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▶ To cite this version:

Mostafa Bendahmane, Fatima Mroue, Mazen Saad, Raafat Talhouk. Mathematical analysis of cardiac electromechanics with physiological ionic model. Discrete and Continuous Dynamical Systems - Series B, American Institute of Mathematical Sciences, 2019, 24 (9), pp.34. 10.3934/dcdsb.2019035 . hal-01680593

HAL Id: hal-01680593 https://hal.inria.fr/hal-01680593

Submitted on 30 Oct 2018

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1 MATHEMATICAL ANALYSIS OF CARDIAC ELECTROMECHANICS WITH 2 PHYSIOLOGICAL IONIC MODEL

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ABSTRACT. This paper is concerned with the mathematical analysis of a coupled elliptic-parabolic system modeling the interaction between the propagation of electric potential coupled with general physiological ionic models and subsequent deformation of the cardiac tissue. A prototype system belonging to this class is provided by the electromechanical bidomain model, which is frequently used to study and simulate electrophysiological waves in cardiac tissue. The coupling between muscle contraction, biochemical reactions and electric activity is introduced with a so-called active strain decomposition framework, where the material gradient of deformation is split into an active (electrophysiology-dependent) part and an elastic (passive) one. We prove existence of weak solutions to the underlying coupled electromechanical bidomain model under the assumption of linearized elastic behavior and a truncation of the updated nonlinear diffusivities. The proof of the existence result, which constitutes the main thrust of this paper, is proved by means of a non-degenerate approximation system, the Faedo-Galerkin method, and the compactness method.

1. INTRODUCTION

The heart is the muscular organ that contracts to pump blood throughout the body. Failure 5 in its contraction leads to sudden cardiac death which is classified as the main cause of mortality 6 in the world. The contraction of the heart is initiated by an electrical signal called action poten-7 tial starting in the sinoatrial node. The electrical signal then travels through the atria and the 8 ventricles. When the cardiac myocytes are electrically stimulated, the electrical potential inside 9 the cell changes: they depolarize. This fast depolarization allows the transmission of the electrical 10 signal through gap junctions and lateral junctions to the neighboring cells and their subsequent 11 contraction. 12

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The goal of the present paper is to investigate the existence of solutions of a model describing 14 the interaction between the propagation of the action potential through the cardiac tissue and the 15 subsequent elastic mechanical response. The propagation of the electrical signal is described at 16 the macroscale by the bidomain model which is the most complete model used in numerical simu-17 lations of the electrical activity of the heart [1]. It represents the averaged intra- and extracellular 18 potentials by a reaction-diffusion system of degenerate parabolic type. Its equations are derived 19 from the conservation of fluxes between the intra- and extracellular media separated by the cellular 20 membrane that acts as a capacitor. The conductivities in these two media reflect their anisotropic 21 properties. They are of different magnitude and they depend on the orientation of the cardiac 22 fibers. The equations of the bidomain model are coupled with phenomenological or physiological 23 ionic models. The bidomain system was proposed fourty years ago [1] and was extensively studied 24 from a well-posedness point of view in the last decade. A variational approach was first introduced 25 by Savaré and Franzone [2]. Later analyses took different directions: Bendahmane and Karlsen 26

Date: September 7, 2018.

²⁰⁰⁰ Mathematics Subject Classification. 74F99, 35K57, 92C10, 65M60.

 $Key \ words \ and \ phrases.$ Electro-mechanical coupling; Bidomain equations; Active deformation; Weak solutions; Weak compactness method.

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used nondegenerate approximation systems to which they applied the Faedo-Galerkin scheme [3], Bourgault et al. introduced a "Bidomain" operator and used a semigroup approach [4], Matano and Mori derived global classical solutions [5] and Veneroni proved the existence and uniqueness of a strong solution with more involved ionic models using a fixed point approach with strong assumptions on the initial data [6]. Still at the macroscopic level, cardiac deformation can be modeled by the equations of motion for a hyperelastic material, written in the reference configuration. However, like any living tissue,

7 there is a difficulty in applying the principles of force balance to cardiac tissue due to its ability to 8 actively deform. In other words, its contraction is influenced by intrinsic mechanisms taking place q at the microscopic level. This ability is taken into account in the literature following different 10 approaches. One common option is to assume that stresses are additively decomposed into active 11 and passive parts and it is called the active stress formulation ([7, 8, 9, 10, 11])). In this paper, 12 we follow the active strain formulation, [12, 13], where the deformation gradient is factorized into 13 active and passive factors, and fiber contraction rewrites in the mechanical balance of forces as 14 a prescribed *active* deformation. Furthermore, this decomposition incorporates the micro-level 15 information on fiber contraction and fiber directions in the kinematics [14]. These mechanisms 16 essentially translate into a dependence of the strain energy function on auxiliary internal state 17 variables, which represent the level of mechanical tissue activation passed across scales [15]. For 18 comparisons between the two approaches in terms of numerical implementation, constitutive is-19 sues, and stability, we refer the reader to [16, 17]. 20

Mathematical analysis of general nonlinear elasticity can be found in [18, 19], whereas applica-21 tions of those theories to the particular case of hyperelastic materials and cardiac mechanics are 22 available in [9, 20, 21, 17, 22, 23]. Despite the large availability of references related to numerical 23 methods and models for cardiac electromechanics (e.g. [7, 8, 10, 24, 11]), there are open questions 24 in their mathematical validity. To our knowledge, some existence results have been established by 25 Pathmanatan et al. [25, 26] and Andreianov et al. [27]. Pathmanatan et al. analyzed a general 26 model involving the active stress formulation where the activation depends on local stretch rate 27 and derived constraints on the initial data. Andreianov et al. also assumed linearized elasticity 28 equations but they adopted the active strain formulation and employed the bidomain model cou-29 pled with FitzHugh-Nagumo ionic model. This is the setting we employ in the present work, but 30 we use a general physiological ionic model which kinetics overlap with Beeler-Reuter model [28] or 31 Luo-Rudy model [29]. The electrical to mechanical coupling is obtained by considering that the 32 active part of deformation incorporates the effect of calcium dynamics. We also consider that the 33 evolution of electrical potential, governed by the bidomain equations, depends on the displacement 34 which enters into the equations upon a change of coordinates from Eulerian to Lagrangian. 35

Putting our contributions into perspective, we first note that up to the author's knowledge, exis-36 tence of solution of an electromechanical model coupled with physiological ionic model has never 37 been rigourously mathematically analyzed. Moreover our paper admits a rigorous mathematical 38 treatment, yielding the existence of weak solutions of our model. We point out that our model is 39 degenerate, strongly nonlinear and so no maximum principle applies. We want to mention that 40 we have not been able to prove uniqueness of weak solutions because of the presence of nonlinear 41 42 lower-order terms in our model. Furthermore, comparing to the work [6] (where the author proves the existence of strong solutions without mechanics), here we give a different and constructive 43 proof of the existence of weak solutions to the electromechanical bidomain model. Moreover, in 44 comparison to the phenomenological ionic model used in [27], the physiological model considered 45 herein contains a concentration variable z that appears as argument of a logarithm both in the 46 dynamics of the concentration and in the ionic currents, and therefore it is necessary to bound z47 far from zero. 48

In the present work, we prove the existence of weak solutions to the coupled electromechanical problem by introducing non-degenerate approximation systems including an "artificial compressibility" condition. We prove existence of solutions to those approximation systems (for each fixed $\varepsilon > 0$) by applying the Faedo-Galerkin method, deriving a priori estimates, and then passing to the limit in the approximate solutions using compactness arguments. Having proved existence for the approximation systems, the goal is to send the regularization parameter ε to zero in sequences of such solutions to fabricate weak solutions of the original systems. Again convergence is achieved
by a priori estimates and compactness arguments. On the technical side, we point out that the
passage to the limit in the pressure term is not straightforward due to the artificial compressibility

⁴ assumption along with the use of "Navier-type" boundary conditions.

The contents of this paper are organized as follows. Section 2 describes the cardiac electrome-5 chanical model we adopt, presenting the equations of passive nonlinear mechanics, the bidomain 6 system, and the active-strain-based coupling strategy. We also list the basic assumptions of the 7 model and provide a definition of weak solution. In Section 3 we state and prove the solvability 8 of the continuous problem employing Faedo-Galerkin approximations and compactness theory to 9 obtain the existence of solution of a regularized problem in the first place. Then the existence of 10 weak solutions for the original problem is given in Section 4 by using (one more time) a priori 11 estimates and compactness arguments. In Section 5, we close our contribution with some remarks 12 and discussion of future directions. 13

2. Governing equations for the electromechanical coupling

2.1. A general nonlinear elasticity problem. From the mechanical view point, we consider the heart as a homogeneous continuous material occupying in the initial undeformed configuration a bounded domain $\Omega_R \subset \mathbb{R}^d$ (d = 3) with Lipschitz continuous boundary $\partial \Omega_R$. Its deformation is described by the equations of motion written in the reference configuration Ω_R . The current configuration is the deformed configuration denoted by Ω . We look for the deformation field $\phi : \Omega_R \to \mathbb{R}^d$ that maps a material particle occupying initially the position \mathbf{X} to its current position $\mathbf{x} = \phi(\mathbf{X})$. We denote by $\mathbf{F} := \nabla_X \phi$, the deformation gradient tensor where ∇_X is the gradient operator with respect to the material coordinates \mathbf{X} , noting that det $(\mathbf{F}) > 0$.

The cardiac tissue is also assumed to be a hyperelastic incompressible material. In other words, there exists a strain stored energy function $\mathcal{W} = \mathcal{W}(\mathbf{X}, \mathbf{F})$, differentiable with respect to \mathbf{F} , from which constitutive relations between strain and stresses are obtained. In addition, the first Piola stress tensor \mathbf{P} , which represents force per unit undeformed surface is given by:

$$\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} - p \operatorname{Cof} \left(\mathbf{F} \right),$$

where Cof (·) is the cofactor matrix, and p is the Lagrange multiplier associated to the incompressibility constraint: det(**F**) = 1 and interpreted as "hydrostatic pressure". The balance equations in the reference configuration for deformations and pressure read as: Find ϕ , p such that

$$\nabla \cdot \mathbf{P}(\mathbf{F}, p) = \mathbf{g} \quad \text{in } \Omega_R, \det(\mathbf{F}) = 1 \quad \text{in } \Omega_R,$$
(2.1)

¹⁵ completed with the Robin boundary condition

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$$\mathbf{P}\boldsymbol{n} = -\alpha\boldsymbol{\phi} \quad \text{on } \partial\Omega_R. \tag{2.2}$$

These are the steady state equations of motion to describe conservation of linear and angular momentum where **g** is a prescribed body force, **n** stands for the unit outward normal vector to $\partial\Omega_R$, and $\alpha > 0$ is a constant parameter. The choice of boundary conditions as (2.2) is due to the fact that they can be tuned to mimic the global motion of the cardiac muscle [15], unlike the unphysiological boundary treatment typically found in the literature, as using excessively rigid boundary conditions, or fixing the atrioventricular plane, or leaving the tissue completely free to move.

Clearly, in order to obtain a precise form of the first equation in (2.1), we need a particular constitutive relation defining \mathcal{W} . We consider herein the case of Neo-Hookean materials, where \mathcal{W} is defined by:

$$\mathcal{W} = \frac{1}{2}\mu \mathrm{tr}[\mathbf{F}^T \mathbf{F} - \mathbf{I}],$$

with μ being the shear modulus. Hence, $\frac{\partial W}{\partial \mathbf{F}} = \mu \mathbf{F}$ and $\mathbf{P} = \mu \mathbf{F} - p \operatorname{Cof}(\mathbf{F})$. Although simplified, such a description of the passive response of the muscle features, so far, a nonlinear strain-stress 1 relationship arising from the incompressibility constraint. The forthcoming discussion will also

² reveal another form of strain-stress nonlinearity as a result of anisotropy inherited from the active

³ strain incorporation. More involved models can be found in e.g. Refs. [9, 17, 15].

2.2. The bidomain equations. The electrophysiological aspect of the heart is incorporated in the model through the widely used bidomain equations [1]. The unknowns are the intracellular (i) and extracellular (e) electric potentials $v_i = v_i(t, \boldsymbol{x})$, $v_e = v_e(t, \boldsymbol{x})$ respectively, the transmembrane potential $v = v(t, \boldsymbol{x}) := v_i - v_e$, the gating or recovery variables $\boldsymbol{w} = \boldsymbol{w}(t, \boldsymbol{x}) = (w_1, \dots, w_k)$, and the concentration variable $z = z(t, \boldsymbol{x}) = (z_1, \dots, z_m)$ at $(t, \boldsymbol{x}) \in \Omega_T := (0, T) \times \Omega$, where T is the final time instant. Cardiac electrical conductivity is represented in the global coordinate system by the orthotropic tensors

$$\mathbf{K}_k(\boldsymbol{x}) = \sigma_k^l \boldsymbol{d}_l \otimes \boldsymbol{d}_l + \sigma_k^t \boldsymbol{d}_t \otimes \boldsymbol{d}_t + \sigma_k^n \boldsymbol{d}_n \otimes \boldsymbol{d}_n, \quad k \in \{e, i\},$$

where $\sigma_k^s = \sigma_k^s(\boldsymbol{x}) \in \boldsymbol{C}^1(\mathbb{R}^3)$, $k \in \{e, i\}$, $s \in \{l, t, n\}$, are the intra- and extracellular conductivities along, transversal, and normal to the fibers' direction, respectively. The direction of the fibers is a local quantity used to determine the principal directions of propagation, thus we have $\boldsymbol{d}_s =$ $\boldsymbol{d}_s(\boldsymbol{x}), s \in \{l, t, n\}$. The externally applied stimulation currents corresponding to the intra- and extracellular spaces are represented by the functions I_s^i and I_s^e , respectively. The bidomain equations are given by:

$$\chi c_{\rm m} \partial_t v - \nabla \cdot \left(\mathbf{K}_{\rm i} \nabla v_i \right) + \chi I_{\rm ion}(v, \boldsymbol{w}, z) = I_s^i \qquad \text{in } \Omega_T,$$

$$\chi c_{\rm m} \partial_t v + \nabla \cdot \left(\mathbf{K}_{\rm e} \nabla v_e \right) + \chi I_{\rm ion}(v, \boldsymbol{w}, z) = I_s^e \qquad \text{in } \Omega_T,$$

$$\partial_t \boldsymbol{w} - \mathbf{R}(v, \boldsymbol{w}) = 0 \qquad \text{in } \Omega_T,$$

$$\partial_t z - G(v, \boldsymbol{w}, z) = 0 \qquad \text{in } \Omega_T,$$
(2.3)

where $v = v_i - v_e$. Here c_m is the capacitance and χ is the membrane surface area per unit volume. For simplicity, we shall suppose that $\chi = 1$ and $c_m = 1$. Problem (2.3) is provided with homogeneous Neumann boundary conditions on the intra- and extracellular potentials. In the physiological membrane model, the ionic current I_{ion} has the following general form

$$I_{\rm ion}(v, \boldsymbol{w}, z) := \sum_{i=1}^{m} d_i f_i(v) \prod_{j=1}^{k} w_j^{n_{i,j}} \left(v - r_i \log\left(\frac{z_e}{z_i}\right) \right).$$

Herein, d_i is the maximal conductance associated with the $i^t h$ current, f_i is a gating function depending on the transmembrane potentiel v, $n_{i,j}$ is positive integer and $E := r_i \log\left(\frac{z_e}{z_i}\right)$ is equilibrium (Nernst) potential (r_i is a constant and z_e is an extracellular concentration). Moreover, the dynamics of the gating variable \boldsymbol{w} is described in the Hodgkin-Huxley formalism by a system of ODEs governed by the following equation

$$\partial_t w_j = \alpha_j(v)(1 - w_j) - \beta_j(v)w_j$$

for j = 1, ..., k. The functions α_j and β_j are positive with the following form

$$\frac{\rho_{1,\kappa}e^{\rho_{2,\kappa}(v-\overline{v})}+\rho_{3,\kappa}(v-\overline{v})}{1+\rho_{4,\kappa}e^{\rho_{5,\kappa}(v-\overline{v})}}$$

4 where $\rho_{1,\kappa}, \rho_{3,\kappa}, \rho_{4,\kappa}, \overline{v} \ge 0$ and $\rho_{2,\kappa}, \rho_{5,\kappa} > 0$ are constants.

The choice of the membrane model to be used is reflected in the functions $I_{ion}(v, \boldsymbol{w}, z)$, $\mathbf{R}(v, \boldsymbol{w})$ and

 $G(v, \boldsymbol{w}, z)$. For a physiological description of the action potential, we will consider a fairly general

ionic model that corresponds for instance to the dynamics of Luo-Rudy model or Beeler-Reuter
model [29, 28], given as in assumption (A.6) below.

2.3. The active strain model for the coupling of elasticity and bidomain equations. The electrical to mechanical coupling is done through the "active strain model" [13] where the deformation gradient \mathbf{F} is factorized into a passive component \mathbf{F}_p and an active component \mathbf{F}_a , $\mathbf{F} = \mathbf{F}_p \mathbf{F}_a$. The tensor \mathbf{F}_p acts at the tissue level and accounts for both deformation of the material needed to insure compatibility and possible tension due to external loads. The tensor \mathbf{F}_a represents

the distortion that dictates deformation at the fiber level and depends on the electrophysiology through the relation, [14]:

$$\mathbf{F}_a = \mathbf{I} + \gamma_l \boldsymbol{d}_l \otimes \boldsymbol{d}_l + \gamma_t \boldsymbol{d}_t \otimes \boldsymbol{d}_t + \gamma_n \boldsymbol{d}_n \otimes \boldsymbol{d}_n$$

where $\gamma_s, s \in \{l, t, n\}$ are quantities that depend on the electrophysiology equations. Such a factorization of the deformation tensor \mathbf{F} assumes the existence of an intermediate configuration between the reference and the current frames. In that configuration, the strain energy function depends solely on the deformation at the macroscale \mathbf{F}_{p} , [30]:

$$\mathcal{W} = \mathcal{W}(\mathbf{F}_p) = \mathcal{W}(\mathbf{F}\mathbf{F}_a^{-1}) = \frac{\mu}{2} \operatorname{tr}[\mathbf{F}_p^T \mathbf{F}_p - \mathbf{I}] = \frac{\mu}{2} \operatorname{tr}[\mathbf{F}_a^{-T} \mathbf{F}^T \mathbf{F}\mathbf{F}_a^{-1} - \mathbf{I}],$$

and the Piola stress tensor is given by :

$$\mathbf{P} = \mu \mathbf{F} \mathbf{C}_a^{-1} - p \mathrm{Cof}(\mathbf{F})$$

1

where $\mathbf{C}_a^{-1} := \det(\mathbf{F}_a)\mathbf{F}_a^{-1}\mathbf{F}_a^{-T}$ (see also Refs. [14, 30]). Further examining the expression of \mathbf{F}_a , we notice that mechanical activation is mainly influenced 2 by intracellular calcium release [24, 26, 31], and in particular, the dynamics of local strain follow 3 closely those of calcium release rather than those from the transmembrane potential, as reported 4 in Ref. [32]. Using a physiological ionic model, the aforementioned fact suggests that, ideally the 5 recovery variables \boldsymbol{w} and the concentration variable z approximate the spatio-temporal structure 6 of calcium. More physiologically-involved activation models require a dependence of γ_s not only 7 on calcium, but also on local stretch, local stretch rate, sliding velocity of crossbridges, and on 8 other force-length experimental relations [26, 15, 33], but for the sake of simplicity we restrict 9 ourselves to a phenomenological description of local activation in terms of the gating variables. 10 The scalar fields γ_l , γ_t and γ_n can be written as functions of a parameter γ : 11

$$\gamma_{l,t,n} = \gamma_{l,t,n}(\gamma), \tag{2.4}$$

where $\gamma_{l,t,n}: \mathbb{R} \mapsto [-\Gamma_{l,t,n}, 0]$ are Lipschitz continuous monotone functions. The values $\Gamma_{l,t,n}$ should be small enough, in order to ensure that $\det(\mathbf{F}_a)$ stays uniformly far from zero, for $\gamma \in \mathbb{R}$. The scalar field γ is the solution of the following ODE associated to the solution (v_i, v_e, w) of the bidomain system (2.3):

$$\partial_t \gamma - S(\gamma, \boldsymbol{w}) = 0 \quad \text{in } \Omega_T,$$

where $S(\gamma, \boldsymbol{w}) = \beta(\sum_{j=1}^{k} \eta_j w_j - \eta_0 \gamma)$, for positive physiological parameters $\beta, \eta_j, j = 0, 1, \dots, k$ (see Ref. [34]). Moreover, the functions $\gamma_{l,t,n}$ are assumed to be of the form:

$$\gamma_{l,t,n} = -\Gamma_{l,t,n} \frac{2}{\pi} \arctan(\gamma^+ / \gamma_R)$$
, where γ_R is a reference value.

