - \boldsymbol{G}(\bar{\varrho}^{(2)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)}). & (4.15)
\end{aligned}
$$

In the next, we denote

$$
R(x,t) = R(v^{(1)}, \mathbf{w}^{(1)}, \mathbf{z}^{(1)}, v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)})(x,t), \quad \mathbf{S}(x,t) = \mathbf{S}^{\top}(v^{(2)}, \mathbf{w}^{(2)}, \mathbf{z}^{(2)})(x,t),
\tag{4.16}
$$

and

$$
h(x,t) := \mathbf{S}^{\top}(x,t) \cdot \bar{\varrho}(x) + R(x,t).
\tag{4.17}
$$

Our Carleman estimate for the bidomain equations (4.10) is as follow.

Lemma 4.3. *Let the Assumptions 2.1 be fulfilled and the function φ, η be defined by (4.1)-(4.3). Then there exists a number $\lambda_0 > 0$ such that for an arbitrary $\lambda \geq \lambda_0$, we can choose $s_0(\lambda) \geq 0$ such that for each $s \geq s_0(\lambda)$, a solution $(v, u_e) \in H^{2,1}(Q)$ of the problem (4.10) satisfies the following inequality:*

$$
\begin{aligned}
\int_Q \Bigg\{ & s\varphi(|\partial_t v|^2 + \sum_{i,j=1}^{n} |\partial_i \partial_j v|^2) + (s\varphi)^3 \lambda^2 |\nabla v|^2 + (s\varphi)^5 \lambda^4 |v|^2 + \sum_{i,j=1}^{n} |\partial_i \partial_j u_e|^2 \\
& + (s\varphi)^2 \lambda^2 |\nabla u_e|^2 + (s\varphi)^4 \lambda^4 |u_e|^2 \Bigg\} e^{-2s\eta} dx \, dt \leq C \int_Q (s\varphi)^2 |h|^2 e^{-2s\eta} dx \, dt \\
& + \tilde{C} \int_{\Sigma_0} \Big\{ |\partial_t v|^2 + |\nabla v|^2 + |v|^2 + |\nabla u_e|^2 + |u_e|^2 \Big\} dS dt, \quad (4.18)
\end{aligned}
$$

where the constant C depends continuously on λ_0.

Proof 4.3. *From the boundary conditions of the Problem (4.10), we can write $\sigma_i \nabla v . \nu = 0$ on Σ. Then applying estimate (4.7) with $p = 2$ to the solution v of (4.10), we have the estimate*

$$
\begin{aligned}
\int_Q \Bigg\{ & s\varphi(|\partial_t v|^2 + \sum_{i,j=1}^{n} |\partial_i \partial_j v|^2) + (s\varphi)^3 \lambda^2 |\nabla v|^2 + (s\varphi)^5 \lambda^4 |v|^2 \Bigg\} e^{-2s\eta} dx \, dt \\
& \leq C \int_Q (s\varphi)^2 (|\nabla u_e|^2 + |h|^2) e^{-2s\eta} dx \, dt + C e^{C(\lambda)s} \int_{\Sigma_0} \Big\{ |\partial_t v|^2 + |\nabla v|^2 + |v|^2 \Big\} dS dt. \quad (4.19)
\end{aligned}
$$

Similarly, applying estimate (4.7) with $p = 1$ to the solution u_e of (4.10), we get

$$\int_Q \left\{ \sum_{i,j=1}^n |\partial_i \partial_j u_e|^2 + (s\varphi)^2 \lambda^2 |\nabla u_e|^2 + (s\varphi)^4 \lambda^4 |u_e|^2 \right\} e^{-2s\eta} dx\, dt$$

$$\leq C \int_Q (s\varphi)(|\partial_t v|^2 + |h|^2) e^{-2s\eta} dx\, dt + Ce^{C(\lambda)s} \int_{\Sigma_0} \left\{ |\nabla u_e|^2 + |u_e|^2 \right\} dSdt. \quad (4.20)$$

By $\frac{4}{T^2} \leq \varphi \leq (\frac{T}{2})^2 \varphi^2$, $(2C) \times (4.19) + (4.20)$, and λ sufficiently large, we obtain the Lemma 4.3.

5. STABILITY ESTIMATE OF CONDUCTANCES PARAMETERS

This section is devoted to proof Theorem 3.1. Since the proof technically looks very awkward firstly we demonstrate some preliminary lemma.

Lemma 5.1. *Under the same hypothesis of Lemma 4.3, we have*

$$\int_Q \left\{ |\partial_t^2 v|^2 + \sum_{i,j=1}^n |\partial_i \partial_j \partial_t v|^2 + (s\varphi)^2 \lambda^2 |\nabla \partial_t v|^2 + (s\varphi)^4 \lambda^4 |\partial_t v|^2 + (s\varphi)(|\partial_t v|^2 + \sum_{i,j=1}^n |\partial_i \partial_j v|^2) \right.$$

$$+ (s\varphi)^3 \lambda^2 |\nabla v|^2 + (s\varphi)^5 \lambda^4 |v|^2 + (s\varphi)^{-1} \sum_{i,j=1}^n |\partial_i \partial_j \partial_t u_e|^2 + (s\varphi)\lambda^2 |\nabla \partial_t u_e|^2 + (s\varphi)^3 \lambda^4 |\partial_t u_e|^2$$

$$+ \sum_{i,j=1}^n |\partial_i \partial_j u_e|^2 + (s\varphi)^2 \lambda^2 |\nabla u_e|^2 + (s\varphi)^4 \lambda^4 |u_e|^2 \left. \right\} e^{-2s\eta} dx\, dt \leq C \int_Q (s\varphi |\partial_t h|^2 + (s\varphi)^2 |h|^2) e^{-2s\eta} dx\, dt$$

$$+ \tilde{C} \int_{\Sigma_0} \left\{ |\partial_t^2 v|^2 + |\partial_t v|^2 + |\nabla \partial_t v|^2 + |\nabla v|^2 + |v|^2 + |\nabla \partial_t u_e|^2 + |\partial_t u_e|^2 + |\nabla u_e|^2 + |u_e|^2 \right\} dSdt. \quad (5.1)$$

Proof 5.1. *Taking the time derivative of the first equation of (4.10), we see that*

$$(1 + \sigma_i \sigma_e^{-1}) \partial_t^2 v - div(\sigma_i \nabla \partial_t v) = -\boldsymbol{A}(x) \cdot \nabla \partial_t u_e - (1 + \sigma_i \sigma_e^{-1}) \partial_t h. \quad (5.2)$$

Applying Lemma 4.2 with $p = 1$ to the solution $\partial_t v$ of (5.2), we have the estimate

$$\int_Q \left\{ |\partial_t^2 v|^2 + \sum_{i,j=1}^n |\partial_i \partial_j \partial_t v|^2 + (s\varphi)^2 \lambda^2 |\nabla \partial_t v|^2 + (s\varphi)^4 \lambda^4 |\partial_t v|^2 \right\} e^{-2s\eta} dx\, dt$$

$$\leq C \int_Q (s\varphi)(|\nabla \partial_t u_e|^2 + |\partial_t h|^2) e^{-2s\eta} dx\, dt + Ce^{C(\lambda)s} \int_{\Sigma_0} \left\{ |\partial_t^2 v|^2 + |\nabla \partial_t v|^2 + |\partial_t v|^2 \right\} dSdt. \quad (5.3)$$

