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MATHEMATICAL ANALYSIS OF CARDIAC ELECTROMECHANICS WITH
PHYSIOLOGICAL IONIC MODEL

MOSTAFA BENDAHMANE¹, FATIMA MROUE²,³, MAZEN SAAD², AND RAAFAT TALHOUK³

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 in its contraction leads to sudden cardiac death which is classified as the main cause of mortality in the world. The contraction of the heart is initiated by an electrical signal called action potential starting in the sinoatrial node. The electrical signal then travels through the atria and the ventricles. When the cardiac myocytes are electrically stimulated, the electrical potential inside the cell changes: they depolarize. This fast depolarization allows the transmission of the electrical signal through gap junctions and lateral junctions to the neighboring cells and their subsequent contraction.

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

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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, there is a difficulty in applying the principles of force balance to cardiac tissue due to its ability to actively deform. In other words, its contraction is influenced by intrinsic mechanisms taking place at the microscopic level. This ability is taken into account in the literature following different approaches. One common option is to assume that stresses are additively decomposed into active and passive parts and it is called the active stress formulation (\[7, 8, 9, 10, 11\]). In this paper, we follow the active strain formulation, \[1, 12, 13\], where the deformation gradient is factorized into active and passive parts, and fiber contraction rewrites in the mechanical balance of forces as a prescribed active deformation. Furthermore, this decomposition incorporates the micro-level information on fiber contraction and fiber directions in the kinematics \[14\]. These mechanisms essentially translate into a dependence of the strain energy function on auxiliary internal state variables, which represent the level of mechanical tissue activation passed across scales \[15\]. For comparisons between the two approaches in terms of numerical implementation, constitutive issues, and stability, we refer the reader to \[16, 17\].

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

Putting our contributions into perspective, we first note that up to the author’s knowledge, existence of solution of an electromechanical model coupled with physiological ionic model has never been rigourously mathematically analyzed. Moreover our paper admits a rigorous mathematical treatment, yielding the existence of weak solutions of our model. We point out that our model is degenerate, strongly nonlinear and so no maximum principle applies. We want to mention that we have not been able to prove uniqueness of weak solutions because of the presence of nonlinear 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 proof of the existence of weak solutions to the electromechanical bidomain model. Moreover, in comparison to the phenomenological ionic model used in \[27\], the physiological model considered herein contains a concentration variable \(z\) that appears as argument of a logarithm both in the dynamics of the concentration and in the ionic currents, and therefore it is necessary to bound \(z\) far from zero.

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 \(\varepsilon\) 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
assumption along with the use of “Navier-type” boundary conditions.

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

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 \( \Omega_R \). The current configuration is the deformed configuration denoted by \( \Omega \). We look for the deformation field \( \phi : \Omega_R \rightarrow \mathbb{R}^d \) that maps a material particle occupying initially the position \( X \) to its current position \( x = \phi(X) \). We denote by \( F := \nabla_X \phi \), the deformation gradient tensor where \( \nabla_X \) is the gradient operator with respect to the material coordinates \( X \), noting that \( \det(F) > 0 \).

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

\[
P = \frac{\partial W}{\partial F} - p \text{Cof}(F),
\]

where \( \text{Cof}(\cdot) \) 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 \( \phi, p \) such that

\[
\nabla \cdot P(F,p) = g \quad \text{in } \Omega_R,
\]

\[
\det(F) = 1 \quad \text{in } \Omega_R,
\]

(2.1)

completed with the Robin boundary condition

\[
Pn = -\alpha \phi \quad \text{on } \partial \Omega_R.
\]