Further details can be found in e.g. Refs. [35, 33].

The *mechanical-to-electrical* coupling is achieved by a change of variables in the bidomain equations from the current configuration (Eulerian coordinates) to the reference configuration (Lagrangian coordinates), which leads to a conduction term depending on the deformation gradient \mathbf{F} . Summarizing, the active strain formulation for the electromechanical activity in the heart is written as follows [30]:

$$-\nabla \cdot \left(a(\boldsymbol{x}, \boldsymbol{\gamma}, \mathbf{F}, p)\right) = \mathbf{g} \qquad \text{in } \Omega_R,$$

$$\det(\mathbf{F}) = 1 \qquad \text{in } \Omega_R \text{ for a.e. } t \in (0, T),$$

$$\partial_t v + \nabla \cdot \left(\mathbf{M}_e(\boldsymbol{x}, \mathbf{F}) \nabla v_e\right) + I_{\text{ion}} = I_s^e \qquad \text{in } Q_T,$$

$$\partial_t v - \nabla \cdot \left(\mathbf{M}_i(\boldsymbol{x}, \mathbf{F}) \nabla v_i\right) + I_{\text{ion}} = I_s^i \qquad \text{in } Q_T,$$

$$v_i - v_e = v \qquad \text{in } Q_T,$$

$$\partial_t \boldsymbol{w} - \mathbf{R}(v, \boldsymbol{w}) = 0 \qquad \text{in } Q_T,$$

$$\partial_t z - G(v, \boldsymbol{w}, z) = 0 \qquad \text{in } Q_T,$$

$$\partial_t \gamma - S(\boldsymbol{\gamma}, \boldsymbol{w}) = 0 \qquad \text{in } Q_T,$$

(2.5)

where $Q_T := (0,T) \times \Omega_R$. Here, according to the above discussion, we should take

$$a(\boldsymbol{x}, \gamma, \mathbf{F}, p) := \mu \mathbf{F} \mathbf{C}_{a}^{-1}(\boldsymbol{x}, \gamma) - p \operatorname{Cof}(\mathbf{F}), \qquad (2.6)$$

2 and

$$\mathbf{M}_k(\boldsymbol{x}, \mathbf{F}) := (\mathbf{F})^{-1} \mathbf{K}_k(\boldsymbol{x}) (\mathbf{F})^{-T}, \quad k \in \{i, e\}$$
(2.7)

The system of equations (2.5) has to be completed with suitable initial conditions for v, w, γ, z and with boundary conditions on $v_{i,e}$ and on the elastic flux $a(\cdot, \cdot, \cdot, \cdot)$.

5 2.4. Linearizing the elasticity equations. For the sake of simplicity of the mathematical anal-6 ysis of the problem, the incompressibility condition $det(\mathbf{F}) = 1$ and the flux in the equilibrium 7 equation are linearized. To linearize the determinant, we use:

$$det(\mathbf{F}) = det(\mathbf{I}) + \frac{\partial(det)}{\partial \mathbf{F}}(\mathbf{I})(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I})$$
$$= 1 + tr(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I}).$$

But $det(\mathbf{F}) = 1$, so one can use the approximation

$$\operatorname{tr}(\mathbf{F}-\mathbf{I})\simeq 0,$$

hence, $\nabla \cdot \boldsymbol{\phi} = \operatorname{tr}(\mathbf{F}) \simeq \operatorname{tr}(\mathbf{I}) = n.$

Now, when \boldsymbol{u} denotes the displacement i.e. $\boldsymbol{u} = \boldsymbol{\phi}(X) - X$, the above condition becomes $\nabla \cdot \boldsymbol{u} = 0$, which is the linearized incompressibility condition. We also linearize the flux in (2.6) with respect to \mathbf{F} using Taylor series' expansion of Cof(\mathbf{F}) about \mathbf{I} , given by:

$$Cof(\mathbf{F}) = Cof(\mathbf{I}) + \frac{\partial Cof}{\partial \mathbf{F}}(\mathbf{I})(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I})$$

= $\mathbf{I} + tr(\mathbf{F} - \mathbf{I})\mathbf{I} - (\mathbf{F} - \mathbf{I})^T + o(\mathbf{F} - \mathbf{I}).$

8 and we obtain

$$a(\boldsymbol{x}, \gamma, \mathbf{F}, p) := \mu \mathbf{F} \mathbf{C}_a^{-1}(\boldsymbol{x}, \gamma) - p \mathbf{I}.$$
(2.8)

Introducing the notation $\sigma(\boldsymbol{x}, \gamma)$ for $\mu \mathbf{C}_a^{-1}(\boldsymbol{x}, \gamma)$, and using the displacement gradient $\nabla \boldsymbol{u}$ we rewrite the first equation of (2.5) as

$$-\nabla \cdot ((\mathbf{I} + \nabla \boldsymbol{u})\sigma(\boldsymbol{x}, \gamma)) + \nabla p = \mathbf{g}$$

then we reformulate the last equation to obtain a Stokes' like equation of the form:

$$-\nabla \cdot (\nabla \boldsymbol{u} \, \sigma(\boldsymbol{x}, \gamma)) + \nabla p = \boldsymbol{f}(t, \boldsymbol{x}, \gamma)$$
$$\boldsymbol{f}(t, \boldsymbol{x}, \gamma) = \nabla \cdot (\sigma(\boldsymbol{x}, \gamma)) + \mathbf{g}.$$
(2.9)

9 where

2.5. The problem to be solved and its weak formulation. For simplicity of notation, we will use Ω and Ω_T to denote Ω_R and Q_T respectively in all what follows, unless otherwise specified. Let us consider the following class of problems:

$$-\nabla \cdot \left(\nabla \boldsymbol{u}\,\boldsymbol{\sigma}(\boldsymbol{x},\boldsymbol{\gamma})\right) + \nabla p = \boldsymbol{f}(t,\boldsymbol{x},\boldsymbol{\gamma}), \quad \text{ in } \Omega, \text{ for a.e. } t \in (0,T), \quad (2.10)$$

$$\nabla \cdot \boldsymbol{u} = 0$$
 in Ω , for a.e. $t \in (0, T)$, (2.11)

$$\partial_t v - \nabla \cdot \left(\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}) \nabla v_i \right) + I_{\text{ion}}(v, \boldsymbol{w}, z) = I_s^i(t, \boldsymbol{x}) \qquad \text{in } \Omega_T,$$
(2.12)

$$\partial_t v + \nabla \cdot \left(\mathbf{M}_e(\boldsymbol{x}, \nabla \boldsymbol{u}) \nabla v_e \right) + I_{\text{ion}}(v, \boldsymbol{w}, z) = I_s^e(t, \boldsymbol{x}) \qquad \text{in } \Omega_T,$$
(2.13)

$$v = v_i - v_e \qquad \text{in } \Omega_T, \qquad (2.14)$$

$$\partial_t \boldsymbol{w} = \mathbf{R}(v, \boldsymbol{w}, z) \quad \text{in } \Omega_T, \tag{2.15}$$

$$\partial_t z = G(v, \boldsymbol{w}, z) \quad \text{in } \Omega_T,$$
(2.16)

$$\partial_t \gamma = S(\gamma, \boldsymbol{w}) \qquad \text{in } \Omega_T.$$
 (2.17)

Equations (2.10), (2.12), (2.13) are complemented with the boundary data (including the linearization of (2.2)):

$$\nabla \boldsymbol{u}\,\sigma(\boldsymbol{x},\gamma)\boldsymbol{n} - p\boldsymbol{n} = -\alpha\boldsymbol{u} \text{ on } \partial\Omega, \text{ for a.e. } t \in (0,T)$$
(2.18)

1 for some $\alpha > 0$ and

$$(\mathbf{M}_k(\boldsymbol{x}, \nabla \boldsymbol{u}) \nabla \boldsymbol{v}_k) \cdot \boldsymbol{n} = 0 \text{ on } (0, T) \times \partial \Omega, \quad k = i, e$$
(2.19)

2 (different boundary conditions can be imposed on $v_{i,e}$; the choice of Neumann conditions (2.19) 3 results in the compatibility constraint (2.31) below). The initial data are:

$$v(0,\cdot) = v_0, \ \boldsymbol{w}(0,\cdot) = \boldsymbol{w}_0, \ , z(0,\cdot) = z_0, \ \gamma(0,\cdot) = \gamma_0 \ \text{in } \Omega.$$
 (2.20)

- ⁴ For simplicity we take m = 1 in the concentration variable z. The following properties of the ⁵ model (2.10)–(2.17) and (2.18)–(2.20) are instrumental for the subsequent analysis:
 - (A.1) $(\sigma(\boldsymbol{x},\gamma))_{\boldsymbol{x}\in\Omega,\gamma\in\mathbb{R}}$ is a family of symmetric tensors, uniformly bounded and positive definite:

$$\exists c > 0: \text{ for a.e. } x \in \Omega, \forall \gamma \in \mathbb{R} \ \forall \mathbf{M} \in \mathbb{M}_{3 \times 3} \ \frac{1}{c} |\mathbf{M}|^2 \le (\sigma(\boldsymbol{x}, \gamma)\mathbf{M}): \mathbf{M} \le c |\mathbf{M}|^2;$$

- 6 (A.2) the function $\sigma(\cdot, \cdot)$ is in $C^1(\bar{\Omega} \times \mathbb{R})$;
 - (A.3) $\left(\mathbf{M}_{i,e}(\boldsymbol{x},\mathbf{M})\right)_{\boldsymbol{x}\in\Omega,\mathbf{M}\in\mathbb{M}_{3\times3}}$ is a family of symmetric matrices, uniformly bounded and positive definite:

$$\exists c > 0: \text{ for a.e. } x \in \Omega, \forall \mathbf{M} \in \mathbb{M}_{3 \times 3} \ \forall \xi \in \mathbb{R}^3 \ \frac{1}{c} |\xi|^2 \le (\mathbf{M}_{i,e}(\boldsymbol{x}, \mathbf{M})\xi) \cdot \xi \le c |\xi|^2;$$

- 7 (A.4) the maps $\mathbf{M} \mapsto \mathbf{M}_{i,e}(\cdot, \mathbf{M})$ are uniformly Lipschitz continuous;
- * (A.5) the function S is given by $S(\gamma, \boldsymbol{w}) = \beta(\sum_{j=1}^{k} \eta_j w_j \eta_0 \gamma)$, for positive physiological parameters $\beta, \eta_j, j = 0, 1, \cdots, k$;
 - (A.6) the functions \mathbf{R} , G and I_{ion} are given by the kinetics of a general physiological ionic model and it can be verified that the assumptions, stated below, are satisfied by several gating and ionic concentration variables in Beeler-Reuter or Luo-Rudy ionic models. We assume that the function $\mathbf{R}(v, \boldsymbol{w}) := (R_1(v, w_1), ..., R_k(v, w_k))$ where $R_j : \mathbb{R}^2 \to \mathbb{R}$ are locally Lipschitz continuous functions defined by

$$R_j(v, \boldsymbol{w}) = \alpha_j(v)(1 - w_j) - \beta_j(v)w_j$$

where α_j and β_j , $j = 1, \dots, k$ are positive rational functions of exponentials in v such that:

$$0 < \alpha_j(v), \beta_j(v) \le C_{\alpha,\beta}(1+|v|),$$

$$\frac{d\alpha_j}{dv} \text{ and } \frac{d\beta_j}{dv} \text{ are uniformly bounded},$$
(2.21)

for some constant $C_{\alpha,\beta} > 0$. The function $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty) \to \mathbb{R}$ has the general form:

$$I_{\rm ion}(v, \boldsymbol{w}, z) = \sum_{j=1}^{k} I_{\rm ion}^{j}(v, w_j) + I_{\rm ion}^{z}(v, \boldsymbol{w}, z, \ln z)$$
(2.22)

where $I_{ion}^j \in C^0(\mathbb{R} \times \mathbb{R}^k)$ and satisfies the condition:

$$|I_{ion}^{j}(v, w_{j})| \le C_{1,I}(1 + |w_{j}| + |v|), \qquad (2.23)$$

15 and I_{ion}^z is such that:

$$I_{\text{ion}}^{z} \in C^{1}(\mathbb{R} \times \mathbb{R}^{k} \times \mathbb{R}^{+} \times \mathbb{R}),$$

$$I_{\text{ion}}^{z}(v, \boldsymbol{w}, z, \ln z) \le C_{2,I}(1 + |v| + |w| + |z| + \ln z),$$
(2.24)

$$I_{\rm ion}^{z}(v, \boldsymbol{w}, z, \ln z) \ge C_{3, I} \sum_{j=1}^{\infty} (|v| + w_j + w_j \ln z),$$
(2.25)

$$0 < \underline{\Theta}(\boldsymbol{w}) \le \frac{\partial}{\partial \zeta} I_{\text{ion}}^{z}(v, \boldsymbol{w}, z, \zeta) \le \bar{\Theta}(\boldsymbol{w}), \qquad (2.26)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^{z}(v, \boldsymbol{w}, z, \zeta) \right| \leq L(\boldsymbol{w}), \qquad (2.27)$$

$$\frac{\partial}{\partial w_j} I_{\text{ion}}^z \le C_{4,I} (1+|v|+|\ln z|), \quad \forall j = 1, \cdots, k,$$
(2.28)

$$0 \le \frac{\partial}{\partial z} I_{\rm ion}^z \le C_{5,I},\tag{2.29}$$

where $\underline{\Theta}$, $\overline{\Theta}$, L belong to $C^0(\mathbb{R}, \mathbb{R}^+)$ and $C_{1,I}, \ldots, C_{5,I}$ are positive constants. Finally the function G is given by:

$$G(v, \boldsymbol{w}, z) = a_1(a_2 - z) - a_3 I_{\rm ion}^z(v, \boldsymbol{w}, z, \ln z), \qquad (2.30)$$

where a_1 , a_2 , a_3 are positive physiological constants that vary from one ion to another. In our case, we only consider z to correspond to the intracellular calcium concentration.

$_{5}$ (A.7) The following condition holds

$$\int_{\Omega} I_s^i = \int_{\Omega} I_s^e \text{ and } \int_{\Omega} v_e(\boldsymbol{x}, t) \, d\boldsymbol{x} = 0 \text{ for a.e. } t \in (0, T).$$
(2.31)

6 (A.8) The data v_0, w_0, γ_0, z_0 lie in $H^1(\Omega)$ with $z_0 \ge c_0 > 0$ (c_0 is a positive constant) whereas 7 $\mathbf{g} \in L^2(\Omega_T)^3$ (recall definition (2.9)), and $I_s^{i,e} \in L^2(\Omega_T)$.

8 Note that, in practice, one starts with an undeformed configuration, i.e., with $\gamma \equiv 0$. Observe also 9 that the above system (2.5), (2.11) with $a(\cdot, \cdot, \cdot, \cdot)$ and $\mathbf{M}_{i,e}(\cdot, \cdot)$ given by (2.8), (2.7) falls within 10 the framework described by (2.10)–(2.20) and (A.1)–(A.8). Indeed, it is enough to check that 11 assumptions (A.1)–(A.4) are satisfied (assumptions (A.5)–(A.8) are already enforced). Let us 12 stress that due to assertion (2.4), properties (A.1),(A.2) hold. Thanks to properties (A.1)–(A.8), 13 the following weak formulation makes sense.

Definition 2.1. A weak solution of problem (2.10)–(2.20) is $U = (\boldsymbol{u}, p, v_i, v_e, v, \boldsymbol{w}, \gamma, z)$ such that:

16 (i) $\boldsymbol{u} \in L^2(0,T; H^1(\Omega)^3), p \in L^2(\Omega_T), v_i \in L^2(0,T; H^1(\Omega));$

17 $v_e \in L^2(0,T; H^{1,0}(\Omega))$ where $H^{1,0}(\Omega) := \{v_e \in H^1(\Omega) \text{ such that } \int_{\Omega} v_e \, d\boldsymbol{x} = 0\};$

- $v \in E := L^2(0, T; H^1(\Omega))$ with $\partial_t v \in E' := L^2(0, T; (H^1(\Omega))');$
- 19 $\gamma, z \in C([0,T]; L^2(\Omega)) \text{ and } w \in C([0,T]; L^2(\Omega)^k);$
- $z(t,x) > 0 \text{ and } 0 \leq w_j(t,x) \leq 1 \text{ for a.e. } (t,x) \in \Omega_T \text{ and for } j = 1,\ldots,k;$
- (ii) For a.e. $t \in (0,T)$, for all $v \in H^1(\Omega)^3$ there holds:

$$\int_{\Omega} \left(\nabla \boldsymbol{u} \, \sigma(\boldsymbol{x}, \gamma) : \nabla \boldsymbol{v} - p \nabla \cdot \boldsymbol{v} \right) d\boldsymbol{x} = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x} - \int_{\partial \Omega} \alpha \boldsymbol{u} \cdot \boldsymbol{v} \, ds \tag{2.32}$$

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(in the last integral, $\boldsymbol{u}, \boldsymbol{v}$ are shortcuts for the traces of $\boldsymbol{u}, \boldsymbol{v}$ on $\partial \Omega$).

For all $q \in L^2(\Omega)$

$$\int_{\Omega} q(\nabla \cdot \boldsymbol{u}) \, d\boldsymbol{x} = 0. \tag{2.33}$$

(iii) For a.e. $t \in (0,T)$, for all $\xi \in H^1(\Omega)$, $\mu \in H^{1,0}(\Omega)$, there holds

$$\langle \partial_t v, \xi \rangle + \int_{\Omega} \Big(\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}) \nabla v_i \cdot \nabla \xi + I_{\text{ion}}(v, \boldsymbol{w}, z) \xi \Big) = \int_{\Omega} I_s^i \xi, \qquad (2.34)$$

$$\langle \partial_t v, \mu \rangle - \int_{\Omega} \left(\mathbf{M}_e(\boldsymbol{x}, \nabla \boldsymbol{u}) \nabla v_e \cdot \nabla \mu + I_{\text{ion}}(v, \boldsymbol{w}, z) \mu \right) = \int_{\Omega} I_s^e \mu, \qquad (2.35)$$

with $v = v_i - v_e$ a.e. in Ω_T and $v(0, \cdot) = v_0$ a.e. in Ω .

(iv) For a.e.
$$t \in (0,T)$$
 the equations (2.15),(2.17),(2.16) are fulfilled in $L^2(\Omega)$, and $w(0,\cdot) = w_0, \gamma(0,\cdot) = \gamma_0, z(0,\cdot) = z_0$ a.e. in Ω .

27 Our main result in this paper is the following theorem:

Theorem 2.1. Assume that conditions $(\mathbf{A}.1)-(\mathbf{A}.8)$ hold. If $v_0 \in L^2(\Omega)$, $w_0 \in H^1(\Omega)^k$, γ_0 , $z_0 \in H^1(\Omega)$, with $z_0 \ge c_0 > 0$, $\mathbf{g} \in L^2(\Omega_T)^3$, $I_s^{i,e} \in L^2(\Omega_T)$ then there exists a weak solution $U = (\mathbf{u}, p, v_i, v_e, v, \mathbf{w}, \gamma, z)$ to (2.10)–(2.17) with the boundary and initial data specified as in (2.18)-(2.20).

5 **Remark 2.1.** In definition 2.1, the integrals are well defined since the tensors $\boldsymbol{\sigma}$ and $\mathbf{M}_{i,e}$ are 6 uniformly bounded and the functions $\boldsymbol{u}(t,\cdot)$, $v_{i,e}(t,\cdot)$ are in $H^1(\Omega)^3$ and $H^1(\Omega)$ respectively.

7 We also note that passage to the limit in the pressure term p is not straightforward because it is

¹ We also note that passage to the time in the pressure term p is not stratightfor adda occurse it is ⁸ not possible to establish an a priori uniform estimate in $L^2(\Omega_T)$ due to the use of the "artificial ⁹ compressibility" which attility becomes closer in the following section

9 compressibility" which utility becomes clearer in the following section.

10

3. EXISTENCE FOR A REGULARIZED PROBLEM

The proof of existence of solutions is introduced in this section using a Faedo-Galerkin method in space. A parabolic regularization similar to the one in [3] is used to ensure existence of Faedo-Galerkin solutions. A priori estimates are obtained on the Faedo-Galerkin solutions followed by compactness results to secure their convergence towards a weak solution of the regularized problem.

¹⁶ 3.1. Faedo-Galerkin approximations for the regularized problem. We use classical Hilbert ¹⁷ bases orthonormal in $L^2(\Omega)$ and orthogonal in $H^1(\Omega)$, denoted by $(\psi_l)_{l \in \mathbb{N}}$ and $(\omega_l)_{l \in \mathbb{N}}$ such that ¹⁸ span $(\psi_l)_{l \in \mathbb{N}}$ is dense in $L^2(\Omega)^3$ and $H^1(\Omega)^3$, and span $(\omega_l)_{l \in \mathbb{N}}$ is dense in $L^2(\Omega)$ and $H^1(\Omega)$ (see ¹⁹ for example [36]).