Taking the time derivative to the second equation of (4.10), we get

$$-div(\sigma_e \nabla \partial_t u_e) = \partial_t^2 v + \partial_t h \quad (5.4)$$

Applying Lemma 4.2 with $p = 0$ to the solution $\partial_t u_e$ of (5.4), we have

$$\int_Q \left\{ (s\varphi)^{-1} \sum_{i,j=1}^n |\partial_i \partial_j \partial_t u_e|^2 + (s\varphi)\lambda^2 |\nabla \partial_t u_e|^2 + (s\varphi)^3 \lambda^4 |\partial_t u_e|^2 \right\} e^{-2s\eta} dx\, dt$$

$$\leq C \int_Q (|\partial_t^2 v|^2 + |\partial_t h|^2) e^{-2s\eta} dx\, dt + C e^{C(\lambda)s} \int_{\Sigma_0} \left\{ |\nabla \partial_t u_e|^2 + |\partial_t u_e|^2 \right\} dS dt. \quad (5.5)$$

Using $\varphi \geq \dfrac{4}{T^2}$, $(2C) \times (5.3) + (5.5)$, and λ sufficiently large, we obtain

$$\int_Q \left\{ |\partial_t^2 v|^2 + \sum_{i,j=1}^n |\partial_i \partial_j \partial_t v|^2 + (s\varphi)^2 \lambda^2 |\nabla \partial_t v|^2 + (s\varphi)^4 \lambda^4 |\partial_t v|^2 + (s\varphi)^{-1} \sum_{i,j=1}^n |\partial_i \partial_j \partial_t u_e|^2 \right.$$

$$\left. + (s\varphi)\lambda^2 |\nabla \partial_t u_e|^2 + (s\varphi)^3 \lambda^4 |\partial_t u_e|^2 \right\} e^{-2s\eta} dx\, dt \leq C \int_Q (s\varphi) |\partial_t h|^2 e^{-2s\eta} dx\, dt$$

$$+ \tilde{C} \int_{\Sigma_0} \left\{ |\partial_t^2 v|^2 + |\nabla \partial_t v|^2 + |\partial_t v|^2 + |\nabla \partial_t u_e|^2 + |\partial_t u_e|^2 \right\} dS dt. \quad (5.6)$$

Summing (4.18), (5.6) and for λ sufficiently large, we deduce the Lemma 5.1.

Lemma 5.2. *We assume that $t_0 = T/2$ without loss of generality by changing the scale of t. We get*

$$\int_\Omega e^{-2s\eta(x,t_0)} \left| \mathbf{S}^\top(x,t_0) \cdot \overline{\varrho}(x) \right|^2 dx \leq C \left(\int_Q s^{-1} |\overline{\varrho}(x)|^2 e^{-2s\eta} dx\, dt + \|v(\cdot,t_0)\|_{H^2(\Omega)}^2 \right.$$

$$\left. + \|u_e(\cdot,t_0)\|_{H^2(\Omega)}^2 + \|\mathbf{w}(\cdot,t_0)\|_{L^2(\Omega)^k}^2 + \|\mathbf{z}(\cdot,t_0)\|_{L^2(\Omega)^m}^2 + \|v\|_{H^2(0,T;H^1(\Gamma_0))}^2 + \|u_e\|_{H^1(0,T;H^1(\Gamma_0))}^2 \right). \quad (5.7)$$

Proof 5.2. *We evaluate the first equation of (4.10) at a fixed time t_0, we have*

$$(1 + \sigma_i \sigma_e^{-1}) \partial_t v(x,t_0) - div(\sigma_i \nabla v(x,t_0)) + (1 + \sigma_i \sigma_e^{-1}) h(x,t_0) = -\boldsymbol{A}(x) \cdot \nabla u_e(x,t_0). \quad (5.8)$$

Then, we integrate over Ω the square of (5.8) with the weight function $e^{-2s\eta(x,t_0)}$, we obtain

$$\int_\Omega e^{-2s\eta(x,t_0)} \left| \mathbf{S}^\top(x,t_0) \cdot \bar{\varrho}(x) \right|^2 dx \leq C \left(\int_\Omega e^{-2s\eta(x,t_0)} |\partial_t v(x,t_0)|^2 dx \right.$$

$$\left. + \int_\Omega e^{-2s\eta(x,t_0)} |div(\sigma_i \nabla v(x,t_0))|^2 dx + \int_\Omega e^{-2s\eta(x,t_0)} |\nabla u_e(x,t_0)|^2 dx + \int_\Omega e^{-2s\eta(x,t_0)} |R(x,t_0)|^2 dx \right)$$

$$\leq C \left(\int_\Omega e^{-2s\eta(x,t_0)} (|\partial_t v(x,t_0)|^2 + |\nabla u_e(x,t_0)|^2 + |R(x,t_0)|^2) dx + \|v(\cdot,t_0)\|_{H^2(\Omega)}^2 \right). \quad (5.9)$$

Similarly, for the second equation of (4.10) at a fixed time t_0, we get

$$-div(\sigma_e \nabla u_e(x,t_0)) = h(x,t_0) + \partial_t v(x,t_0). \quad (5.10)$$

Then

$$\int_{\Omega} e^{-2s\eta(x,t_0)} \left| \mathbf{S}^{\top}(x,t_0) \cdot \bar{\varrho}(x) \right|^2 dx \leq C \left(\int_{\Omega} e^{-2s\eta(x,t_0)} \left| \partial_t v(x,t_0) \right|^2 dx \right.$$

$$\left. + \int_{\Omega} e^{-2s\eta(x,t_0)} \left| div(\sigma_e \nabla u_e(x,t_0)) \right|^2 dx + \int_{\Omega} e^{-2s\eta(x,t_0)} \left| \nabla u_e(x,t_0) \right|^2 dx + \int_{\Omega} e^{-2s\eta(x,t_0)} \left| R(x,t_0) \right|^2 dx \right). \quad (5.11)$$

Combining (5.9) and (5.11), we have

$$\int_{\Omega} e^{-2s\eta(x,t_0)} \left| \mathbf{S}^{\top}(x,t_0) \cdot \bar{\varrho}(x) \right|^2 dx \leq C \left(\int_{\Omega} e^{-2s\eta(x,t_0)} \left| \partial_t v(x,t_0) \right|^2 dx + \|v(\cdot,t_0)\|_{H^2(\Omega)}^2 \right.$$

$$\left. + \|u_e(\cdot,t_0)\|_{H^2(\Omega)}^2 + \|\mathbf{w}(\cdot,t_0)\|_{L^2(\Omega)^k}^2 + \|\mathbf{z}(\cdot,t_0)\|_{L^2(\Omega)^m}^2 \right). \quad (5.12)$$

since

$$\int_{\Omega} e^{-2s\eta(x,t_0)} |R(x,t_0)|^2 dx \leq C \left(\|v(\cdot,t_0)\|_{L^2(\Omega)}^2 + \|\mathbf{w}(\cdot,t_0)\|_{L^2(\Omega)^k}^2 + \|\mathbf{z}(\cdot,t_0)\|_{L^2(\Omega)^m}^2 \right). \quad (5.13)$$