(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 \( W \). We consider herein the case of Neo-Hookean materials, where \( W \) is defined by:

\[
W = \frac{1}{2} \mu \text{tr}[F^T F - I],
\]

with \( \mu \) being the shear modulus. Hence, \( \frac{\partial W}{\partial F} = \mu F \) and \( P = \mu F - p \text{Cof}(F) \). Although simplified, such a description of the passive response of the muscle features, so far, a nonlinear strain-stress
relationship arising from the incompressibility constraint. The forthcoming discussion will also
discover another form of strain-stress nonlinearity as a result of anisotropy inherited from the active
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 \( v_i = v_i(t, x) \), \( v_e = v_e(t, x) \) respectively, the transmembrane potential \( v = v(t, x) := v_i - v_e \), the gating or recovery variables \( w = w(t, x) = (w_1, \ldots, w_k) \), and the concentration variable \( z = z(t, x) = (z_1, \ldots, z_m) \) at \( (t, x) \in \Omega_T := (0, T) \times \Omega \), where \( T \) is the final time instant. Cardiac electrical conductivity is represented in the global coordinate system
by the orthotropic tensors

\[
\mathbf{K}_k(x) = \sigma_k^e \mathbf{d}_e \otimes \mathbf{d}_e + \sigma_k^i \mathbf{d}_i \otimes \mathbf{d}_i + \sigma_k^n \mathbf{d}_n \otimes \mathbf{d}_n, \quad k \in \{c, i\},
\]

where \( \sigma_k^e = \sigma_k^e(x) \in C^1(\mathbb{R}^3) \), \( k \in \{c, i\} \), \( s \in \{l, t, n\} \), 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 \( \mathbf{d}_s = \mathbf{d}_s(x) \), \( s \in \{l, t, n\} \). The externally applied stimulation currents corresponding to the intra- and extracellular spaces are represented by the functions \( I^i_s \) and \( I^e_s \), respectively.

The bidomain equations are given by:

\[
\begin{align*}
\chi c_m \partial_t v - \nabla \cdot (\mathbf{K}_c \nabla v_i) + \chi I_{ion}(v, w, z) &= I^i_s & \text{in } \Omega_T, \\
\chi c_m \partial_t v + \nabla \cdot (\mathbf{K}_e \nabla v_e) + \chi I_{ion}(v, w, z) &= I^e_s & \text{in } \Omega_T, \\
\partial_t w - R(v, w) &= 0 & \text{in } \Omega_T, \\
\partial_t z - G(v, w, z) &= 0 & \text{in } \Omega_T,
\end{align*}
\]

(2.3)

where \( v = v_i - v_e \). Here \( c_m \) is the capacitance and \( \chi \) 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

\[
I_{ion}(v, w, z) := \sum_{i=1}^m d_i f_i(v) \Pi_{j=1}^k w_{i,j}^{n_i,j}(v - r_i \log \left( \frac{z_j}{z_i} \right)).
\]

Herein, \( d_i \) is the maximal conductance associated with the \( i \)th current, \( f_i \) is a gating function depending on the transmembrane potential \( v \), \( n_{i,j} \) is a positive integer and \( E := r_i \log \left( \frac{z_j}{z_i} \right) \) is equilibrium (Nernst) potential \( (r_i \) is a constant and \( z_e \) is an extracellular concentration). Moreover, the dynamics of the gating variable \( w \) 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 \( j = 1, \ldots, k \). The functions \( \alpha_j \) and \( \beta_j \) are positive with the following form

\[
\frac{\rho_{1,K} e^{\rho_{2,K}(v - \bar{v})} + \rho_{3,K} (v - \bar{v})}{1 + \rho_{4,K} e^{\rho_{5,K}(v - \bar{v})}},
\]

where \( \rho_{1,K}, \rho_{3,K}, \rho_{4,K}, \rho_{5,K}, \bar{v} \geq 0 \) and \( \rho_{2,K}, \rho_{5,K} > 0 \) are constants.

The choice of the membrane model to be used is reflected in the functions \( I_{ion}(v, w, z) \), \( R(v, w) \), and
\( G(v, w, z) \). 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 [20] [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, \[14\]:

\[ F_a = I + \gamma_l d_l \otimes d_l + \gamma_t d_t \otimes d_t + \gamma_n d_n \otimes d_n \]

where \( \gamma_s, \ s \in \{ l, t, n \} \) are quantities that depend on the electrophysiology equations. Such a factorization of the deformation tensor \( F \) 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 \( F_p \). \[30\]:

\[ W = W(F_p) = W(FF_a^{-1}) = \frac{\mu}{2} \text{tr}[\gamma_p^T F_p - I] = \frac{\mu}{2} \text{tr}[F_a^{-T} F_p^T F_a^{-1} - I], \]

and the Piola stress tensor is given by:

\[ P = \mu FC_a^{-1} - p \text{Cof}(F) \]

where \( C_a^{-1} := \det(F_a) F_a^{-1} F_a^{-T} \) (see also Refs. \[14\], \[30\]).