In order to impose the compatibility condition (2.31), we let

$$\mu_l = \omega_l - \frac{1}{|\Omega|} \int_{\Omega} \omega_l \, d\boldsymbol{x}$$
, so that $\int_{\Omega} \mu_l \, d\boldsymbol{x} = 0$.

We observe that $\operatorname{span}\{\mu_l\}_{l\in\mathbb{N}}$ is dense in the space $H^{1,0}(\Omega)$, given as in Definition 2.1. Furthermore, we orthonormalize the basis $(\mu_l)_{l\in\mathbb{N}}$ by the Gram-Schmidt process, and we denote the new basis by $(\mu_l)_{l\in\mathbb{N}}$ that is orthonormal in $L^2(\Omega)$. For $m \geq 0$, we introduce the finite dimensional spaces $\mathbf{H}_m = \operatorname{span}\{\psi_0, \cdots, \psi_m\} \subset H^1(\Omega)^3$, $L_m = \operatorname{span}(\mu_0, \cdots, \mu_m) \subset H^{1,0}(\Omega)$ and $W_m = \operatorname{span}(\omega_0, \cdots, \omega_m) \subset H^1(\Omega)$.

We are looking for a discrete solution $\boldsymbol{u}_m = (\boldsymbol{u}_{\varepsilon,m}, p_{\varepsilon,m}, v_m, v_{i,\varepsilon,m}, v_{e,\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}, \gamma_{\varepsilon,m})$ (for fixed $\varepsilon > 0$) of the system (3.2) below with

$$\boldsymbol{u}_{m} = \sum_{l=0}^{m} \boldsymbol{u}_{l,m} \boldsymbol{\psi}_{l}, \qquad p_{m} = \sum_{l=0}^{m} p_{l,m} \omega_{l} \qquad v_{i,m} = \sum_{l=0}^{m} v_{i,l,m} \omega_{l},$$
$$v_{e,m} = \sum_{l=0}^{m} v_{e,l,m} \mu_{l}, \qquad v_{m} = v_{i,m} - v_{e,m}, \qquad \gamma_{m} = \sum_{l=0}^{m} \gamma_{l,m} \omega_{l},$$
$$w_{j,m} = \sum_{l=0}^{m} w_{j,l,m} \omega_{l}, \qquad \forall j = 1, \dots, k, \qquad z_{m} = \sum_{l=0}^{m} z_{l,m} \omega_{l}.$$
(3.1)

²⁸ Upon discretization, we obtain a system of ODEs coupled to a system of algebraic equations to ²⁹ be solved at every time t. Hence, the existence of the discrete solution is not obvious and only ³⁰ the ODE part of the system satisfies the conditions of Cauchy-Lipschitz' theorem. So we resort ³¹ to a time regularization of the Faedo-Galerkin discretization in the spirit of [3]. We obtain the 1 following regularized system

$$\begin{split} \varepsilon \frac{d}{dt} \int_{\Omega} \boldsymbol{u}_{\varepsilon,m} \cdot \boldsymbol{\psi}_{l} + \int_{\Omega} (\nabla \boldsymbol{u}_{\varepsilon,m}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) : \nabla \boldsymbol{\psi}_{l} - p_{\varepsilon,m} \nabla \cdot \boldsymbol{\psi}_{l} \, d\boldsymbol{x} \\ &+ \int_{\partial \Omega} \alpha \boldsymbol{u}_{\varepsilon,m} \cdot \boldsymbol{\psi}_{l} \, d\boldsymbol{s} = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{\psi}_{l} \, d\boldsymbol{x}, \\ \varepsilon \frac{d}{dt} \int_{\Omega} p_{\varepsilon,m} \cdot \omega_{l} + \int_{\Omega} \omega_{l} \nabla \cdot \boldsymbol{u}_{\varepsilon,m} = 0, \\ \frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \omega_{l} + \varepsilon \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_{l} + \int_{\Omega} (\mathbf{M}_{i}(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_{l} \\ &+ I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_{l}) \, d\boldsymbol{x} = \int_{\Omega} I_{s}^{i} \omega_{l} \, d\boldsymbol{x}, \\ \frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \mu_{l} - \varepsilon \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_{l} - \int_{\Omega} (\mathbf{M}_{e}(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_{l} \\ &+ I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_{l}) \, d\boldsymbol{x} = \int_{\Omega} I_{s}^{e} \mu_{l} \, d\boldsymbol{x}, \end{split}$$
(3.2) \\ \frac{d}{dt} \int_{\Omega} \omega_{j,\varepsilon,m} \omega_{l} = \int_{\Omega} R_{j}(v_{\varepsilon,m}, \boldsymbol{w}_{j,\varepsilon,m}) \omega_{l}, \\ \frac{d}{dt} \int_{\Omega} z_{\varepsilon,m} \omega_{l} = \int_{\Omega} G(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_{l}, \\ \frac{d}{dt} \int_{\Omega} \gamma_{\varepsilon,m} \omega_{l} = \int_{\Omega} S(\gamma_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}) \omega_{l}, \end{split}

² for $l = 0, \dots, m$. Having no initial conditions on the functions \boldsymbol{u}, p, v_i and v_e in the original ³ problem, we need to supplement our system with initial conditions. We define the functions:

$$\begin{array}{rcl} v_{i,0} & = & \frac{v_0}{2} + \frac{1}{|\Omega|} \int_{\Omega} \frac{v_0}{2} \, d\boldsymbol{x}, \\ v_{e,0} & = & -\frac{v_0}{2} + \frac{1}{|\Omega|} \int_{\Omega} \frac{v_0}{2} \, d\boldsymbol{x}, \end{array}$$

so that $v_0 = v_{i,0} - v_{e,0}$ and $\int_{\Omega} v_{e,0} d\mathbf{x} = 0$. We further select $\mathbf{u}_0 = 0$ and an arbitrary p_0 . The initial data of the ODE system are then given by

$$\begin{aligned} \boldsymbol{u}_{\varepsilon,m}(0) &= 0, \qquad p_{\varepsilon,m}(0) = \sum_{l=0}^{m} p_{0,l,m}\omega_{l}, \quad \text{where } p_{0,l,m} &= \langle p_{0}, \omega_{l} \rangle_{L^{2}}, \\ v_{i,\varepsilon,m}(0) &= \sum_{l=0}^{m} v_{i,0,l,m}\omega_{l}, \qquad \text{where } v_{i,0,l,m} &= \langle v_{i,0}, \omega_{l} \rangle_{L^{2}}, \\ v_{e,\varepsilon,m}(0) &= \sum_{l=0}^{m} w_{j,0,l,m}\omega_{l}, \qquad \text{where } v_{e,0,l,m} &= \langle v_{e,0}, \mu_{l} \rangle_{L^{2}}, \\ w_{j,\varepsilon,m}(0) &= \sum_{l=0}^{m} w_{j,0,l,m}\omega_{l}, \qquad \text{where } w_{j,0,l,m} &= \langle w_{j,0}, \omega_{l} \rangle_{L^{2}} \\ z_{\varepsilon,m}(0) &= \sum_{l=0}^{m} z_{0,l,m}\omega_{l} \qquad \text{where } z_{0,l,m} &= \langle z_{0}, \omega_{l} \rangle_{L^{2}}, \end{aligned}$$

$$(3.3)$$

for $j = 1, \dots, k$. Using the orthonormality of the bases, we can write (3.2) as a system of ordinary differential equations in the coefficients:

$$\Big\{\{\boldsymbol{u}_{l,m}\}_{l=0}^{m}, \{p_{l,m}\}_{l=0}^{m}, \{v_{i,l,m}\}_{l=0}^{m}, \{v_{e,l,m}\}_{l=0}^{m}, \{\boldsymbol{w}_{l,m}\}_{l=0}^{m}, \{\gamma_{l,m}\}_{l=0}^{m}, \{z_{l,m}\}_{l=0}^{m}\Big\}.$$

¹ To be concise, we detail in the following paragraph how the bidomain equations can be treated to ² obtain the ODE system. We first note that using $v_m = v_{i,m} - v_{e,m}$, we have:

$$\frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_{l} - \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \omega_{l} + \varepsilon \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_{l} + \int_{\Omega} (\mathbf{M}_{i}(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_{l} \quad (3.4) \\
+ I_{\rm ion}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_{l}) d\boldsymbol{x} = \int_{\Omega} I_{s}^{i} \omega_{l} d\boldsymbol{x}, \\
\frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \mu_{l} - \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_{l} - \varepsilon \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_{l} - \int_{\Omega} (\mathbf{M}_{e}(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_{l} \quad (3.5) \\
+ I_{\rm ion}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_{l}) d\boldsymbol{x} = \int_{\Omega} I_{s}^{e} \mu_{l} d\boldsymbol{x},$$

³ Replacing $v_{i,\varepsilon,m}$ and $v_{e,\varepsilon,m}$ by their expressions as in (3.1), we obtain for $l = 0, \cdots, m$:

$$\begin{split} (1+\varepsilon)\sum_{r=0}^{m}v_{i,r,m}'\int_{\Omega}\omega_{r}\omega_{l} &-\sum_{r=0}^{m}v_{e,r,m}'\int_{\Omega}\mu_{r}\omega_{l} + \int_{\Omega}(\mathbf{M}_{i}(\boldsymbol{x},\nabla\boldsymbol{u}_{\varepsilon,m})\nabla v_{i,\varepsilon,m}\cdot\nabla\omega_{l} \\ &+I_{\mathrm{ion}}(v_{\varepsilon,m},\boldsymbol{w}_{\varepsilon,m},z_{\varepsilon,m})\omega_{l})\,d\boldsymbol{x} = \int_{\Omega}I_{s}^{i}\omega_{l}\,d\boldsymbol{x}, \\ \sum_{r=0}^{m}v_{i,r,m}'\int_{\Omega}\omega_{r}\mu_{l} - (1+\varepsilon)\sum_{r=0}^{m}v_{e,r,m}'\int_{\Omega}\mu_{r}\mu_{l} - \int_{\Omega}(\mathbf{M}_{e}(\boldsymbol{x},\nabla\boldsymbol{u}_{\varepsilon,m})\nabla v_{e,\varepsilon,m}\cdot\nabla\mu_{l} \\ &+I_{\mathrm{ion}}(v_{\varepsilon,m},\boldsymbol{w}_{\varepsilon,m},z_{\varepsilon,m})\mu_{l})\,d\boldsymbol{x} = \int_{\Omega}I_{s}^{e}\mu_{l}\,d\boldsymbol{x}, \end{split}$$

⁴ By the L^2 -orthonormality of the bases, the above equations can be rewritten in the form:

$$(1+\varepsilon)v'_{i,r,m} - \sum_{r=0}^{m} \left(\int_{\Omega} \mu_{r}\omega_{l}\right)v'_{e,r,m} = F_{i}\left(\{\boldsymbol{u}_{l,m}\}_{r=0}^{m}, \{v_{i,r,m}\}_{r=0}^{m}, \{v_{e,r,m}\}_{r=0}^{m}, \{\boldsymbol{w}_{r,m}\}_{r=0}^{m}, \{z_{r,m}\}_{r=0}^{m}\right),$$
$$-\sum_{r=0}^{m} v'_{i,r,m} \int_{\Omega} \omega_{r}\mu_{l} + (1+\varepsilon)v'_{e,l,m} = F_{e}\left(\{\boldsymbol{u}_{l,m}\}_{r=0}^{m}, \{v_{i,r,m}\}_{r=0}^{m}, \{v_{e,r,m}\}_{r=0}^{m}, \{\boldsymbol{w}_{r,m}\}_{r=0}^{m}, \{z_{r,m}\}_{r=0}^{m}\right),$$

where F_k , k = i, e assemble all the terms not containing time derivatives. The latter system is equivalent to a system written as:

$$\mathbf{M}\left(\begin{array}{c}v_{i,m}'\\v_{e,m}'\end{array}\right) = b,$$

where

$$\mathbf{M} = \begin{pmatrix} (1+\varepsilon)\mathbf{I}_{m+1} & -\mathbf{A} \\ & \\ & -\mathbf{A}^T & (1+\varepsilon)\mathbf{I}_{m+1} \end{pmatrix},$$

and $\mathbf{A} = (a_{lr})$ with $a_{lr} = \int_{\Omega} \omega_l \mu_r$. In order to write: $\begin{pmatrix} v'_{i,m} \\ v'_{e,m} \end{pmatrix} = \mathbf{M}^{-1}b$, we need to prove that the matrix \mathbf{M} is invertible. For this sake, we expand it as:

$$\mathbf{M} = \begin{bmatrix} \mathbf{I}_{m+1} & -\mathbf{A} \\ -\mathbf{A}^T & \mathbf{I}_{m+1} \end{bmatrix} + \varepsilon \begin{bmatrix} \mathbf{I}_{m+1} & 0 \\ 0 & \mathbf{I}_{m+1} \end{bmatrix}.$$

It is enough to prove that the matrix $\mathbf{N} := \begin{bmatrix} \mathbf{I}_{m+1} & -\mathbf{A} \\ -\mathbf{A}^T & \mathbf{I}_{m+1} \end{bmatrix}$ is positive. Let $\xi = \begin{pmatrix} \xi_i \\ \xi_e \end{pmatrix}$, where $\xi_i = (\xi_{i,0}, \cdots, \xi_{i,m})^T \in \mathbb{R}^{m+1}$ and $\xi_e = (\xi_{e,0}, \cdots, \xi_{e,m})^T \in \mathbb{R}^{m+1}$. Then $\xi^T \mathbf{N} \xi = \xi_i^T \xi_i - \xi_i^T \mathbf{A} \xi_e + \xi_e^T \xi_e - \xi_e^T \mathbf{A}^T \xi_i$ So we have

$$\begin{split} \xi^{T} \mathbf{N} \xi &= \sum_{k,l} \left[\xi_{i,k} \xi_{i,l} \int_{\Omega} \omega_{k} \omega_{l} - 2\xi_{i,k} a_{kl} \xi_{e,l} + \xi_{e,k} \xi_{e,l} \int_{\Omega} \mu_{k} \mu_{l} \right] \\ &= \int_{\Omega} \sum_{k,l} \left[\xi_{i,k} \xi_{i,l} \omega_{k} \omega_{l} - 2\xi_{i,k} \xi_{e,l} \omega_{l} \mu_{k} + \xi_{e,k} \xi_{e,l} \mu_{k} \mu_{l} \right] \\ &= \int_{\Omega} \left(\sum_{l} \xi_{i,l} \omega_{l} \right)^{2} - 2 \sum_{k,l} \xi_{i,k} \xi_{e,l} \omega_{l} \mu_{k} + \left(\sum_{l} \xi_{e,l} \mu_{l} \right)^{2} \\ &= \int_{\Omega} \left[\sum_{l} \xi_{i,l} \omega_{l} - \sum_{l} \xi_{e,l} \mu_{l} \right]^{2} \ge 0. \end{split}$$

¹ Thus the matrix **M** is positive definite, hence invertible. Consequently, the whole system (3.2) ² can be written as a system of ordinary differential equations in the form y'(t) = f(t, y(t)).

⁴ To prove existence of a local solution to the obtained ODE system, we note that by virtue of ⁵ assumptions (A.1)-(A.8), the functions on the right hand side of the system are Carathéodory ⁶ functions bounded by L^1 functions. According to classical ODE theory, the system admits a local in ⁷ time unique solution and the functions defined by (3.1) are well-defined and constitute approximate ⁸ solutions to the regularized system (3.2). The global existence of the Faedo-Galerkin solutions is a ⁹ consequence of the *m*-independent a priori estimates on $\boldsymbol{u}_{\varepsilon,m}, p_{\varepsilon,m}, v_{\varepsilon,m}, v_{i,\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, \gamma_{\varepsilon,m}$ ¹⁰ and $z_{\varepsilon,m}$ that are derived in the next section. For more details, consult [3].

11 3.2. A priori estimates. To prove global existence of the Faedo-Galerkin solutions we de-12 rive m-independent a priori estimates bounding $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $u_{\varepsilon,m}$, $p_{\varepsilon,m}$, $w_{j,\varepsilon,m}$, $z_{\varepsilon,m}$ 13 and $\gamma_{\varepsilon,m}$ in various Banach spaces. Given some (absolutely continuous) coefficients $a_{l,m}(t)$, 14 $c_{l,m}(t)$, $b_{k,l,m}(t)$, k = i, e, and $d_{l,m}^{\kappa}(t)$ we form the functions $\psi_m(t, \boldsymbol{x}) := \sum_{l=1}^m a_{l,m}(t)\psi_l(\boldsymbol{x})$, 15 $\rho_m(t, \boldsymbol{x}) := \sum_{l=1}^m c_{l,m}(t)\omega_l(\boldsymbol{x})$, $\xi_m(t, \boldsymbol{x}) := \sum_{l=1}^m b_{i,l,m}(t)\omega_l(\boldsymbol{x})$, $\mu_m(t, \boldsymbol{x}) := \sum_{l=1}^m b_{e,l,m}(t)\mu_l(\boldsymbol{x})$, 16 and $\omega_m^{\kappa}(t, \boldsymbol{x}) := \sum_{l=1}^m d_{l,m}^{\kappa}(t)\omega_l(\boldsymbol{x})$ for $\kappa := w, z, \gamma$. It follows that the Faedo-Galerkin solutions 17 satisfy the following weak formulations for each fixed t, which will be the starting point for deriving 18 a series of a priori estimates:

$$\begin{split} \varepsilon \int_{\Omega} \partial_t \boldsymbol{u}_{\varepsilon,m} \cdot \boldsymbol{\psi}_m + \int_{\Omega} \Big((\nabla \boldsymbol{u}_{\varepsilon,m}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) : \nabla \boldsymbol{\psi}_m - p_{\varepsilon,m} \nabla \cdot \boldsymbol{\psi}_m \Big) d\boldsymbol{x} \\ &+ \int_{\partial \Omega} \alpha \boldsymbol{u}_{\varepsilon,m} \cdot \boldsymbol{\psi}_m \, ds = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{\psi}_m \, d\boldsymbol{x}, \\ \varepsilon \int_{\Omega} \partial_t p_{\varepsilon,m} \rho_m + \int_{\Omega} \rho_m \nabla \cdot \boldsymbol{u}_{\varepsilon,m} = 0, \\ &\int_{\Omega} \partial_t v_{\varepsilon,m} \xi_m + \varepsilon \int_{\Omega} \partial_t v_{i,\varepsilon,m} \xi_m + \int_{\Omega} \Big(\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \xi_m \\ &+ I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \xi_m \Big) \, d\boldsymbol{x} = \int_{\Omega} I_s^i \xi_m \, d\boldsymbol{x}, \\ &\int_{\Omega} \partial_t v_{\varepsilon,m} \mu_m - \varepsilon \int_{\Omega} \partial_t v_{e,\varepsilon,m} \mu_m - \int_{\Omega} \Big(\mathbf{M}_e(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_m \\ &+ I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_m \Big) \, d\boldsymbol{x} = \int_{\Omega} I_s^e \mu_m \, d\boldsymbol{x}, \end{split}$$

$$\int_{\Omega} \partial_t w_{j,\varepsilon,m} \omega_m^w = \int_{\Omega} R_j (v_{\varepsilon,m}, w_{j,\varepsilon,m}) \omega_m^w,
\int_{\Omega} \partial_t z_{\varepsilon,m} \omega_m^z = \int_{\Omega} G(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_m^z,
\int_{\Omega} \partial_t \gamma_{\varepsilon,m} \omega_m^\gamma = \int_{\Omega} S(\gamma_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}) \omega_m^\gamma,$$
(3.6)

- 1 for $j = 1, \dots, k$. To simplify the notation, we perform the derivations in the following three 2 Lemmata while omitting the subscript ε, m . We start first by obtaining estimates on the gating 3 and concentration variables $(\boldsymbol{w}_{\varepsilon,m} \text{ and } z_{\varepsilon,m})$ that are needed to prove the uniform bounds. In the 4 following Lemma, we show that the gating variables $w_j, j = 1, \dots, k$ satisfy the universal bounds
- 5 $0 \le w_j \le 1.$
- **Lemma 3.1.** Let $w_j \in C([0,T], L^2(\Omega))$ and $v \in H^1(0,T, L^2(\Omega))$ such that for all $\omega_m^w \in H^1(\Omega)$:

$$\int_{\Omega} \partial_t w_j \,\omega_m^w = \int_{\Omega} R_j(v, w_j) \omega_m^w, \tag{3.7}$$

7 where $R_j(v, w_j)$ satisfies assumption (A.6). Assume that $0 \le w_{j,0} \le 1$ for a.e. in Ω , then

$$0 \le w_j \le 1, \qquad a.e. \ in \ \Omega_T. \tag{3.8}$$

8 Proof. We first extend the function $R_j(v, w_j)$ by continuity (for j = 1, ..., k):

$$R_{j}(v, w_{j}) = \begin{cases} -\beta_{j}w_{j} & \text{if } w_{j} > 1, \\ \alpha_{j}(1 - w_{j}) - \beta_{j}w_{j} & \text{if } w_{j} \le 1 \end{cases}$$
(3.9)

We Substitute $\omega_m^w = -w_j^-$ in (3.7) and we use (3.9) to deduce

$$\frac{d}{dt}|w_j^-|^2 \le 0, \text{ for } j = 1, \dots, k$$

9 Using Gronwall's inequality, we get $w_j^- = 0$ and $w_j \ge 0$, for j = 1, ..., k. Similarly, substituting 10 $\omega_m^w = (w_j - 1)^+$ in (3.7) and using (3.9), we obtain by using Gronwall's inequality that $w_j \le 1$, 11 for a.e. $(t, \boldsymbol{x}) \in \Omega_T$ and for j = 1, ..., k.