For the first term in the RHS of (5.12), we have

$$\int_{\Omega} e^{-2s\eta(x,t_0)} |\partial_t v(x,t_0)|^2 dx = \int_0^{t_0} \int_{\Omega} \frac{d}{dt} (e^{-2s\eta(x,t)} |\partial_t v|^2) dx \, dt$$

$$= \int_0^{t_0} \int_{\Omega} \left(-2s\partial_t \eta(x,t) |\partial_t v|^2 + 2p\partial_t^2 v \right) e^{-2s\eta(x,t)} dx \, dt$$

$$\leq C \int_0^{t_0} \int_{\Omega} \left(s^2 \varphi^2 |\partial_t v|^2 + s^{-2} \varphi^{-1} |\partial_t^2 v|^2 \right) e^{-2s\eta(x,t)} dx \, dt. \quad (5.14)$$

Then, we apply the Carleman inequality (5.1) satisfied by $\partial_t v$, using $\frac{4}{T^2} \leq \varphi \leq (\frac{T}{2})^2 \varphi^2$, we obtain for s and λ sufficiently large

$$\int_{\Omega} e^{-2s\eta(x,t_0)} |\partial_t v(x,t_0)|^2 dx \leq \frac{C}{s^2} \int_Q (s\varphi |\partial_t h|^2 + (s\varphi)^2 |h|^2) e^{-2s\eta} dx \, dt$$

$$+ \tilde{C} \int_{\Sigma_0} \left\{ |\partial_t^2 v|^2 + |\partial_t v|^2 + |\nabla \partial_t v|^2 + |\nabla v|^2 + |v|^2 + |\nabla \partial_t u_e|^2 + |\partial_t u_e|^2 + |\nabla u_e|^2 + |u_e|^2 \right\} dS dt. \quad (5.15)$$

Using the Lemma 5.1 given in [2], we have

$$|h|^2 \leq C(\left| \mathbf{S}^{\top} \cdot \bar{\varrho}(x) \right|^2 + |v|^2 + |\mathbf{w}|^2 + |\mathbf{z}|^2), \quad (5.16)$$

and

$$\begin{aligned} |\partial_t h|^2 &\leq C(\left| \partial_{\mathbf{t}} \mathbf{S}^{\top} \cdot \bar{\varrho}(x) \right|^2 + |\partial_t v|^2 + |v|^2 + |\partial_t \mathbf{w}|^2 + |\mathbf{w}|^2 + |\partial_t \mathbf{z}|^2 + |\mathbf{z}|^2) \\ &\leq C(|\bar{\varrho}(x)|^2 + |\partial_t v|^2 + |v|^2 + |\mathbf{w}|^2 + |\mathbf{z}|^2), \end{aligned} \quad (5.17)$$

we complete the proof.

Proof of Theorem 3.1.
In order to prove (3.5), we use the following integro-differential equation

$$v = \{div(\boldsymbol{\sigma}_i \nabla)\}^{-1}(div(\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e) \nabla u_e)) := B u_e,$$

We can see that the operator B is linear and uniformly continuous [11]. Replacing the new expression of v in the right hand side of (5.7) and using the uniform continuity of B, the estimate (5.7) becomes

$$\int_\Omega e^{-2s\eta(x,t_0)} \left| \mathbf{S}^\top(x,t_0) \cdot \overline{\varrho}(x) \right|^2 dx \leq C \left(\int_Q s^{-1} \left| \overline{\varrho}(x) \right|^2 e^{-2s\eta} dx\, dt \right.$$
$$\left. + \|u_e(\cdot,t_0)\|_{H^2(\Omega)}^2 + \|\mathbf{w}(\cdot,t_0)\|_{L^2(\Omega)^k}^2 + \|\mathbf{z}(\cdot,t_0)\|_{L^2(\Omega)^m}^2 + \|u_e\|_{H^2(0,T;H^1(\Gamma_0))}^2 \right). \quad (5.18)$$

Summing up the above estimate over $\ell = 1, \ldots, N$, we get that

$$\int_\Omega e^{-2s\eta(x,t_0)} \left| \Lambda(x) \cdot \bar{\varrho}(x) \right|^2 dx \leq C \left(N s^{-1} \int_\Omega e^{-2s\eta(x,t_0)} \left| \bar{\varrho}(x) \right|^2 dx \right.$$
$$\left. + \sum_{\ell=1}^N \left(\|u_e\|_{H^2(0,T;H^1(\Gamma_0))}^2 + \|u_e(\cdot,t_0)\|_{H^2(\Omega)}^2 + \|\mathbf{w}(\cdot,t_0)\|_{L^2(\Omega)^k}^2 + \|\mathbf{z}(\cdot,t_0)\|_{L^2(\Omega)^m}^2 \right) \right), \quad (5.19)$$

where the $N \times N$ real matrix $\Lambda(x) = \Lambda(v_\ell^{(2)}(x,t_0), \mathbf{w}_\ell^{(2)}(x,t_0), \mathbf{z}_\ell^{(2)}(x,t_0))$, for $x \in \Omega$. Notice that we have

$$\|\Lambda(x)\xi\|_{\mathbb{R}^N} \geq \alpha_1(x) \left| \xi \right|_{\mathbb{R}^N}, \quad x \in \Omega, \quad \xi \in \mathbb{R}^N, \quad (5.20)$$

where $(\alpha_j(x))_{1 \leq j \leq N} \subset \mathbb{R}_+^N$ denotes the increasing sequence of the singular values of $\Lambda(x)$, and $|\xi|_{\mathbb{R}^N}$ stands for the Euclidian norm of ξ. Moreover, by Sobolev embedding theorem (e.g., Thm. 5.4 in [3], Cor. 9.1, p. 46, inVol. 1 of [35]), we see that $H^3(\Omega) \subset \mathcal{C}^1(\overline{\Omega})$, hence $v_\ell^{(2)}(.,t_0)$, $\mathbf{w}_\ell^{(2)}(.,t_0)$ and $\log \mathbf{z}_\ell^{(2)}(.,t_0)$, $\ell = 1, \ldots, N$, being taken in $\mathcal{C}^1(\overline{\Omega})$ thanks to Proposition 2.4. Then, $\alpha_1 \in \mathcal{C}^1(\overline{\Omega}; \mathbb{R}_+)$ from [30] [Thm 6.8 p. 122]. This combined with equation (3.4), yields $\alpha_0 := \inf_{x \in \Omega} \alpha_1(x) > 0$. As a Consequence and by (5.20), we have

$$\int_\Omega e^{-2s\eta(x,t_0)} \left| \Lambda(x)\bar{\varrho}(x) \right|^2 dx \geq \alpha_0^2 \int_\Omega e^{-2s\eta(x,t_0)} \left| \bar{\varrho}(x) \right|^2 dx, \quad (5.21)$$

and Theorem 3.1 follows directly from this and (5.19) by choosing s so large that $CNs^{-1} < \alpha_0^2$. ∎