Further examining the expression of \( F_a \), we notice that mechanical activation is mainly influenced by intracellular calcium release \[24\], \[26\], \[31\], and in particular, the dynamics of local strain follow closely those of calcium release rather than those from the transmembrane potential, as reported in Ref. \[32\]. Using a physiological ionic model, the aforementioned fact suggests that, ideally the recovery variables \( w \) and the concentration variable \( z \) approximate the spatio-temporal structure of calcium. More physiologically-involved activation models require a dependence of \( \gamma_n \) not only on calcium, but also on local stretch, local stretch rate, sliding velocity of crossbridges, and on other force-length experimental relations \[26\], \[15\], \[33\], but for the sake of simplicity we restrict ourselves to a phenomenological description of local activation in terms of the gating variables.

The scalar fields \( \gamma_l, \gamma_t \) and \( \gamma_n \) can be written as functions of a parameter \( \gamma \):

\[ \gamma_{l,t,n} = \gamma_{l,t,n}(\gamma), \quad (2.4) \]

where \( \gamma_{l,t,n} : \mathbb{R} \to [-\Gamma_{l,t,n}, 0] \) are Lipschitz continuous monotone functions. The values \( \Gamma_{l,t,n} \) should be small enough, in order to ensure that \( \det(F_a) \) stays uniformly far from zero, for \( \gamma \in \mathbb{R} \). The scalar field \( \gamma \) is the solution of the following ODE associated to the solution \( (v_l, v_e, w) \) of the bidomain system \[2,3\]:

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

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

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

Further details can be found in e.g. Refs. \[35\], \[36\].

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 \( F \). Summarizing, the active strain formulation for the electromechanical activity in the heart is written as follows \[30\]:

\[
\begin{align*}
-\nabla \cdot (a(x, \gamma, F, p)) &= g & \text{in } \Omega_R, \\
\text{det}(F) &= 1 & \text{in } \Omega_R \text{ for a.e. } t \in (0, T), \\
\partial_t v + \nabla \cdot (M_e(x, F) \nabla v_e) + I_{\text{ion}} &= I^e_s & \text{in } \Omega_T, \\
\partial_t v - \nabla \cdot (M_e(x, F) \nabla v_l) + I_{\text{ion}} &= I^l_s & \text{in } \Omega_T, \\
v_i - v_e &= v & \text{in } \Omega_T, \\
\partial_t w - R(v, w) &= 0 & \text{in } \Omega_T, \\
\partial_t z - G(v, w, z) &= 0 & \text{in } \Omega_T, \\
\partial_t \gamma - S(\gamma, w) &= 0 & \text{in } \Omega_T,
\end{align*}
\]

(2.5)
where \( Q_T := (0, T) \times \Omega_R \). Here, according to the above discussion, we should take

\[
a(x, \gamma, F, p) := \mu C^{-1}_a(x, \gamma) - p \text{Cof} \left( F \right),
\]

and

\[
M_k(x, F) := (F)^{-1}K_k(x)(F)^{-T}, \quad k \in \{i, e\}
\]

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

2.4. **Linearizing the elasticity equations.** For the sake of simplicity of the mathematical analysis of the problem, the incompressibility condition \( \text{det}(F) = 1 \) and the flux in the equilibrium equation are linearized. To linearize the determinant, we use:

\[
\text{det}(F) = \text{det}(I) + \frac{\partial \text{det}}{\partial F} (I)(F - I) + o(F - I) = 1 + \text{tr}(F - I) + o(F - I).
\]

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

\[
\text{tr}(F - I) \simeq 0,
\]

hence, \( \nabla \cdot \phi = \text{tr}(F) \simeq \text{tr}(I) = n \).