¹² Now we establish some estimates on the concentration variable z that will help us in getting ¹³ the uniform bound on $v_{\varepsilon,m}$. The difficulty arises from the presence of a logarithmic term in the ¹⁴ definition of the function G (2.30) and the ionic current I_{ion} (2.22). So we need to bound z far ¹⁵ from zero. We show in the following Lemma that if the concentration variable z is strictly positive ¹⁶ at the initial time t = 0, then it is strictly positive on the interval [0, T] and it cannot approach 0.

18 Lemma 3.2. Let
$$z \in C([0,T], L^2(\Omega)), v \in H^1(0,T, L^2(\Omega))$$
 and $w \in C([0,T], L^2(\Omega)^k)$ such that:
 $\partial_t z = G(v, w, z),$ (3.10)

where G(v, w, z) satisfies assumption (A.6) above. Let $z_0 : \Omega \to (0, +\infty)$ such that:

 $z_0 \in L^2(\Omega), \ z_0 > 0, \ for \ a.e. \ in \ \Omega.$

19 Then for a.e. $(t, \boldsymbol{x}) \in [0, T] \times \Omega, \ z > 0.$

Proof. For a.e. $\boldsymbol{x} \in \Omega$ fixed, we have $z(0, \boldsymbol{x}) = z_0 > 0$ and the map: $t \mapsto z(t, x)$ is in C[0, T]. Assume that at some time $t, z(t, \boldsymbol{x}) = 0$ and let $t_1 = \inf\{t \in (0, T) : z(t, \boldsymbol{x}) = 0\}$. Using (2.24) and (2.30), we see that $G(v, w, z) \to +\infty$ as $t \to t_1$. So, for a given A > 0 there exists $\delta > 0$ such that G(v, w, z) > A for all $t_1 - \delta < t < t_1$. Then using equation (3.10), one obtains $\partial_t z > 0$. Hence, z is strictly increasing over $[t_1 - \delta, t_1]$. Therefore $z(t_1, \boldsymbol{x}) > z(t_1 - \delta, \boldsymbol{x}) > 0$ which is a contradiction. Consequently by diagonalisation and compactness of [0, T], z > 0.

Lemma 3.3. Under the same assumptions as Lemma 3.2, the concentration variable z satisfies the following estimates for a.e. $x \in \Omega$, $t \in (0,T)$:

$$|z(t, \boldsymbol{x})| \le C(1 + |z_0(\boldsymbol{x})| + ||v(\boldsymbol{x})||_{L^2(0, t)}), \qquad \forall t \in [0, T],$$
(3.11)

$$|\ln z(t, \boldsymbol{x})| \le C(1 + |z_0(\boldsymbol{x})| + |v(t, \boldsymbol{x})| + \|v(\boldsymbol{x})\|_{L^2(0, t)})$$
(3.12)

$$\int_0^t |\partial_s z|^2 \le C \Big(1 + |z_0 \ln z_0| + |z_0|^2 + ||v||_{L^2(0,t)}^2 \Big), \tag{3.13}$$

$$\int_0^t |\ln z|^2 \le C \Big(1 + |z_0 \ln z_0| + |z_0|^2 + ||v||_{L^2(0,t)}^2 \Big), \tag{3.14}$$

Proof. In our proof, we follow the idea in [6].

Proof of (3.11):

Fixing $\boldsymbol{x} \in \Omega$ and multiplying equation (3.10) by z, we get

$$z\partial_t z = a_1(a_2 - z)z - a_3 z I_{\text{ion}}^z(v, \boldsymbol{w}, z, \ln z).$$

Next, we use (2.25) to obtain

$$\frac{1}{2}\frac{d}{dt}|z(t,\cdot)|^2 \le a_1(a_2+|z|)|z| - c_1\sum_{j=1}^k w_j(z\ln z) - c_1\sum_{j=1}^k z(|v|+w_j),$$

for some constant $c_1 > 0$. Since $-z \ln z \leq \frac{1}{e}$ for all $z \geq 0$ and $0 \leq w_j \leq 1$ a.e. in Ω_T , we find

$$\frac{1}{2}\frac{d}{dt}|z(t,\cdot)|^2 \le a_1(a_2+|z|)|z| + \frac{kc_1}{e} + kc_1|z||v|.$$

By Young's inequality, we have

$$\frac{1}{2}\frac{d}{dt}|z(t,\cdot)|^2 \le \frac{kc_1}{e} + a_1(a_2^2 + \frac{3}{2}|z(t,\cdot)|)^2) + \frac{kc_1}{2}|z(t,\cdot)|^2 + \frac{kc_1}{2}|v(t,\cdot)|^2,$$

which can be rewritten as

$$\frac{d}{dt}|z(t,\cdot)|^2 \le (3a_1 + kc_1)|z(t,\cdot)|^2 + \frac{2kc_1}{e} + 2a_1a_2^2 + kc_1|v(t,\cdot)|^2.$$

By the differential form of Gronwall's inequality, we obtain:

$$|\mathbf{z}(t,\cdot)|^2 \le \exp^{(kc_1+3a_1)t} \left[|z_0(\cdot)|^2 + \int_0^t \frac{2kc_1}{e} + 2a_1a_2^2 + kc_1|v(s,\cdot)|^2 \, ds \right] \qquad \forall t \in [0,T].$$

Or equivalently, for positive constants c_2 , c_3 and c_4 ,

$$|z(t,\cdot)|^2 \le e^{c_2 t} \left[|\mathbf{z}_0(\cdot)|^2 + c_3 t + c_4 \int_0^t |v(s,\cdot)|^2 ds \right] \qquad \forall t \in [0,T].$$

We conclude that there exists a constant $c_5 > 0$, dependent on T such that

$$|z(t,\cdot)| \le c_5(1+|z_0(\cdot)|+\|v(\cdot)\|_{L^2(0,t)}) \qquad \forall t \in [0,T]$$

Proof of (3.12):

In order to prove this estimate, we fix $x \in \Omega$ and we use definition (2.30) of the function G in equation (3.10) to get

$$\frac{dz}{dt} = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \boldsymbol{w}, z, \ln z).$$

Exploiting (2.24) and the uniform boundedness of \boldsymbol{w} in Lemma 3.1, we get

$$\frac{dz}{dt} \ge c_6 - c_7 |z| - c_8 (|v| + \ln z).$$

1 for some positive constants $c_6, c_7, c_8 > 0$. By (3.11), we have

$$\frac{dz}{dt} \ge c_6 - c_9(1 + |z_0(\cdot)| + ||v||_{L^2(0,t)}) - c_8|v| - c_8\ln z,$$
(3.15)

² for some constant $c_9 > 0$. After rearrangement of the inequality, we obtain:

$$c_8 \ln z \ge c_6 - c_9 (1 + |z_0(\cdot)| + ||v||_{L^2(0,t)}) - c_8 |v| - \frac{dz}{dt}.$$
(3.16)

- ³ Furthermore, since $\frac{dz}{dt}$ is continuous over [0,T], it is bounded below and there exists a constant ⁴ c_{10} such that:
 - $\ln z \ge c_{10}(1+|z_0(\cdot)|+|v(t,\cdot)|+||v||_{L^2(0,t)})$ (3.17)
- 5 On the other hand, knowing that $\ln z < z$, one has by (3.11):

$$\ln z < C(1 + |z_0(\cdot)| + ||v||_{L^2(0,t)}) \le C(1 + |z_0(\cdot)| + |v(t,\cdot)| + ||v||_{L^2(0,t)}).$$
(3.18)

Estimate (3.12) follows easily from (3.17) and (3.18).

Proof of (3.13):

We fix $\boldsymbol{x} \in \Omega$, we multiply equation (3.10) by $\frac{dz}{dt}$ and we use (2.30) to get

$$\left(\frac{dz}{dt}\right)^2 = a_1(a_2 - z)\frac{dz}{dt} - a_3\ln z\frac{dz}{dt} \left[\frac{I_{\rm ion}^z(v, \boldsymbol{w}, z, \ln z) - I_{\rm ion}^z(v, \boldsymbol{w}, z, 0)}{\ln z}\right] - a_3I_{\rm ion}^z(v, \boldsymbol{w}, z, 0)\frac{dz}{dt}.$$

Letting

$$\Theta(t) = \frac{I_{\text{ion}}^z(v, \boldsymbol{w}, z, \ln z) - I_{\text{ion}}^z(v, \boldsymbol{w}, z, 0)}{\ln z}$$

and observing that

$$\frac{dz}{dt}\ln z = \frac{d}{dt}[z\ln z - z].$$

The above equation simplifies to

$$\left(\frac{dz}{dt}\right)^2 = \left[a_1(a_2 - z) - a_3 I_{\rm ion}^z(v, \boldsymbol{w}, z, 0)\right] \frac{dz}{dt} - a_3 \Theta(t) \frac{d}{dt} (z \ln z - z).$$

Therefore

$$\int_{0}^{t} \frac{1}{\Theta(s)} \left(\frac{dz}{ds}\right)^{2} ds = \int_{0}^{t} \left[\frac{a_{1}(a_{2}-z) - a_{3}I_{\text{ion}}^{z}(v, \boldsymbol{w}, z, 0)}{\Theta(s)}\right] \frac{dz}{ds} ds - a_{3}(z\ln z - z - z_{0}\ln z_{0} + z_{0}).$$

Note that by (2.26), the mean value theorem and Lemma 3.1, there exist θ_1 , $\theta_2 > 0$ such that 1

$$\theta_2 \le \Theta(t) \le \theta_1. \tag{3.19}$$

Using $z \ln z - z \ge -1$, (3.19) and (2.24), we get:

$$\int_0^t \frac{1}{\Theta(s)} \left(\frac{dz}{ds}\right)^2 ds \le \frac{1}{\theta_2} \int_0^t \left(a_1 a_2 + a_1 |z| + a_3 C(1 + |v| + |z|)\right) \left|\frac{dz}{ds}\right| ds + a_3(1 + z_0 \ln z_0 - z_0).$$

By (3.19), there holds

$$\frac{1}{\theta_1} \int_0^t \left(\frac{dz}{ds}\right)^2 ds \le \frac{1}{\theta_2} \int_0^t \left(a_1 a_2 + a_1 |z| + a_3 C(1 + |v| + |z|)\right) \left|\frac{dz}{ds}\right| ds + a_3(1 + z_0 \ln z_0 - z_0).$$

Now, by estimate (3.11) with C denoted by C', one gets

$$\frac{1}{\theta_1} \int_0^t \left(\frac{dz}{ds}\right)^2 ds \leq \frac{1}{\theta_2} \int_0^t \left(a_1 a_2 + a_3 C + (a_1 + a_3 C)C'(1 + |z_0| + \|v(\boldsymbol{x})\|_{L^2(0,s)}) + a_3 C|v|)\right) \left|\frac{dz}{ds}\right| ds + a_3(1 + z_0 \ln z_0 - z_0).$$

Applying Cauchy's inequality with $\varepsilon = \frac{1}{2} \frac{\theta_2}{\theta_1}$ on the integrand of the right hand side of this last inequality, we obtain:

$$\frac{1}{\theta_1} \int_0^t \left(\frac{dz}{ds}\right)^2 ds \leq \frac{\theta_1}{2(\theta_2)^2} \int_0^t \left(a_1 a_2 + a_3 C + (a_1 + a_3 C) C'(1 + |z_0| + ||v(\boldsymbol{x})||_{L^2(0,s)}) + a_3 C |v|\right)^2 ds + \frac{1}{2\theta_1} \int_0^t \left|\frac{dz}{ds}\right|^2 ds + a_3 (1 + z_0 \ln z_0 - z_0).$$

Consequently,

$$\frac{1}{2\theta_1} \int_0^t \left(\frac{dz}{ds}\right)^2 ds \leq \frac{\theta_1}{2(\theta_2)^2} \int_0^t \left(a_1 a_2 + a_3 C + (a_1 + a_3 C)C'(1 + |z_0| + ||v(\boldsymbol{x})||_{L^2(0,s)}) + a_3 C|v|\right)^2 ds + a_3(1 + z_0 \ln z_0 - z_0).$$

Finally, one can easily show that there exists $c_{11} > 0$ depending on T such that 2

$$\int_{0}^{t} \left(\frac{dz}{ds}\right)^{2} ds \le c_{11} \left(1 + |z_{0} \ln z_{0} - z_{0}| + |z_{0}|^{2} + \|v(\boldsymbol{x})\|_{L^{2}(0,t)}^{2}\right), \quad \forall t \in (0,T),$$
(3.20)

3 for some constant $c_{11} > 0$.

4

Proof of (3.14): We have by (2.16) and (2.30)

$$I_{\rm ion}^{z}(v, \boldsymbol{w}, z, \ln z) = \frac{1}{a_3} \Big[a_1(a_2 - z) - \frac{dz}{dt} \Big].$$

We rewrite it as:

$$\left(\frac{I_{\rm ion}^z(v, \boldsymbol{w}, z, \ln z) - I_{\rm ion}^z(v, \boldsymbol{w}, z, 0)}{\ln z}\right) \ln z = \frac{1}{a_3} \left[a_1(a_2 - z) - \frac{dz}{dt}\right] - I_{\rm ion}^z(v, \boldsymbol{w}, z, 0).$$

After squaring both sides, we obtain:

$$\underline{\Theta}^2 (\ln z)^2 \le 3 \Big(\frac{a_1^2 (a_2 - z)^2}{a_3^2} + \frac{1}{a_3^2} \Big(\frac{dz}{dt} \Big)^2 + I_{\rm ion}^z (v, \boldsymbol{w}, z, 0)^2 \Big).$$

Then we integrate over (0, t), to get:

$$\int_0^t \underline{\Theta}^2 (\ln z)^2 ds \le 3 \int_0^t \left(\frac{a_1^2 (a_2 - z)^2}{a_3^2} + \frac{1}{a_3^2} \left(\frac{dz}{dt} \right)^2 + I_{\text{ion}}^z (v, \boldsymbol{w}, z, 0)^2 \right) ds.$$

Therefore, by (3.11), (3.20) and (2.24) we find

$$\int_{0}^{t} (\ln z(s))^{2} ds \leq c_{12} \Big(1 + |z_{0} \ln z_{0} - z_{0}| + |z_{0}|^{2} + ||v||_{L^{2}(0,t)}^{2} \Big),$$

$$c_{12} > 0.$$

1 for some constant $c_{12} > 0$.

² Using the above estimates on z and w, we shall control the L^2 norm of I_{ion} by the L^2 norm of ³ v and this result will be later used to reach a uniform in ε and m estimate on $v_{\varepsilon,m}$.

4 Lemma 3.4. Under the same conditions of Lemma 3.3, there exists a constant C > 0 (dependent 5 on T) such that

$$\|I_{\rm ion}(v, \boldsymbol{w}, z, \ln(z))\|_{L^2(\Omega_T)}^2 \le C(1 + \|v\|_{L^2(\Omega_T)}^2).$$
(3.21)

Proof. By definition (2.22) of I_{ion} , by properties (2.23) and (2.24), and by the uniform bound obtained on w_j (3.8), there holds:

$$|I_{\rm ion}(v, \boldsymbol{w}, z, \ln(z))|^2 \le C \Big(\sum_{j=1}^k (1+|v|^2) + 1 + |v|^2 + |z|^2 + |\ln z|^2\Big) \qquad (C \text{ is a generic constant}).$$

6 Using (3.11) and (3.12), one obtains

$$|I_{\rm ion}(v, \boldsymbol{w}, z, \ln(z))|^2 \le C(1 + |z_0|^2 + |v|^2 + \|v\|_{L^2(0,t)}^2)$$
(3.22)

7 Finally, integrate (3.22) over $(0, t) \times \Omega$ and use (3.14) along with the condition that z_0 is in $L^2(\Omega)$, 8 to get (3.21).

We recall that in order to establish the passage to the limit as $m \to \infty$, we need to bound the solutions of the discrete regularized problem in various Banach spaces, making use of the preceding estimates.

12 **Lemma 3.5.** There exist constants C_1, C_2 and $C_3 > 0$ independent of ε and m such that

$$\max_{t\in[0,T]} \left(\|v_{\varepsilon,m}(t)\|_{L^2(\Omega)} + \sum_{j=i,e} \|\sqrt{\varepsilon}v_{j,\varepsilon,m}(t)\|_{L^2(\Omega)} \right) \leq \mathcal{C}_1,$$
(3.23)

$$\left(\sum_{j=i,e} \|v_{j,\varepsilon,m}\|_{L^2(0,T;H^1(\Omega))} + \|v_{\varepsilon,m}\|_{L^2(0,T;H^1(\Omega))}\right) \le \mathcal{C}_2, \tag{3.24}$$

$$\|\partial_t (v_{\varepsilon,m} + \varepsilon v_{i,\varepsilon,m})\|_{L^2(0,T;(H^1(\Omega))')} + \|\partial_t (v_{\varepsilon,m} - \varepsilon v_{e,\varepsilon,m})\|_{L^2(0,T;(H^1(\Omega))')} \le \mathcal{C}_3, \tag{3.25}$$

- 1 Proof.
- 2 Proofs of (3.23) and (3.24):
- ³ First, we make use of the relation $v_{\varepsilon,m} = v_{i,\varepsilon,m} v_{e,\varepsilon,m}$. We take $\xi_m := v_{i,\varepsilon,m}$ and $\mu_m := -v_{e,\varepsilon,m}$
- 4 as test functions in (3.6) to get

.

$$\int_{\Omega} v_{i,\varepsilon,m} \partial_t v_{\varepsilon,m} + \varepsilon \int_{\Omega} v_{i,\varepsilon,m} \partial_t v_{i,\varepsilon,m} + \int_{\Omega} \left(\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla v_{i,\varepsilon,m} + I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{i,\varepsilon,m} \right) d\boldsymbol{x} = \int_{\Omega} I_s^i v_{i,\varepsilon,m} d\boldsymbol{x},$$
(3.26)

$$-\int_{\Omega} v_{e,\varepsilon,m} \partial_t v_{\varepsilon,m} + \varepsilon \int_{\Omega} v_{e,\varepsilon,m} \partial_t v_{e,\varepsilon,m} + \int_{\Omega} \left(\mathbf{M}_e(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla v_{e,\varepsilon,m} - I_{\mathrm{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{e,\varepsilon,m} \right) d\boldsymbol{x} = -\int_{\Omega} I_s^e v_{e,\varepsilon,m} d\boldsymbol{x}.$$
(3.27)

⁵ Secondly, we add equations (3.26) and (3.27) to obtain

$$\int_{\Omega} \left(I_{\text{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{\varepsilon,m} + \sum_{j=i,e} \mathbf{M}_{j}(x, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{j,\varepsilon,m} \cdot \nabla v_{j,\varepsilon,m} \right) \\ + \frac{1}{2} \int_{\Omega} \left| \partial_{t} v_{\varepsilon,m} \right|^{2} + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} \left| \sqrt{\varepsilon} \partial_{t} v_{k,\varepsilon,m} \right|^{2} = \int_{\Omega} (I_{s}^{i} v_{i,\varepsilon,m} - I_{s}^{e} v_{e,\varepsilon,m}).$$

$$(3.28)$$

6 Then we integrate equation (3.28) on (0, s) for every $s \leq T$, to get:

$$\int_{0}^{s} \int_{\Omega} \left(I_{\text{ion}}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{\varepsilon,m} + \sum_{j=i,e} \mathbf{M}_{j}(x, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{j,\varepsilon,m} \cdot \nabla v_{j,\varepsilon,m} \right) \\
+ \frac{1}{2} \int_{\Omega} |v_{\varepsilon,m}(s, \cdot)|^{2} + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,\varepsilon,m}(s, \cdot)|^{2} \\
= \frac{1}{2} \int_{\Omega} |v_{0,\varepsilon,m}|^{2} + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,0,\varepsilon,m}|^{2} + \int_{0}^{s} \int_{\Omega} (I_{s}^{i} v_{i,\varepsilon,m} - I_{s}^{e} v_{e,\varepsilon,m}) \\
= \frac{1}{2} \int_{\Omega} |v_{0,\varepsilon,m}|^{2} + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,0,\varepsilon,m}|^{2} + \int_{0}^{s} \int_{\Omega} (I_{s}^{i} v_{\varepsilon,m} + (I_{s}^{i} - I_{s}^{e}) v_{e,\varepsilon,m}).$$
(3.29)