6. Discussion and conclusions

Personalizing a numerical model in cardiac electrophysiology simulation allows to assimilate the electrophysiology conditions of a patient, including anatomical information but also functional conditions. These functional conditions are generally observed in the electrical signals measured either invasively in the heart domain or non-invasively on the body surface. The underlying substrate behind the electrical changes could be related to macroscopic parameters like the conductivity distribution of the tissue, but also and most importantly to the microscopic parameters at the cell and sub-cell levels. In particular, the conductances of the ion channels play an important role in the modulation of the transmembrane potential and consequently the ECGs. In this paper, we addressed the problem of identifying ion channels conductances from a set of extracellular potentials measurements on the boundary of the heart. Our result says that it is possibly to uniquely identify the conductances parameters if the mathematical model governing the electrical activity satisfies some hypothesis. Our approach is based on a Carleman inequality for the bidomain reaction diffusion model coupled to a general form of ordinary differential equation system. This result is a step further in the parameters identification problem compared to the existing results [2, 4, 10, 33, 51]. There are two novelties in our result compared to the results in those paper. First the cited papers deal with simpler models either by simplifying the ionic model or by simplifying the anisotropy of the bidomain model to reach the condition of the monodomain model approximation. In our case, we only remove the anisotropy but we keep ratio between intra and extracellular conductivities space dependent and we consider physiologically detailed ionic model. Second, we consider that the observations are

given on a part of the accessible boundary of the domain which is more realistic compared to observations on a sub-domain of the heart.

7. Appendix

Proof of Proposition 2.4.
First, we propose a parabolic-elliptic formulation of (2.1) given as follow:

$$
\begin{cases}
\partial_t v - div(\boldsymbol{\sigma}_i \nabla v) + I_{ion}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) = div(\boldsymbol{\sigma}_i \nabla u_e) + I_i^s & \text{in } Q, \\
-div(\boldsymbol{\sigma}_i \nabla v + (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\nabla u_e) = I_i^s + I_e^s & \text{in } Q, \\
\partial_t \mathbf{w} = \boldsymbol{F}(v, \mathbf{w}) & \text{in } Q, \\
\partial_t \mathbf{z} = \boldsymbol{G}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) & \text{in } Q, \\
\boldsymbol{\sigma}_i \nabla v.\nu + \boldsymbol{\sigma}_i \nabla u_e.\nu = 0 & \text{on } \Sigma, \\
\boldsymbol{\sigma}_i \nabla v.\nu + (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\nabla u_e.\nu = 0 & \text{on } \Sigma, \\
v(x,0) = v_0(x), \ u_e(x,0) = u_{e,0}(x), \ \mathbf{w}(x,0) = \mathbf{w}_0(x), \ \mathbf{z}(x,0) = \mathbf{z}_0(x) & \text{in } \Omega.
\end{cases}
\tag{7.1}
$$

Taking the time derivative of equations system (7.1), we obtain

$$
\begin{cases}
\partial_{tt} v - div(\boldsymbol{\sigma}_i \nabla \partial_t v) + \partial_t I_{ion} = div(\boldsymbol{\sigma}_i \nabla \partial_t u_e) + \partial_t I_i^s & \text{in } Q, \\
-div(\boldsymbol{\sigma}_i \nabla \partial_t v + (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\nabla \partial_t u_e) = \partial_t I_i^s + \partial_t I_e^s & \text{in } Q, \\
\partial_{tt} \mathbf{w} = \partial_t \boldsymbol{F}(v, \mathbf{w}) & \text{in } Q, \\
\partial_{tt} \mathbf{z} = \partial_t \boldsymbol{G}(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) & \text{in } Q, \\
\boldsymbol{\sigma}_i \nabla \partial_t v.\nu + \boldsymbol{\sigma}_i \nabla \partial_t u_e.\nu = 0 & \text{on } \Sigma, \\
\boldsymbol{\sigma}_i \nabla \partial_t v.\nu + (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\nabla \partial_t u_e.\nu = 0 & \text{on } \Sigma,
\end{cases}
\tag{7.2}
$$

with initial conditions

$$
\begin{aligned}
\partial_t v(t=0) &= div(\boldsymbol{\sigma}_i \nabla v_0) + div(\boldsymbol{\sigma}_i \nabla u_e(t=0)) + I_i^s(t=0) - I_{ion}(t=0) & \text{in } \Omega, \\
\partial_t u_e(t=0) &= \partial_t u_{e,0} & \text{in } \Omega, \\
\partial_t \mathbf{w}(t=0) &= \boldsymbol{F}(v_0, w_0) & \text{in } \Omega, \\
\partial_t \mathbf{z}(t=0) &= \boldsymbol{G}(\bar{\varrho}, v_0, \mathbf{w}_0, \mathbf{z}_0)
\end{aligned}
\tag{7.3}
$$

Using the hypothesis $v_0 \in H^2(\Omega)$, $u_e(t=0) \in H^2(\Omega)$, $\mathbf{w}_0 \in L^2(\Omega)^k$ and $\mathbf{z}_0 \in L^2(\Omega)^m$, we deduce that

$$
div(\boldsymbol{\sigma}_i \nabla v_0) \in L^2(\Omega), \quad div(\boldsymbol{\sigma}_i \nabla u_e(t=0)) \in L^2(\Omega), \quad I_{ion}(t=0) \in L^2(\Omega),
\tag{7.4}
$$

and then $\partial_t v(t=0) \in L^2(\Omega)$ since $I_{i,e}^s$ satisfy the hypothesis (2.14). Also we deduce that

$$\partial_t \mathbf{w}(t=0) \in L^2(\Omega)^k, \quad \text{and} \quad \partial_t \mathbf{z}(t=0) \in L^2(\Omega)^m. \tag{7.5}$$

We integrate over Ω the sum of the first equation of (7.2) multiplied by $\partial_t v$, the $2^{nd}, 3^{rd}$ and the 4th one multiplied by $\partial_t u_e, \partial_t \mathbf{w}$ and $\partial_t \mathbf{z}$, respectively, we obtain

$$\frac{1}{2}\frac{d}{dt}(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t \mathbf{z}\|_{L^2(\Omega)^m}^2) + <\boldsymbol{\sigma}_i \nabla \partial_t(v+u_e), \nabla \partial_t(v+u_e)> + <\boldsymbol{\sigma}_e \nabla \partial_t u_e, \nabla \partial_t u_e> =$$
$$\int_\Omega \partial_t v \partial_t I_i^s dx + \int_\Omega \partial_t u_e(\partial_t I_i^s + \partial_t I_e^s)dx + \int_\Omega \partial_t v \partial_t I_{ion}dx + \int_\Omega \partial_t \mathbf{w}.\partial_t \boldsymbol{F}dx + \int_\Omega \partial_t \mathbf{z}.\partial_t \boldsymbol{G}dx. \tag{7.6}$$

where $<\boldsymbol{\sigma}\nabla\vartheta, \nabla\vartheta> = \int_\Omega (\boldsymbol{\sigma}\nabla\vartheta)^T \nabla\vartheta dx$. From Assumptions 2.1, we consider

$$<\boldsymbol{\sigma}_i \nabla \partial_t(v+u_e), \nabla \partial_t(v+u_e)> \geq \underline{\sigma_i}\|\nabla \partial_t v + \nabla \partial_t u_e\|_{L^2(\Omega)}^2, \tag{7.7}$$

and

$$<\boldsymbol{\sigma}_e \nabla \partial_t u_e, \nabla \partial_t u_e> \geq \underline{\sigma_e}\|\nabla \partial_t u_e\|_{L^2(\Omega)}^2. \tag{7.8}$$