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

\[
\text{Cof}(F) = \text{Cof}(I) + \frac{\partial \text{Cof}}{\partial F} (I)(F - I) + o(F - I) = I + \text{tr}(F - I)I - (F - I)^T + o(F - I).
\]

and we obtain

\[
a(x, \gamma, F, p) := \mu C^{-1}_a(x, \gamma) - p .
\]

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

\[
- \nabla \cdot ((I + \nabla u)\sigma(x, \gamma)) + \nabla p = g,
\]

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

\[
- \nabla \cdot (\nabla u \sigma(x, \gamma)) + \nabla p = f(t, x, \gamma)
\]

where

\[
f(t, x, \gamma) = \nabla \cdot (\sigma(x, \gamma)) + g.
\]

2.5. **The problem to be solved and its weak formulation.** For simplicity of notation, we will use \( \Omega \) and \( \Omega_T \) to denote \( \Omega_R \) and \( Q_T \) respectively in all what follows, unless otherwise specified. Let us consider the following class of problems:

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

\[
\nabla \cdot u = 0 \quad \text{in} \ \Omega, \ \text{for a.e.} \ t \in (0, T),
\]

\[
\partial_t v - \nabla \cdot (M_i(x, \nabla u)\nabla v_i) + I_{ion}(v, w, \gamma, z) = I_s(t, x) \quad \text{in} \ \Omega_T, \quad (2.11)
\]

\[
\partial_t v + \nabla \cdot (M_e(x, \nabla u)\nabla v_e) + I_{ion}(v, w, \gamma, z) = I_{s}(t, x) \quad \text{in} \ \Omega_T, \quad (2.12)
\]

\[
v = v_i - v_e \quad \text{in} \ \Omega_T, \quad (2.13)
\]

\[
\partial_t w = R(v, w, \gamma, z) \quad \text{in} \ \Omega_T, \quad (2.14)
\]

\[
\partial_t z = G(v, w, \gamma, z) \quad \text{in} \ \Omega_T, \quad (2.15)
\]

\[
\partial_t \gamma = S(\gamma, w) \quad \text{in} \ \Omega_T. \quad (2.16)
\]

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

\[
\nabla u \sigma(x, \gamma) n - \alpha u = 0 \quad \text{on} \ \partial \Omega, \ \text{for a.e.} \ t \in (0, T) \quad (2.18)
\]
For simplicity we take \( m = \alpha > 0 \) and (different boundary conditions can be imposed on \( v_{i,c} \); the choice of Neumann conditions \text{[2.19]} \) results in the compatibility constraint \text{[2.31]} below. The initial data are:

\[
v(0, \cdot) = v_0, \quad w(0, \cdot) = w_0, \quad z(0, \cdot) = z_0, \quad \gamma(0, \cdot) = \gamma_0 \quad \text{in} \; \Omega.
\]  

For simplicity we take \( m = 1 \) in the concentration variable \( z \). The following properties of the model \text{[2.10]–[2.17]} and \text{[2.18]–[2.20]} are instrumental for the subsequent analysis:

(A.1) \( (\sigma(x, \gamma))_{x \in \Theta, \gamma, x \in \mathbb{R}} \) is a family of symmetric tensors, uniformly bounded and positive definite:

\[
\exists c > 0 : \quad \forall x \in \Omega, \forall \gamma \in \mathbb{R}, \forall \mathbf{M} \in \mathbb{M}_{3 \times 3}, \quad \frac{1}{c} |\mathbf{M}|^2 \leq (\sigma(x, \gamma) \mathbf{M}) : \mathbf{M} \leq c |\mathbf{M}|^2;
\]

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

\[
\exists c > 0 : \quad \forall x \in \Omega, \forall \mathbf{M} \in \mathbb{M}_{3 \times 3}, \forall \xi \in \mathbb{R}^3, \quad \frac{1}{c} |\xi|^2 \leq (\mathbf{M}_{i,c}(x, \mathbf{M}) \xi) : \xi \leq c |\xi|^2;
\]

(A.4) the maps \( \mathbf{M} \mapsto \mathbf{M}_{i,c}(\cdot, \cdot, \mathbf{M}) \) are uniformly Lipschitz continuous;