Note that, by construction, $|v_{j,0,\varepsilon,m}| \leq \frac{|v_{0,\varepsilon,m}|}{2} + \frac{1}{|\Omega|} \left| \int_{\Omega} \frac{v_{0,\varepsilon,m}}{2} \right|, j = i, e$. Using this, the ellipticity condition (A.3), Young's and Hölder's inequalities, and in addition estimate (3.21) on I_{ion} in Lemma 3.4 and Poincaré's inequality with compatibility condition (2.31), we get

$$\begin{split} \frac{1}{c} \sum_{j=i,e} \|\nabla v_{j,\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} + \frac{1}{2} \|v_{\varepsilon,m}(s)\|_{L^{2}(\Omega)}^{2} + \frac{1}{2} \sum_{j=i,e} \|\sqrt{\varepsilon}v_{j,\varepsilon,m}\|_{L^{2}(\Omega)}^{2} \\ &\leq \left(\varepsilon + \frac{1}{2}\right) \|v_{0,\varepsilon,m}\|_{L^{2}(\Omega)}^{2} + \|I_{i}^{s}\|_{L^{2}(\Omega_{s})} \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})} + \sum_{j=i,e} \|I_{j}^{s}\|_{L^{2}(\Omega_{s})} \|v_{e,\varepsilon,m}\|_{L^{2}(\Omega_{s})} \\ &\quad + \frac{1}{2} \|I_{ion}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, \boldsymbol{z}_{\varepsilon,m})\|_{L^{2}(\Omega_{s})}^{2} + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} \\ &\leq \left(\varepsilon + \frac{1}{2}\right) \|v_{0,\varepsilon,m}\|_{L^{2}(\Omega)}^{2} + \frac{1}{2} \|I_{i}^{s}\|^{2} + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} + \frac{C}{2} \sum_{j=i,e} \|I_{j}^{s}\|_{L^{2}(\Omega_{s})}^{2} + \frac{1}{2c} \|\nabla v_{e,\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} \\ &\quad + \frac{C}{2} \left(1 + \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2}\right) + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} \\ &\leq \left(\varepsilon + \frac{1}{2}\right) \|v_{0}\|_{L^{2}(\Omega)}^{2} + \frac{1}{2} \left((1+c)\|I_{i}^{s}\|^{2} + \|I_{e}^{s}\|^{2}\right) + \frac{1}{2c} \|\nabla v_{e,\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} \\ &\quad + \left(\frac{C}{2} + 1\right) \|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} + \frac{C}{2}, \end{split}$$

where C > 0 is the constant of estimate (3.21). Or equivalently:

$$\|v_{\varepsilon,m}(s)\|_{L^{2}(\Omega)}^{2} + \sum_{j=i,e} \|\sqrt{\varepsilon}v_{j,\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} - c_{13}\|v_{\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} + \frac{2}{c}\|\nabla v_{i,\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} + \frac{1}{c}\|\nabla v_{e,\varepsilon,m}\|_{L^{2}(\Omega_{s})}^{2} \le c_{14},$$
(3.30)

where $c_{13} = \left(C + \frac{1}{2}\right)$ and $c_{14} > 0$ is obtained from the L^2 -norms of $I_{i,e}^s$ and v_0 . This implies

$$\|v_{\varepsilon,m}(s)\|_{L^{2}(\Omega)}^{2} - c_{15} \int_{0}^{s} \|v_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} dt \le c_{16},$$

for some constants $c_{15}, c_{16} > 0$. An application of Gronwall's inequality yields

$$\|v_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} \leq c_{16}(1+c_{15}t\mathrm{e}^{c_{15}t}), \qquad \forall t \in (0,T).$$

Hence, one obtains

$$\max_{t \in [0,T]} \|v_{\varepsilon,m}(t)\|_{L^2(\Omega)}^2 \le c_{17},$$

for some constant $c_{17} > 0$. Using this and (3.30), (3.23) is proved. Again using (3.30), we have for all $t \in (0, T)$

$$c_{18} \sum_{j=i,e} \|\nabla v_{j,\varepsilon,m}\|_{L^2(\Omega)}^2 + \|v_{\varepsilon,m}(t)\|_{L^2(\Omega)}^2 \le c_{14} + c_{13} \|v_{\varepsilon,m}\|_{L^2(\Omega_t)}^2 := c_{19},$$
(3.31)

4 for some constants $c_{18}, c_{19} > 0$. The last inequality implies the bound on $v_{i,\varepsilon,m}, v_{e,\varepsilon,m}$ and $v_{\varepsilon,m}$

5 in $L^2(0,T; H^1(\Omega))$ (recall that $v_{\varepsilon,m} = v_{i,\varepsilon,m} - v_{e,\varepsilon,m}$). The proof of estimate (3.24) is thus achieved.

Proof of (3.25):

In order to prove (3.25), we introduce the sequences $U_{i,\varepsilon,m} = v_{\varepsilon,m} + \varepsilon v_{i,\varepsilon,m}$ and $U_{e,\varepsilon,m} = v_{\varepsilon,m} - \varepsilon v_{e,\varepsilon,m}$. Indeed, $\partial_t U_{i,\varepsilon,m}$ and $\partial_t U_{e,\varepsilon,m}$ are bounded (independent of ε) in $L^2(0,T; (H^1(\Omega))')$; this is easily seen by the following argument:

We let $\varphi \in L^2(0,T; H^1(\Omega))$, we take $\xi_m := \varphi$ in (3.6) and we exploit assumption (A.3) to get from (3.23) and (3.24)

$$\begin{split} \int_0^T \left| \langle \partial_t U_{i,\varepsilon,m}, \varphi \rangle_{(H^1)',H^1} \right| \, dt &= \int_0^T \left| (\partial_t U_{i,\varepsilon,m}, \varphi)_{L^2} \right| \, dt \\ &= \int_0^T \left| -(\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m}, \nabla \varphi)_{L^2} + (-I_{\mathrm{ion}} + I_s^i, \varphi)_{L^2} \right| \, dt \\ &\leq \int_0^T \left(\| \mathbf{M}_i(\cdot, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \|_{L^2} \| \nabla \varphi \|_{L^2} + \| - I_{\mathrm{ion}} + I_s^i \|_{L^2} \| \varphi \|_{L^2} \right) \, dt \\ &\leq c_{20} \left(\| \nabla v_{i,\varepsilon,m} \|_{L^2(\Omega_T)} + \| I_{\mathrm{ion}} \|_{L^2(\Omega_T)} + \| I_s^i \|_{L^2(\Omega_T)} \right) \| \varphi \|_{L^2(0,T;H^1(\Omega))} \\ &\leq c_{21} \| \varphi \|_{L^2(0,T;H^1(\Omega))} \,, \end{split}$$

7 for some constants $c_{20}, c_{21} > 0$. This implies that $\partial_t U_{i,\varepsilon,m}$ is uniformly bounded in $L^2(0,T;(H^1(\Omega))')$.

8 The bound of ∂_tU_{e,ε,m} in L²(0, T; (H¹(Ω))') follows by a similar argument.
9
10

11 Regarding the gating, the activation and the concentration variables, we have the following 12 result.

13 Lemma 3.6. There exist constants C_4 and $C_5 > 0$ independent of ε and m such that:

$$\|\boldsymbol{w}_{\varepsilon,m}\|_{L^{2}(0,T;H^{1}(\Omega)^{k})} + \|\boldsymbol{z}_{\varepsilon,m}\|_{L^{2}(0,T;H^{1}(\Omega))} + \|\boldsymbol{\gamma}_{\varepsilon,m}\|_{L^{2}(0,T;H^{1}(\Omega))} \leq \mathcal{C}_{4},$$
(3.32)

$$\|\partial_t \boldsymbol{w}_{\varepsilon,m}\|_{L^2(\Omega_T)^k} + \|\partial_t z_{\varepsilon,m}\|_{L^2(\Omega_T)} + \|\partial_t \gamma_{\varepsilon,m}\|_{L^2(\Omega_T)} \le \mathcal{C}_5.$$
(3.33)

Proof.

Proof of (3.32):

We turn now to the gating variables $w_{j,\varepsilon,m}$ (recall that $0 \le w_{j,\varepsilon,m} \le 1$). Observe that by differentiation of equation (2.15) with respect to \boldsymbol{x} and by the chain rule, one has

$$\partial_t \nabla w_{j,\varepsilon,m} = \frac{d\alpha_j}{dv} \nabla v_{\varepsilon,m} (1 - w_{j,\varepsilon,m}) - (\alpha_j + \beta_j) \nabla w_{j,\varepsilon,m} - \frac{d\beta_j}{dv} \nabla v_{\varepsilon,m} w_{j,\varepsilon,m}.$$

Multiplying this equation by $\nabla w_{j,\varepsilon,m}$ and using the assumption (A.6) (recall that $\frac{d\alpha_j}{dv}$ and $\frac{d\beta_j}{dv}$ are uniformly bounded in L^{∞}), we get

$$\begin{aligned} \frac{1}{2}\partial_t |\nabla w_{j,\varepsilon,m}|^2 &\leq & |\frac{d\alpha_j}{dv}\nabla v_{\varepsilon,m}\nabla w_{j,\varepsilon,m}| + |\frac{d\beta_j}{dv}\nabla v_{\varepsilon,m}\nabla w_{j,\varepsilon,m}| \\ &\leq & \frac{|\frac{d\alpha_j}{dv}\nabla v_{\varepsilon,m}|^2}{2} + \frac{|\nabla w_{j,\varepsilon,m}|^2}{2} + \frac{|\frac{d\beta_j}{dv}(v_{\varepsilon,m})\nabla v_{\varepsilon,m}|^2}{2} + \frac{|\nabla w_{j,\varepsilon,m}|^2}{2} \\ &\leq & c_{22}(|\nabla v_{\varepsilon,m}|^2 + |\nabla w_{j,\varepsilon,m}|^2), \end{aligned}$$

for some positive constant c_{22} . An application of Gronwall's inequality and (3.24) yield

 $\|\nabla w_{j,\varepsilon,m}(t)\|_{L^{2}(\Omega)} \leq \mathcal{C}(T,\Omega, \|\nabla w_{j,0}\|_{L^{2}(\Omega)}),$

for all $t \in (0,T)$. Estimate (3.32) for $w_{j,\varepsilon,m}$ follows easily. Now to obtain the uniform bound on the concentration variable $z_{\varepsilon,m}$, we integrate (3.11) to get

$$\int_{\Omega} |z_{\varepsilon,m}(x,t)|^2 \le c_{23} \Big(1 + ||z_0||^2_{L^2(\Omega)} + ||v_{\varepsilon,m}||^2_{L^2(\Omega_T)} \Big), \qquad \forall t \in [0,T].$$

Using (3.23) for $v_{\varepsilon,m}$, this implies the uniform bound of $z_{\varepsilon,m}$ in $L^{\infty}(0,T;L^2(\Omega))$. Now we differentiate both sides of equation (2.16) with respect to \boldsymbol{x} and then use (2.30) to obtain

$$\partial_t \nabla z_{\varepsilon,m} = -a_1 \nabla z_{\varepsilon,m} - a_3 \Big(\frac{\partial I_{\rm ion}^z}{\partial v} \nabla v_{\varepsilon,m} + \sum_{j=1}^k \frac{\partial I_{\rm ion}^z}{\partial w_j} \nabla w_{j,\varepsilon,m} + \frac{\partial I_{\rm ion}^z}{\partial z} \nabla z_{\varepsilon,m} + \frac{\partial I_{\rm ion}^z}{\partial \zeta} \frac{1}{z_{\varepsilon,m}} \nabla z_{\varepsilon,m} \Big).$$

Multiplying this equation by $\nabla z_{\varepsilon,m}$, using (2.26) and (2.29), we get

$$\begin{split} \frac{1}{2}\partial_t |\nabla z_{\varepsilon,m}|^2 &= -a_1 |\nabla z_{\varepsilon,m}|^2 - a_3 \left(\frac{\partial I_{\rm ion}^z}{\partial v} \nabla v_{\varepsilon,m} \cdot \nabla z_{\varepsilon,m} + \sum_{j=1}^k \frac{\partial I_{\rm ion}^z}{\partial w_j} \nabla w_{j,\varepsilon,m} \cdot \nabla z_{\varepsilon,m} \right. \\ &\quad + \frac{\partial I_{\rm ion}^z}{\partial z} |\nabla z_{\varepsilon,m}|^2 + \frac{\partial I_{\rm ion}^z}{\partial \zeta} \frac{1}{z_{\varepsilon,m}} |\nabla z_{\varepsilon,m}|^2 \right) \\ &\leq -a_3 \left(\frac{\partial I_{\rm ion}^z}{\partial v} \nabla v_{\varepsilon,m} \cdot \nabla z_{\varepsilon,m} + \sum_{j=1}^k \frac{\partial I_{\rm ion}^z}{\partial w_j} \nabla w_{j,\varepsilon,m} \cdot \nabla z_{\varepsilon,m} \right) \\ &\leq a_3 \left(\left| \frac{\partial I_{\rm ion}^z}{\partial v} \nabla v_{\varepsilon,m} \cdot \nabla z_{\varepsilon,m} \right| + \sum_{j=1}^k \left| \frac{\partial I_{\rm ion}^z}{\partial w_j} \nabla w_{j,\varepsilon,m} \cdot \nabla z_{\varepsilon,m} \right| \right) \\ &\leq \frac{a_3}{2} \left| \frac{\partial I_{\rm ion}^z}{\partial v} \nabla v_{\varepsilon,m} \right|^2 + \frac{a_3}{2} |\nabla z_{\varepsilon,m}|^2 + \frac{a_3}{2} \sum_{j=1}^k \left| \frac{\partial I_{\rm ion}^z}{\partial w_j} \nabla w_{j,\varepsilon,m} \right|^2 + \frac{ka_3}{2} |\nabla z_{\varepsilon,m}|^2 \,. \end{split}$$

By assumptions (2.27) and (2.28), we deduce

$$\partial_t |\nabla z_{\varepsilon,m}|^2 \le c_{24} \Big(1 + |\nabla z_{\varepsilon,m}|^2 + |\nabla v_{\varepsilon,m}|^2 + |v_{\varepsilon,m}|^2 + |\ln z_{\varepsilon,m}|^2 + \sum_{j=1}^k |\nabla w_{j,\varepsilon,m}|^2 \Big),$$

for some constant $c_{24} > 0$. Using Gronwall's inequality, we get

$$|\nabla z_{\varepsilon,m}(t)|^2 \le e^{c_{24}t} \Big(|\nabla z_0|^2 + c_{24} \int_0^t (|\nabla v_{\varepsilon,m}|^2 + |v_{\varepsilon,m}|^2 + |\ln z_{\varepsilon,m}|^2 + \sum_{j=1}^k |\nabla w_{j,\varepsilon,m}|^2 + 1) \, ds \Big),$$

1 for all $t \in (0, T)$. Estimate (3.32) for $z_{\varepsilon,m}$ is a consequence of (3.14), (3.24) and the uniform bound 2 of $w_{j,\varepsilon,m}$ in $L^2(H^1)$ for $j = 1, \ldots, k$.

3

Now, we substitute $\omega_m^{\gamma} := \gamma_{\varepsilon,m}$ into the equation satisfied by γ in (3.6) to deduce after an integration in time t and an application of Young's inequality (recall the definition of the function S in (A.5))

$$\begin{split} \frac{1}{2} \|\gamma_{\varepsilon,m}(s)\|_{L^{2}(\Omega)}^{2} + \beta\eta_{0} \int_{0}^{s} \|\gamma_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} dt \\ &= \frac{1}{2} \|\gamma_{\varepsilon,m}(0)\|_{L^{2}(\Omega)}^{2} + \beta \sum_{j=1}^{k} \eta_{j} \int_{0}^{s} \int_{\Omega} \gamma_{\varepsilon,m} w_{j,\varepsilon,m} \, d\boldsymbol{x} \, dt \\ &\leq \frac{1}{2} \|\gamma_{\varepsilon,m}(0)\|_{L^{2}(\Omega)}^{2} + \frac{k\beta\eta}{2} \int_{0}^{s} \|\gamma_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} \, dt + \frac{\beta\eta}{2} \sum_{j=1}^{k} \int_{0}^{s} \|w_{j,\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} \, dt. \end{split}$$

for $s \in (0,T)$., where $\eta = \max_{j=1,\cdots,k} \eta_j$. This implies

$$\begin{aligned} \|\gamma_{\varepsilon,m}(s)\|_{L^{2}(\Omega)}^{2} &\leq (k\beta\eta - 2\beta\eta_{0}) \int_{0}^{s} \|\gamma_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} dt + \|\gamma_{\varepsilon,m}(0)\|_{L^{2}(\Omega)}^{2} \\ &+ \beta\eta \sum_{j=1}^{k} \|w_{j,\varepsilon,m}\|_{L^{2}(\Omega_{T})}^{2} \\ &\leq c_{25} \int_{0}^{s} \|\gamma_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2} dt + \|\gamma(0)\|_{L^{2}(\Omega)}^{2} + \beta\eta kc_{26}, \end{aligned}$$

where $c_{25} = -2\beta\eta_0 + k\beta\eta$ and $c_{26} > 0$. Let $\tilde{C} = \|\gamma(0)\|_{L^2(\Omega)}^2 + \beta\eta kc_{26}$, by Gronwall's lemma, we obtain

$$\|\gamma_{\varepsilon,m}(t)\|_{L^2(\Omega)}^2 \le \tilde{C}(1 + c_{25}te^{c_{25}t}) < c_{27},$$

for $t \in (0,T)$ and c_{27} a positive constant. This gives the $L^2(\Omega_T)$ uniform bound of $\gamma_{\varepsilon,m}$. Now, differentiating (2.17) with respect to \boldsymbol{x} and multiplying by $\nabla \gamma_{\varepsilon,m}$, we get

$$\frac{1}{2}\partial_t |\nabla\gamma_{\varepsilon,m}|^2 \leq \beta \sum_{\substack{j=1\\j=1}}^k \eta_j |\nabla\gamma_{\varepsilon,m} \cdot \nabla w_{j,\varepsilon,m}| + \beta\eta_0 |\nabla\gamma_{\varepsilon,m}|^2 \\ \leq \left(\frac{\beta k\eta}{2} + \beta\eta_0\right) |\nabla\gamma_{\varepsilon,m}|^2 + \frac{\beta\eta}{2} |\nabla w_{\varepsilon,m}|^2.$$

An application of Gronwall's inequality, we deduce

$$|\nabla \gamma_{\varepsilon,m}|^2 \leq e^{(\beta k\eta + 2\beta \eta_0)t} |\nabla \gamma_0|^2 + \beta \eta \int_0^t |\nabla \boldsymbol{w}_{\varepsilon,m}|^2 \, ds.$$

⁴ Upon integration of this inequality over Ω_T , we get the uniform bound of $\nabla \gamma_{\varepsilon,m}$ in L^2 . This ⁵ concludes the proof of (3.32)

6

Proof of (3.33):

To prove the L^2 uniform bound of $\partial_t w_{j,\varepsilon,m}$ we exploit $0 \leq w_{j,\varepsilon,m} \leq 1$ and $\beta_j(v) > 0$ in the following equation

$$\begin{array}{ll} \partial_t w_{j,\varepsilon,m} &= \alpha_j(v_{\varepsilon,m})(1-w_{j,\varepsilon,m}) - \beta_j(v_{\varepsilon,m})w_{j,\varepsilon,m} \\ &\leq \alpha_j(v_{\varepsilon,m}) \\ &\leq C(1+|v_{\varepsilon,m}|), \end{array}$$

where the last inequality follows from (2.21). Squaring both sides, integrating over Ω_T and using the uniform estimate on $\|v_{\varepsilon,m}\|_{L^2(\Omega_T)}^2$, we obtain (for a positive constant c_{28} dependent on T)

$$\|\partial_t w_{j,\varepsilon,m}\|_{L^2(\Omega_T)}^2 \le c_{28}(T).$$

Now the $L^2(\Omega_T)$ uniform estimate on $\partial_t z_{\varepsilon,m}$ is a direct consequence of the structure of the governing equation along with (2.30), (2.24) and Lemmata 3.1 and 3.3. Actually, squaring both sides of (2.16), and using the inequality $(a-b)^2 \leq 2a^2 + 2b^2$ twice, we have

$$|\partial_t z_{\varepsilon,m}|^2 \le 4a_1^2(a_2^2 + z_{\varepsilon,m}^2) + 2a_3^2(I_{\text{ion}}^z)^2$$

and by (2.24) and Lemma 3.1, we can find a positive constant C such that

$$\left|\partial_t z_{\varepsilon,m}\right|^2 \le C \Big(1 + \left|z_{\varepsilon,m}\right|^2 + \left|v_{\varepsilon,m}\right|^2 + \left|\ln z_{\varepsilon,m}\right|^2\Big).$$