Using Cauchy-Schwarz inequality, we have

$$\int_\Omega \partial_t v \partial_t I_i^s dx \leq \frac{1}{2}(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t I_i^s\|_{L^2(\Omega)}^2) \tag{7.9}$$

$$\int_\Omega \partial_t u_e \partial_t(I_i^s + I_e^s)dx \leq \epsilon\|\partial_t u_e\|_{L^2(\Omega)}^2 + C_\epsilon(\|\partial_t I_i^s\|_{L^2(\Omega)}^2 + \|\partial_t I_e^s\|_{L^2(\Omega)}^2), \tag{7.10}$$

Computing the time derivative of the ionic curren I_{ion}, we get

$$\begin{aligned}
\partial_t I_{ion} = & \sum_{i=1}^{N} \bar{\varrho}_i \, \partial_t v \, y_i'(v) \prod_{j=1}^{k} w_j^{p_{j,i}}(v - E_i(\mathbf{z})) \\
& + \sum_{i=1}^{N} \bar{\varrho}_i y_i(v)(\sum_{l=1}^{k} p_{l,i}w_l^{p_{l,i}-1}\partial_t w_l \prod_{j \neq l} w_j^{p_{j,i}})(v - E_i(\mathbf{z})) \\
& + \sum_{i=1}^{N} \bar{\varrho}_i y_i(v)\partial_t v \prod_{j=1}^{k} w_j^{p_{j,i}} + \sum_{i=1}^{N} \bar{\varrho}_i \frac{\partial_t z_i}{z_i} y_i(v) \prod_{j=1}^{k} w_j^{p_{j,i}}.
\end{aligned} \tag{7.11}$$

Thanks to Lemma 2.3, we have $v \in L^\infty(Q)$, $\log \mathbf{z} \in L^\infty(Q)^m$, $\mathbf{w} \in [0,1]^k$ and y_i is $\mathcal{C}^\infty$. Applying Cauchy-Schwarz inequality, we deduce from (7.9) and (7.11) that

$$\int_\Omega \partial_t v \partial_t I_i^s dx + \int_\Omega \partial_t v \partial_t I_{ion}dx \leq C(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t \mathbf{z}\|_{L^2(\Omega)^m}^2 + \|\partial_t I_i^s\|_{L^2(\Omega)}^2). \tag{7.12}$$

We recall that the function F_j given by (2.5) is $\mathcal{C}^2(\mathbb{R}^2)$ for $j = 1, \ldots, k$, and then we can write

$$\partial_t F_j(v, w_j) = \partial_t v \partial_1 F_j + \partial_t w_j \partial_2 F_j, \tag{7.13}$$

where ∂_l is the partial derivative with respect the lth variable, $l = 1, 2$. Since α_j, β_j are $\mathcal{C}^\infty(\mathbb{R})$, $v \in L^\infty(Q)$ and $w_j \in [0,1]$, $j = 1, \ldots, k$, we deduce that

$$\partial_1 F_j(v, w_j) = \alpha'(v)(1 - w_j) - \beta'(v)w_j, \quad \text{and} \quad \partial_2 F_j(v, w_j) = -\alpha(v) - \beta(v), \quad j = 1, \ldots, k, \tag{7.14}$$

are bounded. Then, by Cauchy-Schwarz inequality and Young inequality, we have

$$\int_\Omega \partial_t \mathbf{w}.\partial_t \boldsymbol{F} dx \le C(\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k}). \tag{7.15}$$

Similarly for the variable $\mathbf{z}$, for $i = 1, \ldots, m$, we can write

$$\begin{aligned}
\partial_t G_i(\bar{\varrho}, v, \mathbf{w}, \mathbf{z}) = \quad & -\big(\partial_t v \partial_2 J_i + \sum_{j=1}^{k} (\partial_t w_j \partial_{j+2} J_i) + \partial_t \log z_i \partial_{k+3} J_i\big) \\
& + \partial_t v \partial_2 H_i + \sum_{j=1}^{k} \partial_t w_j \partial_{j+2} H_i + \sum_{j=1}^{m} \partial_t \log z_j \partial_{k+2+j} H_i.
\end{aligned} \tag{7.16}$$

By hypothesis (2.8) and (2.9), we deduce that $\partial_l J_i$, $l = 1, \ldots, k+3$, and $\partial_l H_i$, $l = 1, \ldots, m+k+2$, are bounded since $v \in L^\infty(Q)$, $\mathbf{w} \in [0,1]^k$, $\mathbf{z} \in L^\infty(Q)^m$. Then, we have

$$\int_\Omega \partial_t \mathbf{z}.\partial_t \boldsymbol{G} dx \le C(\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_t \mathbf{z}\|^2_{L^2(\Omega)^m}). \tag{7.17}$$

Thus, substituting (7.7), (7.8), (7.10), (7.12), (7.15) and (7.17) in (7.6), and applying Poincaré inequality by choosing $\epsilon = \dfrac{1}{2C_p}\underline{\sigma_e}$, with C_p is the Poincaré constant depending on Ω, we obtain

$$\begin{aligned}
&\frac{d}{dt}(\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_t \mathbf{z}\|^2_{L^2(\Omega)^m}) + \underline{\sigma_i}\|\nabla\partial_t v + \nabla\partial_t u_e\|^2_{L^2(\Omega)} + \frac{1}{2}\underline{\sigma_e}\|\nabla\partial_t u_e\|^2_{L^2(\Omega)} \\
&\le C(\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_t \mathbf{z}\|^2_{L^2(\Omega)^m} + \|\partial_t I_i^s\|^2_{L^2(\Omega)} + \|\partial_t I_e^s\|^2_{L^2(\Omega)}).
\end{aligned} \tag{7.18}$$

Applying Gronwall Lemma, we deduce

$$\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_t \mathbf{z}\|^2_{L^2(\Omega)^m} + \underline{\sigma_i}\|\nabla\partial_t v + \nabla\partial_t u_e\|^2_{L^2(\Omega)} + \frac{1}{2}\underline{\sigma_e}\|\nabla\partial_t u_e\|^2_{L^2(\Omega)} \le C_0, \quad \forall t \in [0,T], \tag{7.19}$$

where

$$C_0 = C(\|v_0\|_{H^2(\Omega)}, \|\mathbf{w}_0\|_{L^2(\Omega)^k}, \|\mathbf{z}_0\|_{L^2(\Omega)^m}, \|I_{i,e}^s\|_{H^1(0,T;L^2(\Omega))}) > 0. \tag{7.20}$$

Thus,

$$v, u_e \in W^{1,\infty}(0,T;H^1(\Omega)), \quad \mathbf{w} \in W^{1,\infty}(0,T;L^2(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in W^{1,\infty}(0,T;L^2(\Omega))^m. \tag{7.21}$$