(A.5) the function \( S(\gamma, \mathbf{w}) = \beta(\sum_{j=1}^{k} \eta_j w_j - \eta_0 \gamma) \), for positive physiological parameters \( \beta, \eta, j = 0, 1, \ldots, k \);

(A.6) the functions \( \mathbf{R} \), \( \mathbf{G} \) and \( I_{\text{ion}} \) 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 \( \mathbf{R}(v, \mathbf{w}) := (R_1(v, w_1), \ldots, R_k(v, w_k)) \) where \( R_j : \mathbb{R}^2 \rightarrow \mathbb{R} \) are locally Lipschitz continuous functions defined by

\[
R_j(v, w) = \alpha_j(v)(1 - w_j) - \beta_j(v)w_j
\]

where \( \alpha_j \) and \( \beta_j, j = 1, \ldots, k \) are positive rational functions of exponentials in \( v \) such that:

\[
0 < \alpha_j(v), \beta_j(v) \leq C_{\alpha, \beta}(1 + |v|),
\]

\[
\frac{d\alpha_j}{dv} \quad \text{and} \quad \frac{d\beta_j}{dv} \quad \text{are uniformly bounded,}
\]

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

\[
I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{j=1}^{k} I_{\text{ion}}^j(v, w_j) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z)
\]

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

\[
|I_{\text{ion}}^j(v, w_j)| \leq C_{1,j}(1 + |w_j| + |v|),
\]

and \( I_{\text{ion}}^z \) is such that:

\[
I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \leq C_{2,z}(1 + |v| + |w| + |z| + \ln z),
\]

\[
I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3,z}(\sum_{j=1}^{k} (|v| + w_j + w_j \ln z),
\]

\[
0 < \Theta(v) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(v),
\]
where \( \Theta, \bar{\Theta}, L \) belong to \( C^0(\mathbb{R}, \mathbb{R}^+) \) and \( C_{1,j}, \ldots, C_{5,j} \) are positive constants. Finally the function \( G \) is given by:
\[
G(v, w, z) = a_1(a_2 - z) - a_3I_{\text{ion}}^2(v, w, z, \ln z),
\]
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.

(A.7) The following condition holds
\[
\int_{\Omega} I_s^1 = \int_{\Omega} I_s^5 \text{ and } \int_{\Omega} v_e(x, t) \, dx = 0 \text{ for a.e. } t \in (0, T). 
\]

(A.8) The data \( v_0, w_0, \gamma_0, z_0 \) lie in \( H^1(\Omega) \) with \( z_0 \geq c_0 > 0 \) (\( c_0 \) is a positive constant) whereas \( g \in L^2(\Omega_T)^3 \) (recall definition (2.9)), and \( I^e_s \in L^2(\Omega_T) \).

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

**Definition 2.1.** A weak solution of problem \([2.10]--[2.20]\) is \( U = (u, p, v, v_z, v, w, \gamma, z) \) such that:

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

(ii) \( v \in L^2(0, T; H^{1,0}(\Omega)) \) where \( H^{1,0}(\Omega) := \{ v_e \in H^1(\Omega) \mid \int_{\Omega} v_e \, dx = 0 \} \);

(iii) for a.e. \( t \in (0, T) \), for all \( v \in H^1(\Omega)^3 \) there holds:
\[
\int_{\Omega} (\nabla u \sigma(x, \gamma) : \nabla v - p \nabla \cdot v) \, dx = \int_{\Omega} f \cdot v \, dx - \int_{\partial \Omega} \alpha u \cdot v \, ds 
\]
\[
(\text{in the last integral, } u, v \text{ are shortcuts for the traces of } u, v \text{ on } \partial \Omega). 
\]

For all \( q \in L^2(\Omega) \)
\[
\int_{\Omega} q(\nabla \cdot u) \, dx = 0. 
\]

(iii) For a.e. \( t \in (0, T) \), for all \( \xi \in H^1(\Omega), \ \mu \in H^{1,0}(\Omega) \), there holds
\[
\langle \partial_t v, \xi \rangle + \int_{\Omega} (M_i(x, \nabla u) \nabla v_i : \nabla \xi + I_{\text{ion}}(v, w, z) \xi) = \int_{\Omega} I_s^1 \xi, 
\]
\[
\langle \partial_t v, \mu \rangle - \int_{\Omega} (M_i(x, \nabla u) \nabla v_c : \nabla \mu + I_{\text{ion}}(v, w, z) \mu) = \int_{\Omega} I_s^5 \mu, 
\]

with \( v = v_i - v_e \) a.e. in \( \Omega_T \) and \( v(0, \cdot) = v_0 \) a.e. in \( \Omega \).