Integrating the above inequality over Ω_T and exploiting the estimates of Lemma 3.3 along with 1 estimate (3.23), we obtain (3.33) for $z_{\varepsilon,m}$. Similarly, we get the $L^2(\Omega_T)$ uniform bound of $\partial_t \gamma_{\varepsilon,m}$. 2 3

Lemma 3.7. There exist constants C_6 and $C_7 > 0$ independent of ε and m such that: 4

$$\max_{t\in[0,T]} \left(\|\sqrt{\varepsilon}\boldsymbol{u}_{\varepsilon,m}\|_{L^{2}(\Omega)^{3}}^{2} + \|\sqrt{\varepsilon}p_{\varepsilon,m}\|_{L^{2}(\Omega)}^{2} \right) + \|\boldsymbol{u}_{\varepsilon,m}\|_{L^{2}(0,T;H^{1}(\Omega)^{3})} \leq \mathcal{C}_{6},$$
(3.34)

 $\|\varepsilon\partial_t p_{\varepsilon,m}\|_{L^2(0,T;(H^1(\Omega))')} + \|\varepsilon\partial_t u_{\varepsilon,m}\|_{L^2(0,T;(H^1(\Omega)^3)')} \le \mathcal{C}_7.$ (3.35)

Proof. Proof of (3.34):

In this proof, we first substitute $\psi_m := u_{\varepsilon,m}$ and $\rho_m := \rho_{\varepsilon,m}$ in the first two equations of system (3.6) and we add them to obtain

$$\frac{\varepsilon}{2} \frac{d}{dt} \int_{\Omega} |\boldsymbol{u}_{\varepsilon,m}|^2 d\boldsymbol{x} + \int_{\Omega} (\nabla \boldsymbol{u}_{\varepsilon,m}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) : \nabla \boldsymbol{u}_{\varepsilon,m} d\boldsymbol{x} \\ + \frac{\varepsilon}{2} \frac{d}{dt} \int_{\Omega} |p_{\varepsilon,m}|^2 d\boldsymbol{x} + \alpha \int_{\partial \Omega} |\boldsymbol{u}_{\varepsilon,m}|^2 ds = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{u}_{\varepsilon,m} d\boldsymbol{x}.$$

Next, we define the continuous bilinear form

$$a(\boldsymbol{u}, \boldsymbol{v}) = \int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{v} \, d\boldsymbol{x} + \int_{\partial \Omega} \alpha \boldsymbol{u} \cdot \boldsymbol{v} \, ds.$$

- Furthermore, we claim and we prove the following statement: 5
- Claim: The bilinear form a is coercive on $(H^1(\Omega))^3$. 6
- Proof of Claim 7
- By the uniform ellipticity of σ (A.1), we have: 8

$$a(\boldsymbol{u}, \boldsymbol{u}) = \int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma} : \nabla \boldsymbol{u} \, d\boldsymbol{x} + \alpha \|\boldsymbol{u}\|_{L^{2}(\partial\Omega)}^{2}$$
$$\simeq \|\nabla \boldsymbol{u}\|^{2} + \alpha \|\boldsymbol{u}\|_{L^{2}(\partial\Omega)}^{2}$$

We want to show that there exists c > 0 such that $c(\|\nabla \boldsymbol{u}\|_{(L^2(\Omega))^{3\times 3}}^2 + \alpha \|\boldsymbol{u}\|_{L^2(\partial\Omega)}^2) \geq \|\boldsymbol{u}\|_{(H^1(\Omega))^3}$, $\forall \boldsymbol{u} \in (H^1(\Omega))^3$. We proceed by contradiction.

Assume that

$$\forall n > 0, \quad \exists \ \boldsymbol{u}_n \in (H^1(\Omega))^3 \text{ such that } \|\nabla \boldsymbol{u}_n\|_{(L^2(\Omega))^{3\times 3}}^2 + \alpha \|\boldsymbol{u}_n\|_{(L^2(\partial\Omega))^3}^2 \leq \frac{1}{n} \|\boldsymbol{u}\|_{(H^1(\Omega))^3}^2$$

and let $\mathbf{v}_n = \frac{\mathbf{u}_n}{\|\mathbf{u}_n\|_{(H^1(\Omega))^3}}$ so that $\|\mathbf{v}_n\|_{(H^1(\Omega))^3} = 1$ and

$$\|\nabla \mathbf{v}_n\|_{(L^2(\Omega))^{3\times 3}}^2 + \alpha \|\mathbf{v}_n\|_{(L^2(\partial\Omega))^3}^2 \le \frac{1}{n},$$

which implies that

$$\nabla \mathbf{v}_n \to 0 \quad \text{in } (L^2(\Omega))^{3 \times 3},$$
(3.36)

and 10

$$\mathbf{v}_n \to 0 \quad \text{in } (L^2(\partial\Omega))^3.$$
 (3.37)

On the other hand, since \mathbf{v}_n is bounded in $(H^1(\Omega))^3$ and Ω is bounded and smooth, there exists $\mathbf{v} \in (H^1(\Omega))^3$ and a subsequence \mathbf{v}_{n_k} in $(H^1(\Omega))^3$ such that

$$\mathbf{v}_{n_k} \to \mathbf{v} \quad \text{in } (L^2(\Omega))^3$$

and

$$\nabla \mathbf{v}_{\mathbf{n}_{\mathbf{k}}} \to \nabla \mathbf{v} \text{ in } \boldsymbol{D'}(\Omega).$$

Now using (3.36), we deduce that $\nabla \mathbf{v} = 0$, hence $\mathbf{v} = C$, since Ω is connected. Also, using (3.36) and the convergence of \mathbf{v}_{n_k} to C in $(L^2(\Omega))^3$, we obtain

 $\mathbf{v_{n_k}} \to C \text{ in } (H^1(\Omega))^3$

which implies by the continuity of the trace map γ_0 that

$$\gamma_0 \mathbf{v_{n_k}} \to C \text{ in } (L^2(\partial \Omega))^3.$$

1 On the other hand, by (3.37), we have $\mathbf{v_{n_k}} \to 0$ in $(L^2(\partial \Omega))^3$. So C = 0, hence we obtain a 2 contradiction since $\|\mathbf{v}_n\|_{(H^1(\Omega))^3} = 1$. \Box

³ By the coercivity of the bilinear form a and Young's inequality, we have

$$\frac{1}{2}\frac{d}{dt}\left(\|\sqrt{\varepsilon}\boldsymbol{u}_{\varepsilon,m}\|_{L^{2}(\Omega)^{3}}^{2}+\|\sqrt{\varepsilon}p_{\varepsilon,m}\|_{L^{2}(\Omega)}^{2}\right)+\frac{c}{2}\|\boldsymbol{u}_{\varepsilon,m}\|_{H^{1}(\Omega)^{3}}^{2}\leq\frac{1}{2c}\|\boldsymbol{f}\|_{L^{2}(\Omega)}^{2}.$$
(3.38)

Integrating (3.38) over (0,t) with $0 < t \leq T$, noting that $u_{\varepsilon,m}(0) = 0$ and $||p_{0,\varepsilon,m}||_{L^2(\Omega)} \leq ||p_0||_{L^2(\Omega)}$, we obtain

$$\|\sqrt{\varepsilon}\boldsymbol{u}_{\varepsilon,m}(t)\|_{L^{2}(\Omega)^{3}}^{2}+\|\sqrt{\varepsilon}p_{\varepsilon,m}(t)\|_{L^{2}(\Omega)}^{2}\leq c_{28}(\|\boldsymbol{f}\|_{L^{2}(\Omega_{t})}^{2}+\varepsilon\|p_{0}\|_{L^{2}(\Omega)}^{2}).$$

Hence,

$$\max_{t \in [0,T]} \left(\|\sqrt{\varepsilon} \boldsymbol{u}_{\varepsilon,m}\|_{L^2(\Omega)^3}^2 + \|\sqrt{\varepsilon} p_{\varepsilon,m}\|_{L^2(\Omega)}^2 \right) \le c_{29}.$$

4 We also have upon integration of (3.38)

$$c \int_{0}^{T} \|\boldsymbol{u}_{\varepsilon,m}(t)\|_{H^{1}(\Omega)^{3}}^{2} \leq c_{30}(T)(\|\boldsymbol{f}\|_{L^{2}(\Omega_{T})}^{2} + \varepsilon \|p_{0}\|_{L^{2}(\Omega_{T})}^{2}).$$
(3.39)

As a result, estimate (3.34) follows.

In order to obtain estimate (3.35), we let $\psi \in L^2(0,T; H^1(\Omega))$ and we take $\rho_m = \psi$ in (3.6) to get

$$\begin{split} \int_0^T \left| \langle \varepsilon \partial_t p_{\varepsilon,m}, \psi \rangle_{(H^1)',H^1} \right|^2 dt &= \int_0^T \left| (\partial_t p_{\varepsilon,m}, \psi)_{L^2} \right|^2 dt \\ &= \int_0^T \left| (\psi, \nabla \cdot \boldsymbol{u}_{\varepsilon,m})_{L^2} \right|^2 dt \\ &\leq \int_0^T \|\psi\|_{L^2}^2 \|\nabla \cdot \boldsymbol{u}_{\varepsilon,m}\|_{L^2}^2 dt \\ &\leq \|\boldsymbol{u}_{\varepsilon,m}\|_{L^2(0,T;H^1(\Omega)^3)}^2 \|\psi\|_{L^2(0,T;H^1(\Omega))}^2 \\ &\leq \mathcal{C}_6 \|\psi\|_{L^2(0,T;H^1(\Omega))}^2. \end{split}$$

Similarly, we get

$$\int_0^T \left| \langle \varepsilon \partial_t \boldsymbol{u}_{\varepsilon,m}, \psi \rangle_{(H^1)', H^1} \right|^2 dt \le \mathcal{C}_6' \|\psi\|_{L^2(0,T; H^1(\Omega))}^2$$

5 for some constant $C'_6 > 0$. Therefore, estimate (3.35) follows directly.

7 Remark 3.1. We note that one can exploit the structure of the equations to obtain upper bounds 8 on $\|\varepsilon \partial_t u_{\varepsilon,m}\|_{L^1(0,T;(H^1(\Omega))')}$ and $\|p_{\varepsilon,m}\|_{L^1(0,T;L^2(\Omega))}$. With a wise choice of a sequence of test 9 functions in $H^1_0(0,T)$ along with the Ladyzhenskaya-Babuška-Brezzi condition, we can bound $p_{\varepsilon,m}$ 10 in $L^1(0,T;L^2(\Omega))$ and consequently $\varepsilon \partial_t u_{\varepsilon,m}$.

3.3. Compactness properties and Convergence. Having proved that the Faedo-Galerkin so lutions (3.1) are well defined, we are ready to prove existence of solutions to the regularized
 system.

Theorem 3.1. Assume (A.1)-(A.8) hold. Then the regularized system possesses a weak solution
for each ε > 0.

⁶ The remaining part of this subsection is devoted to proving Theorem 3.1.

7 In view of Lemma 3.5, we can construct subsequences of $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $\boldsymbol{w}_{\varepsilon,m}$, $\gamma_{\varepsilon,m}$, $z_{\varepsilon,m}$, 8 $\boldsymbol{u}_{\varepsilon,m}$, $p_{\varepsilon,m}$ which we do not bother to relabel, such that:

• $v_{\varepsilon,m} \rightharpoonup v_{\varepsilon}$, weakly in $L^2(0,T; H^1(\Omega))$,

• $\boldsymbol{w}_{\varepsilon,m} \rightharpoonup \boldsymbol{w}_{\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega)^k)$ and $\partial_t \boldsymbol{w}_{\varepsilon,m} \rightharpoonup \partial_t \boldsymbol{w}_{\varepsilon}$ weakly in $(L^2(\Omega_T))^k$,

• $\gamma_{\varepsilon,m} \rightharpoonup \gamma_{\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega))$ and $\partial_t \gamma_{\varepsilon,m} \rightharpoonup \partial_t \gamma_{\varepsilon}$ weakly in $L^2(\Omega_T)$,

• $z_{\varepsilon,m} \rightharpoonup z_{\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega))$ and $\partial_t z_{\varepsilon,m} \rightharpoonup \partial_t z_{\varepsilon}$ weakly in $L^2(\Omega_T)$,

- $v_{i,\varepsilon,m} \rightharpoonup v_{i,\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega))$ and $\nabla v_{i,\varepsilon,m} \rightharpoonup \nabla v_{i,\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $v_{e,\varepsilon,m} \rightharpoonup v_{e,\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega))$ and $\nabla v_{e,\varepsilon,m} \rightharpoonup \nabla v_{e,\varepsilon}$ weakly in $L^2(\Omega_T)$,

• $\boldsymbol{u}_{\varepsilon,m} \rightharpoonup \boldsymbol{u}_{\varepsilon}$ weakly in $L^2(0,T; H^1(\Omega)^3)$ and $\nabla \boldsymbol{u}_{\varepsilon,m} \rightharpoonup \nabla \boldsymbol{u}_{\varepsilon}$ weakly in $L^2(\Omega_T)^{3\times 3}$

• and $p_{\varepsilon,m} \rightharpoonup p_{\varepsilon}$ weak star in $L^{\infty}(0,T;L^2(\Omega))$ and weakly in $L^2(\Omega_T)$.

¹⁷ We also observe that from the sequences $U_{i,\varepsilon,m}$ and $U_{e,\varepsilon,m}$ introduced in the proof of Lemma ¹⁸ 3.5, we can extract subsequences such that:

- 19 $U_{i,\varepsilon,m} \rightharpoonup v_{\varepsilon} + \varepsilon v_{i,\varepsilon} \text{ in } L^2(0,T;H^1(\Omega)),$
- 20 $U_{e,\varepsilon,m} \rightharpoonup v_{\varepsilon} \varepsilon v_{e,\varepsilon} \text{ in } L^2(0,T;H^1(\Omega))$.

Moreover, knowing that $\partial_t U_{i,\varepsilon,m}$ and $\partial_t U_{e,\varepsilon,m}$ are uniformly bounded in $L^2(0,T;(H^1(\Omega))')$, we obtain, by compactness and uniqueness of the limit, the following strong convergence:

 $U_{i,\varepsilon,m} \to U_{i,\varepsilon} = v_{\varepsilon} + \varepsilon v_{i,\varepsilon}$ in $L^2(\Omega_T)$ and a.e. in Ω_T ,

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$$U_{e,\varepsilon,m} \to U_{e,\varepsilon} := v_{\varepsilon} - \varepsilon v_{e,\varepsilon}$$
 in $L^2(\Omega_T)$ and a.e. in Ω_T

As a result, $U_{i,\varepsilon,m} + U_{e,\varepsilon,m} = (1+\varepsilon)v_{\varepsilon,m} \to U_{i,\varepsilon} + U_{e,\varepsilon} := (1+\varepsilon)v_{\varepsilon}$ in $L^2(\Omega_T)$ and a.e. in Ω_T . Hence, $v_{\varepsilon,m} \to v_{\varepsilon}$ in $L^2(\Omega_T)$ and a.e. in Ω_T .

²⁷ Also from classical compactness results, (see [37] Theorem 5.1 p58), we have

• $\boldsymbol{w}_{\varepsilon,m} \to \boldsymbol{w}_{\varepsilon}$ strongly in $L^2(\Omega_T)^k$ and a.e. in Ω_T ,

• $\gamma_{\varepsilon,m} \to \gamma_{\varepsilon}$ strongly in $L^2(\Omega_T)$ and a.e. in Ω_T ,

so • $z_{\varepsilon,m} \to z_{\varepsilon}$ strongly in $L^2(\Omega_T)$ and a.e. in Ω_T ,

where $\boldsymbol{u}_{\varepsilon} \in L^{2}(0,T; H^{1}(\Omega)^{3}), v_{\varepsilon} \in L^{\infty}(0,T; L^{2}(\Omega)) \cap L^{2}(0,T; H^{1}(\Omega)), \boldsymbol{w}_{\varepsilon} \in L^{\infty}(\Omega_{T})^{k} \cap L^{2}(0,T; H^{1}(\Omega)^{k}),$ $\gamma_{\varepsilon} \in L^{2}(0,T; H^{1}(\Omega)), z_{\varepsilon} \in L^{2}(0,T; H^{1}(\Omega)), \text{ and } p_{\varepsilon}, \text{ in } L^{\infty}(0,T; L^{2}(\Omega)).$ For $l \geq 1$ fixed, $j = 1, \cdots, k$ and $\phi \in \mathcal{D}(0,T)$, we naturally have

$$\varepsilon \int_0^T \int_\Omega \partial_t \boldsymbol{u}_{\varepsilon,m} \boldsymbol{\psi}_l \phi = -\varepsilon \int_0^T \int_\Omega \boldsymbol{u}_{\varepsilon,m} \boldsymbol{\psi}_l \phi' \to -\varepsilon \int_0^T \int_\Omega \boldsymbol{u}_\varepsilon \boldsymbol{\psi}_l \phi',$$

$$\varepsilon \int_0^T \int_\Omega \partial_t p_{\varepsilon,m} \psi_l \phi = -\varepsilon \int_0^T \int_\Omega p_{\varepsilon,m} \omega_l \phi' \to -\varepsilon \int_0^T \int_\Omega p_\varepsilon \omega_l \phi'.$$

As a consequence, we have in the space of distributions $\mathcal{D}'(0,T)$,

$$\varepsilon \int_{\Omega} \partial_t \boldsymbol{u}_{\varepsilon,m} \boldsymbol{\psi}_l \to \varepsilon \int_{\Omega} \partial_t \boldsymbol{u}_{\varepsilon} \boldsymbol{\psi}_l \text{ and } \varepsilon \int_{\Omega} \partial_t p_{\varepsilon,m} \omega_l \to \varepsilon \int_{\Omega} \partial_t p_{\varepsilon} \omega_l$$

Since the electromechanical transmission is provided via variables $\gamma_{\varepsilon,m}$, $\boldsymbol{w}_{\varepsilon,m}$ and $z_{\varepsilon,m}$, we discuss first the passage to the limit in the governing ODE system.

We have $\boldsymbol{w}_{\varepsilon,m} \to \boldsymbol{w}_{\varepsilon}$ and $\gamma_{\varepsilon,m} \to \gamma_{\varepsilon}$ a.e. in Ω_T and S is continuous, so that $S(\gamma_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}) \to S(\gamma_{\varepsilon}, \boldsymbol{w}_{\varepsilon})$ a.e. in Ω_T ; and $S(\gamma_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}) \rightharpoonup S(\gamma_{\varepsilon}, \boldsymbol{w}_{\varepsilon})$ weakly in $L^2(\Omega_T)$ (being a linear continuous form on $L^2(\Omega_T) \times L^2(\Omega_T)^k$).

Using a classical result, see [37] Lemma 1.3 p 12, the continuity of $\mathbf{R}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m})$ and its bound in $L^2(\Omega_T)$ (which is a consequence of assumption (A.6)), (2.21) and assertion (3.23)), yield the weak convergence $\mathbf{R}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}) \rightharpoonup \mathbf{R}(v_{\varepsilon}, \boldsymbol{w}_{\varepsilon},)$ in $L^2(\Omega_T)^k$.

Similarly, by continuity of $G(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m})$ and its boundedness in $L^2(\Omega_T)$ (as a result of (3.14), and (3.23)), we obtain the weak convergence $G(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, z_{\varepsilon,m}) \rightharpoonup G(v_{\varepsilon}, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon})$ in $L^2(\Omega_T)$.