Now, for $t \in (0,T)$, we intergrate (7.18) over $(0,t)$, we obtain

$$\begin{aligned}
\|\partial_t v\|^2_{L^2(\Omega)} + \|\partial_t \mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_t \mathbf{z}\|^2_{L^2(\Omega)^m} + \underline{\sigma_i}\int_0^t \|\nabla\partial_t v + \nabla\partial_t u_e\|^2_{L^2(\Omega)}d\tau \\
+ \frac{1}{2}\underline{\sigma_e}\int_0^t \|\nabla\partial_t u_e\|^2_{L^2(\Omega)}d\tau \le 2C_0,
\end{aligned} \tag{7.22}$$

and then, we conclude

$$v, u_e \in H^1(0,T;H^1(\Omega)). \tag{7.23}$$

On the other hand, from the system (2.10), we have

$$\begin{aligned}
div(\boldsymbol{\sigma_e}\nabla u_e) = -\partial_t v - I_{ion} - I_e^s \in L^2(0,T;L^2(\Omega)), \\
\Rightarrow u_e \in L^2(0,T;H^2(\Omega)).
\end{aligned} \tag{7.24}$$

and

$$div(\boldsymbol{\sigma}_i \nabla v) = \partial_t v + I_{ion} - div(\boldsymbol{\sigma}_i \nabla u_e) - I_i^s \in L^2(0, T; L^2(\Omega)),$$
$$\Rightarrow v \in L^2(0, T; H^2(\Omega)). \tag{7.25}$$

Let us now prove the regularities (2.21). Deriving equations (2.5) and (2.7) over the space variable x, we obtain

$$\partial_t(\partial_x w_j) = \partial_x v \partial_1 F_j + \partial_x w_j \partial_2 F_j, \quad j = 1, \dots, k, \tag{7.26}$$

and

$$\partial_t(\partial_x z_i) = \sum_{j=1}^N \partial_x \varrho_j \partial_j G_i + \partial_x v \partial_{N+1} G_i + \sum_{j=1}^k \partial_x w_j \partial_{j+N+1} G_i + \sum_{j=1}^m \partial_x z_j \partial_{k+N+1+j} G_i, \quad i = 1, \dots, m. \tag{7.27}$$

Without loss of generality, ∂_x is the space derivative over one direction (here could be the first, the second or the third dimension of the space $\mathbb{R}^3$).

According to Lemma 2.3 and the hypothesis (2.7)-(2.9), there exist a constant C depending on T, such that

$$\|\partial_1 F_j\|_{L^2(Q)}^2 + \|\partial_2 F_j\|_{L^2(Q)}^2 \leq C, \quad j = 1, \dots, k, \tag{7.28}$$

and

$$\sum_{j=1}^N \|\partial_x \varrho_j \partial_j G_i\|_{L^2(Q)}^2 + \|\partial_{N+1} G_i\|_{L^2(Q)}^2 + \sum_{j=1}^k \|\partial_{j+N+1} G_i\|_{L^2(Q)}^2 + \sum_{j=1}^m \|\partial_{k+N+1+j} G_i\|_{L^2(Q)}^2 \leq C, \quad i = 1, \dots, m. \tag{7.29}$$

Multiplying the equation (7.26) by $(\partial_x w_j), j = 1, \dots, k$, the equation (7.27) by $(\partial_x z_i), i = 1, \dots, m$, and integrating the sum over Ω, and applying the Young inequality of the right hand side, we obtain

$$\frac{d}{dt}(\|\partial_x \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_x \mathbf{z}\|_{L^2(\Omega)^m}^2) \leq C(\|\partial_x v\|_{L^2(\Omega)}^2 + \|\partial_x \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_x \mathbf{z}\|_{L^2(\Omega)^m}^2). \tag{7.30}$$

Thanks to the regularity (7.23), we have $\|\partial_x v\|_{L^2(\Omega)} \in C^0[0, T]$. Applying Gronwall lemma and using hypothesis (2.20), we obtain

$$\|\partial_x \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_x \mathbf{z}\|_{L^2(\Omega)^m}^2 \leq C(\|\partial_x \mathbf{w}_0\|_{L^2(\Omega)^k}, \|\partial_x \mathbf{z}_0\|_{L^2(\Omega)^m}), \quad \forall t \in [0, T]. \tag{7.31}$$

Thus,

$$\mathbf{w} \in L^\infty(0, T; H^1(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in L^\infty(0, T; H^1(\Omega))^m. \tag{7.32}$$

On the other hand, from (7.26) and (7.27), we deduce

$$\mathbf{w} \in W^{1,\infty}(0, T; H^1(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in W^{1,\infty}(0, T; H^1(\Omega))^m. \tag{7.33}$$

• Let us now consider the initial conditions:

- $\partial_{tt} v(0) = \text{div}(\boldsymbol{\sigma}_i \nabla \partial_t v(0)) + \text{div}(\boldsymbol{\sigma}_i \nabla \partial_t u_e(0)) + \partial_t I_i^s(0) - \partial_t I_{ion}(0),$
- $\partial_{tt} \mathbf{w}(0) = \partial_t \boldsymbol{F}(v(0), \mathbf{w}(0)),$ (7.34)
- $\partial_{tt} \mathbf{z}(0) = \partial_t \boldsymbol{G}(\bar{\boldsymbol{\varrho}}, v(0), \mathbf{w}(0), \mathbf{z}(0)).$

We start by showing that $\partial_t v(t = 0) \in H^2(\Omega)$. Using hypothesis (2.14), $v_0 \in H^4(\Omega)$, and $u_e(t = 0) \in H^4(\Omega)$, we have $\text{div}(\sigma_i \nabla v_0) \in H^2(\Omega)$, and $\text{div}(\sigma_i \nabla u_e(t = 0)) \in H^2(\Omega)$. We also have $I_i^s(t = 0) \in H^2(\Omega)$. It's obvious

that

$$I_{ion}(t=0) = \sum_{i=1}^{N} \bar{\varrho}_i y_i(v_0) \prod_{j=1}^{k} w_{0,j}^{p_{j,i}}(v_0 - E_i(\mathbf{z}_0)) \in L^2(\Omega). \tag{7.35}$$

Since $\bar{\varrho}$ is bounded in $H^3(\Omega)^N$, there exists a constant $C > 0$ such that

$$\begin{aligned}
|\partial_x I_{ion}(t=0)|^2 &\leq C(|\partial_x v_0|^2 + |\partial_x \mathbf{w}_0|^2 + |\partial_x \mathbf{z}_0|^2), \\
|\partial_{xy} I_{ion}(t=0)|^2 &\leq C(|\partial_x v_0|^2 + |\partial_x \mathbf{w}_0|^2 + |\partial_x \mathbf{z}_0|^2 + |\partial_y v_0|^2 + |\partial_y \mathbf{w}_0|^2 + |\partial_y \mathbf{z}_0|^2 \\
&\quad + |\partial_{xy} v_0|^2 + |\partial_{xy} \mathbf{w}_0|^2 + |\partial_{xy} \mathbf{z}_0|^2).
\end{aligned} \tag{7.36}$$

So, from hypothesis $v_0 \in H^4(\Omega)$, $\mathbf{w}_0 \in H^2(\Omega)^k$, $\mathbf{z}_0 \in H^2(\Omega)^m$, we deduce that $\partial_x I_{ion}(t=0)$ and $\partial_{xy} I_{ion}(t=0)$ belong to $L^2(\Omega)$. Thus $I_{ion}(t=0) \in H^2(\Omega)$, and then $\partial_t v(t=0) \in H^2(\Omega)$. From (7.34), we get $\partial_{tt} v(t=0) \in L^2(\Omega)$, $\partial_{tt} \mathbf{w}(t=0) \in L^2(\Omega)^k$, and $\partial_{tt} \mathbf{z}(t=0) \in L^2(\Omega)^m$.