(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 \( \Omega \).

Our main result in this paper is the following theorem:
Theorem 2.1. Assume that conditions (A.1)–(A.8) hold. If \( v_0 \in L^2(\Omega) \), \( w_0 \in H^1(\Omega)^k \), \( \gamma_0 \), and \( z_0 \in H^1(\Omega) \), with \( z_0 \geq c_0 > 0 \), \( g \in L^2(\Omega_R)^3 \), \( f^e \in L^2(\Omega_T) \) then there exists a weak solution \( U = (u, p, v_i, v, w, \gamma, z) \) to \( (2.18) \)–\( (2.20) \) with the boundary and initial data specified as in \( (3.1) \).

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

We also note that passage to the limit in the pressure term \( p \) is not straightforward because it is not possible to establish an a priori uniform estimate in \( L^2(\Omega_T) \) due to the use of the “artificial compressibility” which utility becomes clearer in the following section.

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 \cite{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.

3.1. Faedo-Galerkin approximations for the regularized problem.

We use classical Hilbert 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 \( \text{span}(\phi_l)_{l \in \mathbb{N}} \) is dense in \( L^2(\Omega)^3 \) and \( H^1(\Omega)^3 \), and \( \text{span}(\omega_l)_{l \in \mathbb{N}} \) is dense in \( L^2(\Omega) \) and \( H^1(\Omega) \) (see for example \cite{37}).

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

\[
\mu_l = \omega_l - \frac{1}{|\Omega|} \int_{\Omega} \omega_l \, dx,
\]

so that \( \int_{\Omega} \mu_l \, dx = 0 \).

We observe that \( \text{span}\{\mu_l\}_{l \in \mathbb{N}} \) 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 \( H_m = \text{span}\{\psi_l, \ldots, \psi_m\} \subset H^1(\Omega)^3 \), \( L_m = \text{span}(\mu_0, \ldots, \mu_m) \subset H^{1,0}(\Omega) \) and \( W_m = \text{span}(\omega_0, \ldots, \omega_m) \subset H^1(\Omega) \).

We are looking for a discrete solution \( u_m = (u_{\varepsilon,m}, p_{\varepsilon,m}, v_m, v_{i,\varepsilon,m}, v_{e,\varepsilon,m}, w_{\varepsilon,m}, z_{\varepsilon,m}, \gamma_{\varepsilon,m}) \) (for fixed \( \varepsilon > 0 \)) of the system \( (3.2) \) below with

\[
\begin{align*}
\mathbf{u}_m &= \sum_{l=0}^{m} u_{l,m} \psi_l, \\
p_m &= \sum_{l=0}^{m} p_{l,m} \omega_l, \\
v_{i,m} &= \sum_{l=0}^{m} v_{i,l,m} \mu_l, \\
v_{e,m} &= \sum_{l=0}^{m} v_{e,l,m} \mu_l, \\
w_{j,m} &= \sum_{l=0}^{m} w_{j,l,m} \omega_l, \quad \forall j = 1, \ldots, k, \\
\gamma_m &= \sum_{l=0}^{m} \gamma_{l,m} \omega_l, \\
z_m &= \sum_{l=0}^{m} z_{l,m} \omega_l.
\end{align*}
\]