The strong $L^2(\Omega_T)$ and a.e. Ω_T convergence of $\gamma_{\varepsilon,m}$ implies the strong and a.e. convergence of the uniformly bounded family of tensors $\boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m})$, due to assumptions (A.1) and (A.2). With this information, we can write for all $\varphi \in \mathcal{D}(0,T)$:

$$\int_{0}^{T} \langle \nabla \boldsymbol{u}_{\varepsilon,m} \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m}), \nabla \boldsymbol{\psi}_{l} \rangle_{L^{2}(\Omega), L^{2}(\Omega)} \varphi \, dt = \int_{0}^{T} \langle \nabla \boldsymbol{u}_{\varepsilon,m} (\boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})), \nabla \boldsymbol{\psi}_{l} \rangle \varphi \, dt \\ + \int_{0}^{T} \langle \nabla \boldsymbol{u}_{\varepsilon,m} \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon}), \nabla \boldsymbol{\psi}_{l} \rangle \varphi \, dt \\ = \int_{0}^{T} \langle \nabla \boldsymbol{u}_{\varepsilon,m} (\boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})), \nabla \boldsymbol{\psi}_{l} \rangle \varphi \, dt \\ + \int_{0}^{T} \langle \nabla \boldsymbol{u}_{\varepsilon,m}, \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon}) \nabla \boldsymbol{\psi}_{l} \rangle \varphi \, dt.$$

The weak $L^2(\Omega_T)^{3\times 3}$ convergence of $\nabla \boldsymbol{u}_{\varepsilon,m}$ directly implies the convergence of the last term on the right hand side to $\langle \nabla \boldsymbol{u}_{\varepsilon}, \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon}) \nabla \boldsymbol{\psi}_l \rangle = \langle \nabla \boldsymbol{u}_{\varepsilon} \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon}), \nabla \boldsymbol{\psi}_l \rangle$. It remains to prove that the first term converges to 0; we write

$$\begin{split} \int_0^T \langle \nabla \boldsymbol{u}_{\varepsilon,m}(\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon})), \nabla \boldsymbol{\psi}_l \rangle \left| \varphi \right| \, dt \\ &\leq \int_0^T \| \nabla \boldsymbol{u}_{\varepsilon,m} \|_{L^2} \| (\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon})) \nabla \boldsymbol{\psi}_l \|_{L^2} \left| \varphi \right| \, dt \\ &\leq \mathcal{C} \int_0^T \| (\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon})) \nabla \boldsymbol{\psi}_l \|_{L^2} \left| \varphi \right| \, dt. \end{split}$$

Knowing that $(\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon,m})-\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon}))\nabla \boldsymbol{\psi}_{l} \to 0$ a.e. in Ω and a.e. in (0,T) and that $|(\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon,m})-\boldsymbol{\sigma}(\boldsymbol{x},\gamma_{\varepsilon}))\nabla \boldsymbol{\psi}_{l}|$ is (due to assumption (A.1)) bounded by a constant multiple of $|\nabla \boldsymbol{\psi}_{l}| \in L^{2}(\Omega)$ for a.e. $t \in (0,T)$, we can apply Lebesgue's dominated convergence theorem to obtain $\|[\boldsymbol{\sigma}(\cdot,\gamma_{\varepsilon,m})-\boldsymbol{\sigma}(\cdot,\gamma_{\varepsilon})]\nabla \boldsymbol{\psi}_{l}\|_{L^{2}(\Omega)} \to 0$ for a.e. $t \in (0,T)$. Similarly, one can apply Lebesgue's dominated convergence theorem on (0,T) to reach the required result.

The remaining term in the elasticity equation involves $f(t, x, \gamma_{\varepsilon,m})$, by (2.9) and assumption (A.2) we obtain the a.e. convergence of $f(t, x, \gamma_{\varepsilon,m})$ from the a.e. convergence of $\gamma_{\varepsilon,m}$ in Ω_T . Furthermore, by assumption (A.8) and estimate (3.32) we get:

$$\int_0^T \int_\Omega \boldsymbol{f}(t, \boldsymbol{x}, \gamma_{\varepsilon, m}) \cdot \boldsymbol{\psi}_l \phi(t) \to \int_0^T \int_\Omega \boldsymbol{f}(t, \boldsymbol{x}, \gamma_{\varepsilon}) \cdot \boldsymbol{\psi}_l \phi(t), \quad \forall \phi \in \mathcal{D}(0, T).$$

In order to pass to the limit in the electrical part of the system, the strong L^2 convergence of the gradients $\nabla \boldsymbol{u}_{\varepsilon,m}$ is needed. Indeed, since the limit \boldsymbol{u} solves the limit equation of (3.2), using the Minty-Browder trick (see, e.g. [38, 37, 39]), we are able to assert that $\nabla \boldsymbol{u}_{\varepsilon,m} \to \nabla \boldsymbol{u}_{\varepsilon}$ strongly in $(L^2(\Omega_T))^{3\times 3}$. Indeed, one can also exploit the structure of the elasticity equations and the

coercivity of the bilinear form a to obtain

$$\begin{aligned} \frac{1}{c} \| \boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon} \|_{L^{2}(0,T;H^{1}(\Omega)^{3})}^{2} &\leq \int_{0}^{T} a(\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}, \boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) dt \\ &= -\int_{0}^{T} \langle \varepsilon \partial_{t}(\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}), \boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon} \rangle dt - \varepsilon \| p_{\varepsilon,m}(T) - p_{\varepsilon}(T) \|_{L^{2}(\Omega_{T})}^{2} \\ &+ \varepsilon \| (p_{\varepsilon,m}(0) - p_{0} \|_{L^{2}(\Omega_{T})}^{2}) \\ &- \int_{\Omega_{T}} \nabla \boldsymbol{u}_{\varepsilon} [\boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})] : \nabla (\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) d\boldsymbol{x} dt \\ &- \int_{\Omega_{T}} [f(\boldsymbol{x}, \gamma_{\varepsilon,m}) - f(\boldsymbol{x}, \gamma_{\varepsilon})] \cdot (\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) d\boldsymbol{x} dt \\ &\leq -\int_{0}^{T} \langle \varepsilon \partial_{t}(\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}), \boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon} \rangle dt + \varepsilon \| p_{\varepsilon,m}(0) - p_{0} \|_{L^{2}(\Omega_{T})}^{2} \\ &- \int_{\Omega_{T}} \nabla \boldsymbol{u}_{\varepsilon} [\boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})] : \nabla (\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) d\boldsymbol{x} dt \\ &\leq -\int_{\Omega_{T}} [f(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})] : \nabla (\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) d\boldsymbol{x} dt \\ &- \int_{\Omega_{T}} [f(\boldsymbol{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\boldsymbol{x}, \gamma_{\varepsilon})] : \nabla (\boldsymbol{u}_{\varepsilon,m} - \boldsymbol{u}_{\varepsilon}) d\boldsymbol{x} dt \end{aligned}$$

Exploiting the convergence results obtained above along with the strong convergence of $p_{\varepsilon,m}(0)$ to p_0 and assumptions (A.1) and (A.2), one can show that the right hand side of the last inequality goes to 0 as $m \to \infty$. Therefore, $\nabla \boldsymbol{u}_{\varepsilon,m} \to \nabla \boldsymbol{u}_{\varepsilon}$ strongly in $L^2(\Omega_T)^{3\times 3}$.

Due to assumptions (A.3)-(A.4), strong convergence of $\nabla u_{\varepsilon,m}$ implies a.e. convergence of $\mathbf{M}_{i,e}(x, \nabla u_{\varepsilon,m})$ to the limit $\mathbf{M}_{i,e}(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon})$; hence we can use again the dominated convergence argument to obtain $\forall \phi \in \mathcal{D}(0,T) \text{ and for } k=i,e$

$$\int_0^T \int_\Omega \mathbf{M}_k(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_{k,\varepsilon,m} \cdot \nabla \omega_l \phi(t) \to \int_0^T \int_\Omega \mathbf{M}_k(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon}) \nabla v_{k,\varepsilon} \cdot \nabla \omega_l \phi(t).$$

Moreover, observe that I_{ion} is a continuous function of $v_{\varepsilon,m}$, $w_{\varepsilon,m}$, $z_{\varepsilon,m}$, and that it is uniformly bounded in $L^2(\Omega_T)$, again by standard arguments we have

$$\int_0^T \int_\Omega I_{\rm ion}(v_{\varepsilon,m}, \boldsymbol{w}_{\varepsilon,m}, \boldsymbol{z}_{\varepsilon,m}) \omega_l \phi(t) \to \int_0^T \int_\Omega I_{\rm ion}(v_{\varepsilon}, \boldsymbol{w}_{\varepsilon}, \boldsymbol{z}_{\varepsilon}) \omega_l \phi(t), \quad \forall \phi \in \mathcal{D}(0, T).$$

Gathering all these results, the functions $\boldsymbol{u}_{\varepsilon}, p_{\varepsilon}, v_{\varepsilon}, v_{\varepsilon}, v_{\varepsilon,\varepsilon}, \gamma_{\varepsilon}, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon}$ verify in the space of distri-1 butions $\mathcal{D}'(0,T)$, for all functions $\psi \in H^1(\Omega)^3$, $\rho \in L^2(\Omega)$, $\omega \in H^1(\Omega)$, and $\mu \in H^{1,0}(\Omega)$:

$$\langle \varepsilon \partial_t \boldsymbol{u}_{\varepsilon}, \boldsymbol{\psi} \rangle + \int_{\Omega} (\nabla \boldsymbol{u}_{\varepsilon}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon}) : \nabla \boldsymbol{\psi} - p_{\varepsilon} \nabla \cdot \boldsymbol{\psi} \, d\boldsymbol{x} + \int_{\partial \Omega} \alpha \boldsymbol{u}_{\varepsilon} \cdot \boldsymbol{\psi} \, ds = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{\psi} \, d\boldsymbol{x} \\ \langle \varepsilon p'_{\varepsilon}, \rho \rangle + \int_{\Omega} \rho \nabla \cdot \boldsymbol{u}_{\varepsilon} = 0 \\ \langle \partial_t v_{\varepsilon} + \varepsilon \partial_t v_{i,\varepsilon}, \omega \rangle + \int_{\Omega} (\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon}) \nabla v_{i,\varepsilon} \cdot \nabla \omega + I_{\mathrm{ion}}(v, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon}) \omega) \, d\boldsymbol{x} = \int_{\Omega} I_i^s \omega \, d\boldsymbol{x} \\ \langle \partial_t v_{\varepsilon} - \varepsilon \partial_t v_{e,\varepsilon}, \mu \rangle - \int_{\Omega} (\mathbf{M}_e(\boldsymbol{x}, \boldsymbol{u}_{\varepsilon}) \nabla v_{e,\varepsilon} \cdot \nabla \mu + I_{\mathrm{ion}}(v, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon,m}) \mu) \, d\boldsymbol{x} = \int_{\Omega} I_e^s \mu \, d\boldsymbol{x} \qquad (3.40) \\ \forall j = 1, \cdots, k, \quad \int_{\Omega} \partial_t w_{j,\varepsilon} \omega = \int_{\Omega} R_j(v_{\varepsilon}, \boldsymbol{w}_{\varepsilon}) \omega \\ \int_{\Omega} \partial_t z_{\varepsilon} \omega = \int_{\Omega} G(v_{\varepsilon}, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon}) \omega \\ \int_{\Omega} \partial_t \gamma_{\varepsilon} \omega = \int_{\Omega} S(\gamma_{\varepsilon}, \boldsymbol{w}_{\varepsilon}, z_{\varepsilon}) \omega.$$

 $\text{3} \quad \text{Finally, having } \boldsymbol{u}_{\varepsilon} \in L^{2}(0,T;H^{1}(\Omega)^{3}), U_{i,e,\varepsilon}, \gamma_{\varepsilon}, z_{\varepsilon} \in L^{2}(0,T;H^{1}(\Omega)) \text{ ,} \boldsymbol{w}_{\varepsilon} \in L^{2}(0,T;H^{1}(\Omega)^{k}) \text{ and } L^{2$ 4 $p_{\varepsilon} \in L^{\infty}(0,T;L^{2}(\Omega))$, and their weak derivatives $\partial_{t} u_{\varepsilon} \in L^{2}(0,T;(H^{1}(\Omega)')^{3}), \ \partial_{t} U_{i,e,\varepsilon}, \ \partial_{t} p_{\varepsilon}$ in $\begin{array}{l} {}^{4} \quad p_{\varepsilon} \in D \quad (0, T, D \quad (u_{\varepsilon})), \text{ and then we are derivative } v_{\varepsilon} u_{\varepsilon} \in U \quad (v, T, D \quad (u_{\varepsilon})), v_{\varepsilon} \in u_{\varepsilon}, v_{\varepsilon} \in U \\ \\ {}^{5} \quad L^{2}(0, T; (H^{1}(\Omega))'), \partial_{t} \boldsymbol{w}_{\varepsilon} \text{ in } L^{2}(\Omega_{T})^{k} \text{ and } \partial_{t} \gamma_{\varepsilon}, \partial_{t} z_{\varepsilon} \text{ in } L^{2}(\Omega_{T}), \text{ it is deduced from a classical result,} \\ \\ {}^{6} \quad \text{that the functions } \boldsymbol{u}_{\varepsilon} : t \in [0, T] \mapsto \boldsymbol{u}_{\varepsilon}(t) \in H^{1}(\Omega)^{3}, U_{i,e,\varepsilon} : t \in [0, T] \mapsto U_{i,e,\varepsilon}(t) \in H^{1}(\Omega), \boldsymbol{w}_{\varepsilon} : \\ \\ \\ {}^{6} \quad \text{that the functions } \boldsymbol{u}_{\varepsilon} : t \in [0, T] \mapsto \boldsymbol{u}_{\varepsilon}(t) \in H^{1}(\Omega)^{3}, U_{i,e,\varepsilon} : t \in [0, T] \mapsto U_{i,e,\varepsilon}(t) \in H^{1}(\Omega), \boldsymbol{w}_{\varepsilon} : \\ \\ \end{array}$

- $t \in [0,T] \mapsto \boldsymbol{w}_{\varepsilon}(t) \in L^{2}(\Omega)^{k}, \ \gamma_{\varepsilon}: t \in [0,T] \mapsto \gamma_{\varepsilon}(t) \in L^{2}(\Omega), \text{ and } z_{\varepsilon}: t \in [0,T] \mapsto z_{\varepsilon}(t) \in L^{2}(\Omega)$ 7
- are continuous. For p_{ε} , it only proves that they are weakly continuous in $H^1(\Omega)$. 8
- Furthermore, since $\boldsymbol{u}_{\varepsilon,m}(0) \rightarrow \boldsymbol{u}_0, \ p_{\varepsilon,m}(0) \rightarrow p_0, \ v_{\varepsilon,m}(0) \rightarrow v_0, \ v_{k,\varepsilon,m}(0) \rightarrow v_{k,0}, k = i, e,$

1 $\boldsymbol{w}_{\varepsilon,m}(0) \to \boldsymbol{w}_0, \ \gamma_{\varepsilon,m}(0) \to \gamma_0 \text{ and } z_{\varepsilon,m}(0) \to z_0 \text{ in } L^2(\Omega), \text{ we easily prove that } \boldsymbol{u}_{\varepsilon}(0) = \boldsymbol{u}_0,$ 2 $p_{\varepsilon}(0) = p_0, \ v_{\varepsilon}(0) = v_0, \ v_{k,\varepsilon}(0) = v_{k,0}, \ k = i, e, \ \boldsymbol{w}_{\varepsilon}(0) = \boldsymbol{w}_0, \ \gamma_{\varepsilon}(0) = \gamma_0 \text{ and } z_{\varepsilon}(0) = z_0.$ The proof 3 is by a standard argument given in [39] and one can refer to [3] for further details.

4

4. EXISTENCE OF SOLUTION TO THE ORIGINAL PROBLEM

From the previous section, we know there exist sequences $\{u_{\varepsilon}\}_{\varepsilon>0}, \{v_{\varepsilon}\}_{\varepsilon>0}, \{v_{\varepsilon}\}$

6 $\{w_{\varepsilon}\}_{\varepsilon>0}, \{\gamma_{\varepsilon}\}_{\varepsilon>0}$, and $\{z_{\varepsilon}\}_{\varepsilon>0}$ of solutions of (3.40). Moreover, by the lower semicontinuity of

⁷ norms, the following a priori estimates are immediately obtained as in Lemma 3.5 with $u_{\varepsilon,m}$, $p_{\varepsilon,m}$,

s $v_{\varepsilon,m}, v_{i,\varepsilon,m}, v_{e,\varepsilon,m}, w_{\varepsilon,m}, \gamma_{\varepsilon,m}, z_{\varepsilon,m}$ replaced by $u_{\varepsilon}, p_{\varepsilon}, v_{\varepsilon}, v_{i,\varepsilon}, v_{e,\varepsilon}, w_{\varepsilon}, \gamma_{\varepsilon}, z_{\varepsilon}$, respectively.

Lemma 4.1. There exist constants C_1, \dots, C_6 independent of ε such that

$$\max_{t\in[0,T]} \left(\|v_{\varepsilon}(t)\|_{L^{2}(\Omega)}^{2} + \sum_{j=i,e} \|\sqrt{\varepsilon}v_{j,\varepsilon}\|_{L^{2}(\Omega)}^{2} \right) \leq \mathcal{C}_{1}, \qquad \forall t\in[0,T],$$

$$(4.1)$$

$$\left(\sum_{j=i,e} \|v_{i,\varepsilon}\|_{L^2(0,T;H^1(\Omega))} + \|v_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))}\right) \le \mathcal{C}_2, \tag{4.2}$$

$$\|\partial_t (v_{\varepsilon} + \varepsilon v_{i,\varepsilon})\|_{L^2(0,T;(H^1)'(\Omega))} + \|\partial_t (v_{\varepsilon} - \varepsilon v_{e,\varepsilon})\|_{L^2(0,T;(H^1)'(\Omega))} \le \mathcal{C}_3, \tag{4.3}$$

$$\|\boldsymbol{w}_{\varepsilon}\|_{L^{2}(0,T;H^{1}(\Omega)^{k})} + \|\boldsymbol{z}_{\varepsilon}\|_{L^{2}(0,T;H^{1}(\Omega))} + \|\boldsymbol{\gamma}_{\varepsilon}\|_{L^{2}(0,T;H^{1}(\Omega))} \leq \mathcal{C}_{4},$$
(4.4)

$$\|\partial_t \boldsymbol{w}_{\varepsilon}\|_{\boldsymbol{L}^2(\Omega_T)^k} + \|\partial_t \boldsymbol{z}_{\varepsilon}\|_{\boldsymbol{L}^2(\Omega_T)} + \|\partial_t \gamma_{\varepsilon}\|_{\boldsymbol{L}^2(\Omega_T)} \le \mathcal{C}_5, \tag{4.5}$$

$$\max_{t \in [0,T]} (\|\sqrt{\varepsilon} \boldsymbol{u}_{\varepsilon}\|_{L^{2}(\Omega)^{3}}^{2} + \|\sqrt{\varepsilon} p_{\varepsilon}\|_{L^{2}(\Omega)}^{2}) + \|\boldsymbol{u}_{\varepsilon}\|_{L^{2}(0,T;H^{1}(\Omega)^{3})} \leq \mathcal{C}_{6}.$$
(4.6)

In view of Lemma 4.1, we can assume there exist limit functions \boldsymbol{u} , p, v, v_i , v_e , with $v = v_i - v_e$, \boldsymbol{w} , γ and z such that as $\varepsilon \to 0$, we can extract subsequences (which we do not bother to relabel) with the following convergence properties:

- $v_{\varepsilon} \to v$ strongly in $L^2(\Omega_T)$ and a.e. in Ω_T and weakly in $L^2(0,T; H^1(\Omega))$,
- $v_{i,\varepsilon} \to v_i$ weakly in $L^2(0,T; H^1(\Omega)), v_{e,\varepsilon} \to v_e$ weakly in $L^2(0,T; H^1(\Omega)),$

• $\boldsymbol{w}_{\varepsilon} \to \boldsymbol{w}$ strongly in $L^2(\Omega_T)^k$ and a.e. in Ω_T ,

• $\gamma_{\varepsilon} \to \gamma$ strongly in $L^2(\Omega_T)$ and a.e. in Ω_T ,

• $z_{\varepsilon} \to z$ strongly in $L^2(\Omega_T)$ and a.e. in Ω_T ,

• $\boldsymbol{u}_{\varepsilon} \rightharpoonup \boldsymbol{u}$ weakly in $L^2(0,T; H^1(\Omega)^3)$ and $\nabla \boldsymbol{u}_{\varepsilon} \rightharpoonup \nabla \boldsymbol{u}$ in $L^2(\Omega_T)^{3\times 3}$.

We briefly note that in the distribution sense

 $\varepsilon \langle \partial_t \boldsymbol{u}_{\varepsilon}, \boldsymbol{\psi} \rangle \to 0,$

in $\mathcal{D}'(0,T)$. Similarly,

$$\varepsilon \langle \partial_t p_{\varepsilon}, \psi \rangle \to 0$$

19 in $\mathcal{D}'(0,T)$.