Now, we take the second derivative with respect to time of the system (7.1), we multiply the first (respectively the $2^{nd}, 3^{rd}$ and the 4th) equation by $\partial_{tt} v$ (respectively by $\partial_{tt} u_e$, $\partial_{tt} \mathbf{w}$, $\partial_{tt} \mathbf{z}$), we obtain

$$\begin{aligned}
&\bullet \quad \partial_{ttt} v \partial_{tt} v - \partial_{tt} v \mathrm{div}(\boldsymbol{\sigma}_i \nabla \partial_{tt} v) = \partial_{tt} v \mathrm{div}(\boldsymbol{\sigma}_i \nabla \partial_{tt} u_e) + \partial_{tt} v \partial_{tt} I_i^s - \partial_{tt} v \partial_{tt} I_{ion}, \\
&\bullet \quad -\partial_{tt} u_e \mathrm{div}(\boldsymbol{\sigma}_i \nabla \partial_{tt} v) - \partial_{tt} u_e \mathrm{div}((\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e) \nabla \partial_{tt} u_e) = \partial_{tt} u_e (\partial_{tt} I_i^s + \partial_{tt} I_e^s), \\
&\bullet \quad \partial_{ttt} w_j \, \partial_{tt} w_j = \partial_{tt} F_j(v, w_j) \partial_{tt} w_j, \quad j = 1, \cdots, k, \\
&\bullet \quad \partial_{ttt} z_i \, \partial_{tt} z_i = \partial_{tt} G_i(\bar{\boldsymbol{\varrho}}, v, \mathbf{w}, \mathbf{z}) \partial_{tt} z_i, \quad i = 1, \cdots, m.
\end{aligned} \tag{7.37}$$

Deriving (7.11) with respect to time, integrating over Ω the sum of the first and second equation of (7.37), using Cauchy Schwarz inequality, we get

$$\begin{aligned}
&\frac{1}{2} \frac{d}{dt} \|\partial_{tt} v\|_{L^2(\Omega)}^2 + \frac{1}{2} < \boldsymbol{\sigma}_i \nabla \partial_{tt}(v + u_e), \nabla \partial_{tt}(v + u_e) > + \frac{1}{2} < \boldsymbol{\sigma}_e \nabla \partial_{tt} u_e, \nabla \partial_{tt} u_e > \\
&\leq C_1(\|\partial_{tt} v\|_{L^2(\Omega)}^2 + \|\partial_{tt} u_e\|_{L^2(\Omega)}^2) + C_2 \|\partial_{tt} \mathbf{w}\|_{L^2(\Omega)^k}^2 + C_3 \|\partial_{tt} \mathbf{z}\|_{L^2(\Omega)^m}^2 \\
&+ C_4(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t \mathbf{z}\|_{L^2(\Omega)^m}^2 + \|\partial_{tt} I_i^s\|_{L^2(\Omega)}^2 + \|\partial_{tt} I_e^s\|_{L^2(\Omega)}^2).
\end{aligned} \tag{7.38}$$

Deriving in time (7.13) and (7.16), integrating over Ω the 3rd and the 4th equation of (7.37), using Cauchy Schwarz inequality, for $j = 1, \ldots, k$ and $i = 1, \ldots, m$, we get

$$\begin{aligned}
&\bullet \quad \frac{1}{2} \frac{d}{dt} \|\partial_{tt} w_j\|_{L^2(\Omega)}^2 + C_{\alpha,\beta} \|\partial_{tt} w_j\|_{L^2(\Omega)}^2 \leq C_5 \|\partial_{tt} v\|_{L^2(\Omega)}^2 + C_6 \|\partial_{tt} w_j\|_{L^2(\Omega)}^2 \\
&\qquad + C_7(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t w_j\|_{L^2(\Omega)}^2), \\
&\bullet \quad \frac{1}{2} \frac{d}{dt} \|\partial_{tt} z_i\|_{L^2(\Omega)}^2 + \underline{C} \|\partial_{tt} z_i\|_{L^2(\Omega)}^2 \leq C_8 \|\partial_{tt} v\|_{L^2(\Omega)}^2 + C_9 \|\partial_{tt} \mathbf{w}\|_{L^2(\Omega)^k}^2 + C_{10} \|\partial_{tt} z_i\|_{L^2(\Omega)}^2 \\
&\qquad + C_{11}(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t \mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t z_i\|_{L^2(\Omega)}^2),
\end{aligned} \tag{7.39}$$

where $C_1, C_2, \ldots, C_{11}, C_{\alpha,\beta}, \underline{C}$ positive constants such that $\alpha_j(v) + \beta_j(v) \geq C_{\alpha,\beta}$ and $\dfrac{1}{z_i}\partial_{k+3}J_i \geq \underline{C}$. Summing all equations in (7.38) and (7.39), we get

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}(\|\partial_{tt}v\|_{L^2(\Omega)}^2 + \|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2) + \frac{1}{2}\underline{\sigma_i}\|\nabla\partial_{tt}v + \nabla\partial_{tt}u_e\|_{L^2(\Omega)}^2 + \frac{1}{2}\underline{\sigma_e}\|\nabla\partial_{tt}u_e\|_{L^2(\Omega)}^2 \\
&+C_{\alpha,\beta}\|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 + \underline{C}\|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2 \leq C_{12}(\|\partial_{tt}v\|_{L^2(\Omega)}^2 + \|\partial_{tt}u_e\|_{L^2(\Omega)}^2) + C_{13}\|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 \\
&+C_{14}\|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2 + C_{15}(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t\mathbf{z}\|_{L^2(\Omega)^m}^2 + \|\partial_{tt}I_i^s\|_{L^2(\Omega)}^2 + \|\partial_{tt}I_e^s\|_{L^2(\Omega)}^2).
\end{aligned} \tag{7.40}
$$

Applying Poincaré inequality by choosing $C_{12} = \dfrac{1}{4C_p}\underline{\sigma_i}$, with C_p is the Poincaré constant depending on Ω, $C_{13} = \dfrac{1}{2}C_{\alpha,\beta}$, and $C_{14} = \dfrac{1}{2}\underline{C}$, we obtain