20

21 Remark 4.1. Recuperation of p

²² Due to the "artificial compressibility" used in the proof, we were not able to obtain a bound on ²³ $\partial_t p_{\varepsilon}$ that is independent of ε except in $L^1(0,T;L^2(\Omega))$, (see remark 3.1), which is not a reflexive ²⁴ space. So in order to pass to the limit in the term involving the pressure, we made a detour by ²⁵ exploiting the structure of the equation and making use of De Rham's Lemma. It is important ²⁶ to note that the boundary condition used herein (2.18) determines p uniquely and not up to an ²⁷ additive constant.

Now we recall the following standard lemma (see for instance Theorem IV.3.1 p 245 in [40], see also [41, 42]).

Lemma 4.2. $\forall q \in L^2_0(\Omega) := \{q \in L^2(\Omega) : \int_{\Omega} q \, d\boldsymbol{x} = 0\}$, there exists $\boldsymbol{v} \in (H^1_0(\Omega))^3$ such that $\nabla \cdot \boldsymbol{v} = q$.

³² This lemma will be used to prove the following result.

Lemma 4.3. There exists $p \in L^2(\Omega_T)$ such that for a.e. $t \in (0,T)$ and for all $v \in (H^1(\Omega))^3$

$$\int_{\Omega} p_{\varepsilon} \nabla \cdot v \to \int_{\Omega} p \nabla \cdot v.$$

Proof. For all $\boldsymbol{v} \in (\mathcal{D}(\Omega))^3$ with $\nabla \cdot \boldsymbol{v} = 0$ we have

$$\varepsilon \langle \partial_t \boldsymbol{u}_{\varepsilon}, \boldsymbol{v} \rangle + \int_{\Omega} (\nabla \boldsymbol{u}_{\varepsilon}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon}) : \nabla \boldsymbol{v} \, d\boldsymbol{x} = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x}$$

Passing to the limit in ε we get

$$\int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{v} \, d\boldsymbol{x} = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x}$$

Therefore, by de Rham's Lemma (see Theorem IV.2.5 in [40], see also [43, 44, 45, 46]), there exists, up to an additive constant, $p \in \mathcal{D}'(\Omega)$ such that

$$abla \cdot (\nabla \boldsymbol{u})\boldsymbol{\sigma}(\mathbf{x},\gamma) + \boldsymbol{f} = \nabla p$$

in the distribution sense. Moreover, by Nečas inequality (see Theorem IV.1.1 in [40], see also [47, 48, 46]), for a.e. $t \in (0, T), p \in L^2(\Omega)$ since $\boldsymbol{u} \in (H^1(\Omega))^3$. Hence, $p \in L^2(\Omega_T)$. Now we have, for all $\boldsymbol{v} \in (H^1_0(\Omega))^3$,

$$\int_{\Omega} p_{\varepsilon} \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = \varepsilon \int_{\Omega} \partial_t \boldsymbol{u}_{\varepsilon} \cdot \boldsymbol{v} + \int_{\Omega} (\nabla \boldsymbol{u}_{\varepsilon}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon}) : \nabla \boldsymbol{v} \, d\boldsymbol{x} - \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x}$$

and

$$\int_{\Omega} p \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = \int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{v} \, d\boldsymbol{x} - \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x}$$

Subtracting these two equations, we obtain

$$\int_{\Omega} (p_{\varepsilon} - p) \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = \varepsilon \int_{\Omega} \partial_t \boldsymbol{u}_{\varepsilon} \cdot \boldsymbol{v} + \int_{\Omega} \left((\nabla \boldsymbol{u}_{\varepsilon}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon}) - (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) \right) : \nabla \boldsymbol{v} \, d\boldsymbol{x}$$

¹ Consequently, we get, for all $\boldsymbol{v} \in (H_0^1(\Omega))^3$,

$$\lim_{\varepsilon \to 0} \int_{\Omega} (p_{\varepsilon} - p) \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = 0.$$
(4.7)

Thus, $\nabla p_{\varepsilon} \to \nabla p$ in $H^{-1}(\Omega)$.

In order to complete the passage to the limit and obtain the original weak formulation, it remains to get the following result:

$$\lim_{\varepsilon \to 0} \int_{\Omega} (p_{\varepsilon} - p) \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = 0 \quad \text{for all} \ \boldsymbol{v} \in H^1(\Omega).$$

Let $q \in L^2(\Omega)$, set $\tilde{q} = q - C$ where $C = \frac{1}{|\Omega|} \int_{\Omega} q \, d\boldsymbol{x}$, so $\tilde{q} \in L^2_0(\Omega)$. By Lemma 4.2, there exists $\tilde{\boldsymbol{v}} \in (H^1_0(\Omega))^3$ such that $\nabla \cdot \tilde{\boldsymbol{v}} = \tilde{q}$. By Equation (4.7), we have

$$\lim_{\varepsilon \to 0} \int_{\Omega} (p_{\varepsilon} - p) \tilde{q} \, d\boldsymbol{x} = 0$$

In other words,

$$\int_{\Omega} (p_{\varepsilon} - p) q \, d\boldsymbol{x} - C \int_{\Omega} (p_{\varepsilon} - p) \, d\boldsymbol{x} \to 0 \quad \text{as} \quad \varepsilon \to 0$$

So in order to obtain $\int_{\Omega} (p_{\varepsilon} - p) q \, d\mathbf{x} \to 0$, it is sufficient to show $\int_{\Omega} (p_{\varepsilon} - p) \, d\mathbf{x} \to 0$. In fact, by the first equation of (3.40) we have for all $\mathbf{v} \in (H^1(\Omega))^3$,

$$\lim_{\varepsilon \to 0} \int_{\Omega} p_{\varepsilon} \nabla \cdot \boldsymbol{v} \, d\boldsymbol{x} = \int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{v} + \int_{\partial \Omega} \alpha \boldsymbol{u} \cdot \boldsymbol{v} \, ds - \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v} \, d\boldsymbol{x}.$$

In particular, we can consider the test function $\boldsymbol{v}_1 = (x_1, 0, 0)$ which is in $(H^1(\Omega))^3$ and verifies $\nabla \cdot \boldsymbol{v}_1 = 1$. Thus we obtain

$$\lim_{\varepsilon \to 0} \int_{\Omega} p_{\varepsilon} \, d\boldsymbol{x} = \tilde{\mathcal{C}} := \int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{v}_1 + \int_{\partial \Omega} \alpha \boldsymbol{u} \cdot \boldsymbol{v}_1 \, ds - \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{v}_1 \, d\boldsymbol{x}$$

Since by De Rham's Lemma, p is found up to an additive constant, then we choose it so that we have $\int_{\Omega} p \, d\boldsymbol{x} = \tilde{\mathcal{C}}$. Therefore, we have

$$\lim_{\varepsilon \to 0} \int_{\Omega} p_{\varepsilon} \, d\boldsymbol{x} = \tilde{\mathcal{C}} = \int_{\Omega} p \, d\boldsymbol{x}.$$

Consequently, we have, for all $q \in L^2(\Omega)$,

$$\lim_{\varepsilon \to 0} \int_{\Omega} (p_{\varepsilon} - p) q \, d\boldsymbol{x} = 0.$$

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² Therefore, according to all of the preceding convergence results, and repeating some of the

arguments of the previous section, we have for all $\psi \in H^1(\Omega)^3$, ρ in $L^2(\Omega)$, $\mu \in H^{1,0}(\Omega)$ (given as

4 in Definition 2.1) and ω in $H^1(\Omega)$:

$$\int_{\Omega} (\nabla \boldsymbol{u}) \boldsymbol{\sigma}(\boldsymbol{x}, \boldsymbol{\gamma}) : \nabla \boldsymbol{\psi} - p \nabla \cdot \boldsymbol{\psi} \, d\boldsymbol{x} + \int_{\partial \Omega} \alpha \boldsymbol{u} \cdot \boldsymbol{\psi} \, ds = \int_{\Omega} \boldsymbol{f} \cdot \boldsymbol{\psi} \, d\boldsymbol{x}$$
$$\int_{\Omega} \rho \nabla \cdot \boldsymbol{u} = 0$$
$$\langle \partial_t v, \omega \rangle + \int_{\Omega} (\mathbf{M}_i(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_i \cdot \nabla \omega + I_{\text{ion}}(v, \boldsymbol{w}, z) \omega) \, d\boldsymbol{x} = \int_{\Omega} I_i^s \omega \, d\boldsymbol{x}$$
$$\langle \partial_t v, \mu \rangle - \int_{\Omega} (\mathbf{M}_e(\boldsymbol{x}, \nabla \boldsymbol{u}_{\varepsilon,m}) \nabla v_e \cdot \nabla \mu + I_{\text{ion}}(v, \boldsymbol{w}, z) \mu) \, d\boldsymbol{x} = \int_{\Omega} I_e^s \mu \, d\boldsymbol{x}$$
$$\forall j = 1, \cdots, k, \quad \int_{\Omega} \partial_t w_j \, \omega = \int_{\Omega} R_j(v, \boldsymbol{w}) \omega$$
$$\int_{\Omega} \partial_t z \, \omega = \int_{\Omega} G(v, \boldsymbol{w}, z) \omega.$$
$$(4.8)$$

⁵ Repeating the argument of the previous section, the functions $v : t \in [0,T] \mapsto v(t) \in H^1(\Omega)$, ⁶ $\boldsymbol{w} : t \in [0,T] \mapsto \boldsymbol{w}(t) \in L^2(\Omega)^k$, $\gamma : t \in [0,T] \mapsto \gamma(t) \in L^2(\Omega)$, and $z : t \in [0,T] \mapsto z(t) \in L^2(\Omega)$ ⁷ are continuous and satisfy the initial conditions $v(0, \boldsymbol{x}) = v_0(\boldsymbol{x})$, $\boldsymbol{w}(0, \boldsymbol{x}) = \boldsymbol{w}_0(\boldsymbol{x})$, $\gamma(0, \boldsymbol{x}) = \gamma_0(\boldsymbol{x})$ ⁸ and $z(0) = z_0(\boldsymbol{x})$.

5. Concluding Remarks

In summary, we consider that in our work, we have paved the way towards addressing the 10 solvability of cardiac electromechanics coupled with physiological ionic models. We used a mathe-11 matical model (partially introduced in [27]) for the study of cardiac electromechanical interactions 12 written in fully Lagrangian form, with a linearized description of the passive elastic response of 13 cardiac tissue, a linearized incompressibility constraint, and a truncated approximation of the 14 nonlinear diffusivities appearing in the bidomain equations. The existence proof is done using 15 nondegenerate approximation systems, the Faedo-Galerkin method followed by a compactness 16 argument. The model simplifications are used herein for the sake of the mathematical analysis 17 but more realistic formulations have been addressed numerically. To conclude, deeper theoretical 18 insight is needed to mathematically analyze more realistic models. 19

References

2 [1] L. Tung. A bi-domain model for describing ischemic myocardial D-C potentials. PhD thesis, MIT, 1978.

1

- [2] P. Colli Franzone and G. Savaré. Degenerate evolution systems modeling the cardiac electric field at micro and macroscopic level. In *Evolution equations, semigroups and functional analysis (Milano, 2000)*, volume 50
 of *Progr. Nonlinear Differential Equations Appl.*, pages 49–78. Birkhäuser, 2002.
- [3] M. Bendahmane and K.H. Karlsen. Analysis of a class of degenerate reaction-diffusion systems and the bido main model of cardiac tissue. Netw. Heterog. Media, 1(1):185–218, 2006.
- [4] Y. Bourgault, Y. Coudière, and C. Pierre. Existence and uniqueness of the solution for the bidomain model
 used in cardiac electrophysiology. Nonl. Anal.: Real World Appl., 10(1):458-482, 2009.
- [5] H. Matano and Y. Mori. Global existence and uniqueness of a three-dimensional model of cellular electrophysiology. Discrete Contin. Dyn. Syst., 29(4):1573–1636, 2011.
- [6] M. Veneroni. Reaction-diffusion systems for the macroscopic bidomain model of the cardiac electric field. Nonl.
 Anal.: Real World Appl., 10(2):849–868, 2009.
- [7] S. Göktepe and E. Kuhl. Electromechanics of the heart: a unified approach to the strongly coupled excitation–
 contraction problem. *Comput. Mech.*, 45(2-3):227–243, 2010.
- [8] P. Lafortune, R. Arís, M. Vázquez, and G. Houzeaux. Coupled electromechanical model of the heart: Parallel
 finite element formulation. Int. J. Numer. Methods Biomed. Engrg., 28(1):72–86, 2012.
- [9] M.P. Nash and P.J. Hunter. Computational mechanics of the heart. From tissue structure to ventricular
 function. J. Elasticity, 61(1-3):113-141, 2000.
- [10] M.P. Nash and A.V. Panfilov. Electromechanical model of excitable tissue to study reentrant cardiac arrhythmias. Progr. Biophys. Molec. Biol., 85(23):501-522, 2004.
- [11] N.A. Trayanova. Whole-heart modeling: Applications to cardiac electrophysiology and electromechanics. Circ.
 Res., 108:113–128, 2011.
- 24 [12] P. Nardinocchi and L. Teresi. On the active response of soft living tissues. J. Elasticity, 88(1):27–39, 2007.
- [13] C. Cherubini, S. Filippi, P. Nardinocchi, and L. Teresi. An electromechanical model of cardiac tissue: Constitutive issues and electrophysiological effects. *Progr. Biophys. Molec. Biol.*, 97(23):562 573, 2008.
- [14] D. Ambrosi, G. Arioli, F. Nobile, and A. Quarteroni. Electromechanical coupling in cardiac dynamics: the active strain approach. SIAM J. Appl. Math., 71(2):605–621, 2011.
- [15] S. Rossi, T. Lassila, R. Ruiz-Baier, A. Sequeira, and A. Quarteroni. Thermodynamically consistent orthotropic
 activation model capturing ventricular systolic wall thickening in cardiac electromechanics. *Eur. J. Mechanics* A/Solids, 48:129–142, 2014.
- [16] D. Ambrosi and S. Pezzuto. Active stress vs. active strain in mechanobiology: constitutive issues. J. Elasticity, 107(2):199-212, 2012.
- [17] S. Rossi, R. Ruiz-Baier, L.F. Pavarino, and A. Quarteroni. Orthotropic active strain models for the numerical simulation of cardiac biomechanics. Int. J. Numer. Meth. Biomed. Engrg., 28:761-788, 2012.
- [18] P.G. Ciarlet. Mathematical Elasticity, Vol I: Three-Dimensional Elasticity. North-Holland, Amsterdam, 1978.
 [19] J.M. Ball. Convexity conditions and existence theorems in nonlinear elasticity. Arch. Rational Mech. Anal.,
- 63(4):337-403, 1976/77.
- [20] P. Krejčí, J. Sainte-Marie, M. Sorine, and J.M. Urquiza. Solutions to muscle fiber equations and their long time behaviour. Nonl. Anal.: Real World Appl., 7(4):535 558, 2006.
- [21] G.A. Holzapfel and R.W. Ogden. Constitutive modelling of passive myocardium: a structurally based frame work for material characterization. *Phil. Trans. Royal Soc. Lond. A*, 367:3445–3475, 2009.
- [22] J. Sundnes, S. Wall, H. Osnes, T. Thorvaldsen, and A.D. McCulloch. Improved discretisation and linearisation
 of active tension in strongly coupled cardiac electro-mechanics simulations. *Comput. Meth. Biomech. Biomed. Engrg.*, 17(6):604–615, 2014.
- [23] D. Baroli, A. Quarteroni, and R. Ruiz-Baier. Convergence of a stabilized discontinuous Galerkin method for
 incompressible nonlinear elasticity. Adv. Comput. Math., 39(2):425–443, 2013.
- [24] D.A. Nordsletten, S.A. Niederer, M.P. Nash, P.J. Hunter, and N.P. Smith. Coupling multi-physics models to cardiac mechanics. *Progr. Biophys. Molec. Biol.*, 104(13):77–88, 2011.
- [25] P. Pathmanathan, S.J. Chapman, D.J. Gavaghan, and J.P. Whiteley. Cardiac electromechanics: the effect of
 contraction model on the mathematical problem and accuracy of the numerical scheme. *Quart. J. Mech. Appl. Math.*, 63(3):375–399, 2010.
- [26] P. Pathmanathan, C. Ortner, and D. Kay. Existence of solutions of partially degenerate visco-elastic problems,
 and applications to modelling muscular contraction and cardiac electro-mechanical activity. *Submitted*, 2013.
- [27] Boris Andreianov, Mostafa Bendahmane, Alfio Quarteroni, and Ricardo Ruiz-Baier. Solvability analysis and
 numerical approximation of linearized cardiac electromechanics. *Mathematical Models and Methods in Applied Sciences*, 25(05):959–993, 2015.
- [28] Go W Beeler and H Reuter. Reconstruction of the action potential of ventricular myocardial fibres. The Journal of physiology, 268(1):177–210, 1977.
- [29] Ching-hsing Luo and Yoram Rudy. A dynamic model of the cardiac ventricular action potential. i. simulations
 of ionic currents and concentration changes. *Circulation research*, 74(6):1071–1096, 1994.
- [30] F. Nobile, A. Quarteroni, and R. Ruiz-Baier. An active strain electromechanical model for cardiac tissue. Int.
 J. Numer. Meth. Biomed. Engrg., 28:52-71, 2012.

- 1 [31] J. Sundnes, G.T. Lines, X. Cai, B.F. Nielsen, K.-A. Mardal, and A. Tveito. Computing the electrical activity in 2 the heart, volume 1 of Monographs in Computational Science and Engineering. Springer-Verlag, Berlin, 2006.
- 3 [32] D.M. Bers. Cardiac excitation-contraction coupling. Nature, 415(6868):198-205, 2002.
- 4 [33] R. Ruiz-Baier, A. Gizzi, S. Rossi, C. Cherubini, A. Laadhari, S. Filippi, and A. Quarteroni. Mathematical
- 5 modeling of active contraction in isolated cardiomyocytes. *Math. Medicine Biol.*, 31:259–283, 2014.
- [34] R. Ruiz-Baier, D. Ambrosi, S. Pezzuto, S. Rossi, and A. Quarteroni. Activation models for the numerical simulation of cardiac electromechanical interactions. In G.A. Holzapfel and E. Kuhl, editors, *Computer Models in Biomechanics: From nano to macro*, pages 189–201. Springer-Verlag, Heidelberg, 2013.
- 9 [35] A. Laadhari, R. Ruiz-Baier, and A. Quarteroni. Fully Eulerian finite element approximation of a fluid-structure interaction problem in cardiac cells. Int. J. Numer. Methods Engrg., 96(11):712–738, 2013.
- [36] Pierre-Arnaud Raviart, Jean-Marie Thomas, Philippe G Ciarlet, and Jacques Louis Lions. Introduction à
 l'analyse numérique des équations aux dérivées partielles, volume 2. Dunod Paris, 1998.
- [37] J.-L. Lions. Quelques méthodes de résolution des problèmes aux limites non linéaires. Dunod; Gauthier-Villars,
 Paris, 1969.
- [38] H.W. Alt and S. Luckhaus. Quasilinear elliptic-parabolic differential equations. Mathematische Zeitschrift,
 183:311-342, 1983.
- [39] Lawrence C. Evans. Partial Differential Equations, volume 19 of Graduate Studies in Mathematics. American
 Mathematical Society, Providence, Rhode Island, 1998.
- [40] Franck Boyer and Pierre Fabrie. Mathematical tools for the study of the incompressible Navier-Stokes equations
 and related models, volume 183. Springer Science & Business Media, 2012.
- [41] Jean Bourgain and Haïm Brezis. On the equation divy= f and application to control of phases. Journal of the american mathematical society, 16(2):393–426, 2003.
- [42] Douglas N Arnold, L Ridgway Scott, and Michael Vogelius. Regular inversion of the divergence operator with
 dirichlet boundary conditions on a polygon. 1987.
- [43] Georges de Rham. Differentiable manifolds, volume 266 of grundlehren der mathematischen wissenschaften.
 Berlin: Springer, 1(9):84, 1984.
- [44] Xiaoming Wang. A remark on the characterization of the gradient of a distribution. Applicable Analysis, 51(1-4):35-40, 1993.
- [45] Jacques Simon. Démonstration constructive dun théorème de g. de rham. CR Acad. Sci. Paris Sér. I Math,
 316(11):1167-1172, 1993.
- [46] Roger Temam. Navier-Stokes equations: theory and numerical analysis, volume 343. American Mathematical
 Soc., 2001.
- 33 [47] Jindrich Nečas. Sur les normes équivalentes dans $w_p^k(\omega)$ et sur la coercivité des formes formellement positives.
- 34 Les presses de l'Université de Montréal, 1966.
- 35 [48] Jindrich Nečas. Direct methods in the theory of elliptic equations. Springer Science & Business Media, 2011.
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