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}(\|\partial_{tt}v\|_{L^2(\Omega)}^2 + \|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2) + \underline{\underline{C}}(\|\nabla\partial_{tt}v + \nabla\partial_{tt}u_e\|_{L^2(\Omega)}^2 + \|\nabla\partial_{tt}u_e\|_{L^2(\Omega)}^2 + \|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 \\
&+\|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2) \leq C_{15}(\|\partial_t v\|_{L^2(\Omega)}^2 + \|\partial_t\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_t\mathbf{z}\|_{L^2(\Omega)^m}^2 + \|\partial_{tt}I_i^s\|_{L^2(\Omega)}^2 + \|\partial_{tt}I_e^s\|_{L^2(\Omega)}^2)
\end{aligned} \tag{7.41}
$$

where $\underline{\underline{C}} = \min\{\dfrac{1}{2}C_{\alpha,\beta}, \dfrac{1}{2}\underline{C}, \dfrac{1}{4}\underline{\sigma_i}, \dfrac{1}{2}\underline{\sigma_e}\}$. Using hypothesis (7.34) and inequality (7.19), for $t \in [0,T]$, we integrate over the time interval $(0, t)$, we get

$$
\begin{aligned}
&\|\partial_{tt}v\|_{L^2(\Omega)}^2 + \|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2 + \underline{\underline{C}}\int_0^t \left(\|\nabla\partial_{tt}(v + u_e)\|_{L^2(\Omega)}^2 + \|\nabla\partial_{tt}u_e\|_{L^2(\Omega)}^2\right. \\
&+\|\partial_{tt}\mathbf{w}\|_{L^2(\Omega)^k}^2 + \|\partial_{tt}\mathbf{z}\|_{L^2(\Omega)^m}^2)d\tau \leq C(\|\partial_{tt}I_{i,e}^s\|_{L^2(0,T;L^2(\Omega))}^2 + C_{15}C_0T + \|\partial_{tt}v(t = 0)\|_{L^2(\Omega)}^2 \\
&+\|\partial_{tt}\mathbf{w}(t = 0)\|_{L^2(\Omega)^k}^2 + \|\partial_{tt}\mathbf{z}(t = 0)\|_{L^2(\Omega)^m}^2).
\end{aligned} \tag{7.42}
$$

We obtain
$$
v, u_e \in H^2(0, T; H^1(\Omega)), \quad \mathbf{w} \in H^2(0, T; L^2(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in H^2(0, T; L^2(\Omega))^m. \tag{7.43}
$$
On the other hand, from the system (2.10), we have

$$
\begin{aligned}
div(\boldsymbol{\sigma}_e \nabla \partial_t u_e) &= -\partial_{tt}v - \partial_t I_{ion} - \partial_t I_e^s \in L^2(0, T; L^2(\Omega)), \\
&\Rightarrow u_e \in H^1(0, T; H^2(\Omega)).
\end{aligned} \tag{7.44}
$$

and

$$
\begin{aligned}
div(\boldsymbol{\sigma}_i \nabla \partial_t v) &= \partial_{tt}v + \partial_t I_{ion} - div(\boldsymbol{\sigma}_i \nabla \partial_t u_e) - \partial_t I_i^s \in L^2(0, T; L^2(\Omega)), \\
&\Rightarrow v \in H^1(0, T; H^2(\Omega)).
\end{aligned} \tag{7.45}
$$

Deriving (7.44) and (7.45) with respect to space, we obtain that

$$
\begin{aligned}
\partial_x\big[div(\boldsymbol{\sigma}_e \nabla \partial_t u_e)\big] &= -\partial_x \partial_{tt}v - \partial_x \partial_t I_{ion} - \partial_x \partial_t I_e^s \in L^2(0, T; L^2(\Omega)), \\
&\Rightarrow u_e \in H^1(0, T; H^3(\Omega)).
\end{aligned} \tag{7.46}
$$

and

$$
\begin{aligned}
\partial_x\big[div(\boldsymbol{\sigma}_i \nabla \partial_t v)\big] &= \partial_x \partial_{tt}v + \partial_x \partial_t I_{ion} - \partial_x\big[div(\boldsymbol{\sigma}_i \nabla \partial_t u_e)\big] - \partial_x \partial_t I_i^s \in L^2(0, T; L^2(\Omega)), \\
&\Rightarrow v \in H^1(0, T; H^3(\Omega)).
\end{aligned} \tag{7.47}
$$

Let us now prove the regularities (2.22). Getting second derivatives of equations (2.5) and (2.7) over the space variable x, multiplying both equations by $\partial_{xx} w_j$ and $\partial_{xx} z_i$ respectively and using that fact that $\bar{\varrho}$ is bounded in $H^3(\Omega)^N$, integrating the sum over Ω and applying the Young inequality of the right hand side, we obtain

$$\frac{d}{dt}(\|\partial_{xx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xx}\mathbf{z}\|^2_{L^2(\Omega)^m}) \leq C_1(\|\partial_{xx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xx}\mathbf{z}\|^2_{L^2(\Omega)^m}) + C_2, \tag{7.48}$$

where C_1 and C_2 are two non negative constants. Applying Gronwall Lemma, we obtain

$$\|\partial_{xx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xx}\mathbf{z}\|^2_{L^2(\Omega)^m} \leq C(\|\partial_{xx}\mathbf{w}_0\|_{L^2(\Omega)^k}, \|\partial_{xx}\mathbf{z}_0\|_{L^2(\Omega)^m}). \tag{7.49}$$

Thus,

$$\mathbf{w} \in L^\infty(0, T; H^2(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in L^\infty(0, T; H^2(\Omega))^m. \tag{7.50}$$

Similarly, computing the third space derivatives of (2.5) and (2.7), multiplying both equations by $\partial_{xxx} w_j$ and $\partial_{xxx} z_i$ respectively and using that fact that $\bar{\varrho}$ is bounded in $H^3(\Omega)^N$, integrating the sum over Ω and applying the Young inequality of the right hand side, we obtain

$$\frac{d}{dt}(\|\partial_{xxx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xxx}\mathbf{z}\|^2_{L^2(\Omega)^m}) \leq C_3(\|\partial_{xxx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xxx}\mathbf{z}\|^2_{L^2(\Omega)^m}) + C_4. \tag{7.51}$$

since $v \in L^\infty(0, T; H^3(\Omega))$, where C_3 and C_4 are two non negative constants. Using $\mathbf{w}_0 \in H^3(\Omega)^k$, $\mathbf{z}_0 \in H^3(\Omega)^m$ and applying Gronwall Lemma, we have

$$\|\partial_{xxx}\mathbf{w}\|^2_{L^2(\Omega)^k} + \|\partial_{xxx}\mathbf{z}\|^2_{L^2(\Omega)^m} \leq C(\|\partial_{xxx}\mathbf{w}_0\|_{L^2(\Omega)^k}, \|\partial_{xxx}\mathbf{z}_0\|_{L^2(\Omega)^m}). \tag{7.52}$$

Then

$$\mathbf{w} \in L^\infty(0, T; H^3(\Omega))^k, \quad \text{and} \quad \mathbf{z} \in L^\infty(0, T; H^3(\Omega))^m. \tag{7.53}$$

Moreover, from the expressions of $\partial_t(\partial_{xxx}\mathbf{w})$ and $\partial_t(\partial_{xxx}\mathbf{z})$, we deduce

$$\begin{aligned} \mathbf{w} &\in W^{1,\infty}(0, T; H^3(\Omega))^k \subset H^1(0, T; H^3(\Omega))^k \hookrightarrow \mathcal{C}^0([0, T]; \mathcal{C}^1(\overline{\Omega}))^k, \\ \mathbf{z} &\in W^{1,\infty}(0, T; H^3(\Omega))^m \subset H^1(0, T; H^3(\Omega))^m \hookrightarrow \mathcal{C}^0([0, T]; \mathcal{C}^1(\overline{\Omega}))^m. \end{aligned} \tag{7.54}$$

The proof of Proposition 2.4 is finished. ∎

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