Upon discretization, we obtain a system of ODEs coupled to a system of algebraic equations to be solved at every time \( t \). Hence, the existence of the discrete solution is not obvious and only the ODE part of the system satisfies the conditions of Cauchy-Lipschitz’ theorem. So we resort to a time regularization of the Faedo-Galerkin discretization in the spirit of \cite{3}. We obtain the
following regularized system

\[
\begin{align*}
\varepsilon \frac{d}{dt} \int_{\Omega} u_{\varepsilon,m} & \cdot \psi_t + \int_{\Omega} (\nabla u_{\varepsilon,m}) \sigma(x, \gamma_{\varepsilon,m}) : \nabla \psi_t - p_{\varepsilon,m} \nabla \cdot \psi_t \, dx \\
& + \int_{\partial \Omega} \alpha u_{\varepsilon,m} \cdot \psi_t \, ds = \int_{\Omega} f \cdot \psi_t \, dx,
\end{align*}
\]

\[
\varepsilon \frac{d}{dt} \int_{\Omega} p_{\varepsilon,m} \cdot \omega_t + \int_{\Omega} \omega_t \nabla \cdot u_{\varepsilon,m} = 0,
\]

\[
\frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \omega_t + \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_t + \int_{\Omega} (M_i(x, \nabla u_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_t
\]

\[
+ \int_{\Omega} I_{\text{ion}}(v_{\varepsilon,m}, w_{\varepsilon,m}, z_{\varepsilon,m}) \omega_t \, dx = \int_{\Omega} I^i_{\omega} \omega_t \, dx,
\]

\[
\frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \mu_t - \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \mu_t - \int_{\Omega} (M_i(x, \nabla u_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \mu_t
\]

\[
+ I_{\text{ion}}(v_{\varepsilon,m}, w_{\varepsilon,m}, z_{\varepsilon,m}) \mu_t \, dx = \int_{\Omega} I^i_{\mu} \mu_t \, dx,
\]

\[
\frac{d}{dt} \int_{\Omega} w_{j,\varepsilon,m} \omega_t = \int_{\Omega} R_j(v_{\varepsilon,m}, w_{j,\varepsilon,m}) \omega_t,
\]

\[
\frac{d}{dt} \int_{\Omega} z_{\varepsilon,m} \omega_t = \int_{\Omega} G(v_{\varepsilon,m}, w_{\varepsilon,m}, z_{\varepsilon,m}) \omega_t,
\]

\[
\frac{d}{dt} \int_{\Omega} \gamma_{\varepsilon,m} \omega_t = \int_{\Omega} S(\gamma_{\varepsilon,m}, w_{\varepsilon,m}) \omega_t,
\]

for \( l = 0, \ldots, m \). Having no initial conditions on the functions \( u, p, v_i \) and \( v_e \) in the original problem, we need to supplement our system with initial conditions. We define the functions:

\[
v_{i,0} = \frac{v_0}{2} + \frac{1}{|\Omega|} \int_{\Omega} \frac{v_0}{2} \, dx,
\]

\[
v_{e,0} = -\frac{v_0}{2} + \frac{1}{|\Omega|} \int_{\Omega} \frac{v_0}{2} \, dx,
\]

so that \( v_0 = v_{i,0} - v_{e,0} \) and \( \int_{\Omega} v_{e,0} \, dx = 0 \). We further select \( u_0 = 0 \) and an arbitrary \( p_0 \). The initial data of the ODE system are then given by

\[
u_{i,m}(0) = 0, \quad p_{e,m}(0) = \sum_{l=0}^{m} p_{0,l,m} \omega_l, \quad \text{where} \quad p_{0,l,m} = \langle p_0, \omega_l \rangle_{L^2},
\]

\[
v_{i,m}(0) = \sum_{l=0}^{m} v_{i,0,l,m} \omega_l, \quad \text{where} \quad v_{i,0,l,m} = \langle v_{i,0}, \omega_l \rangle_{L^2},
\]

\[
v_{e,m}(0) = \sum_{l=0}^{m} v_{i,0,l,m} \mu_l, \quad \text{where} \quad v_{e,0,l,m} = \langle v_{e,0}, \mu_l \rangle_{L^2},
\]

\[
w_{j,m}(0) = \sum_{l=0}^{m} w_{j,0,l,m} \omega_l, \quad \text{where} \quad w_{j,0,l,m} = \langle w_{j,0}, \omega_l \rangle_{L^2}
\]

\[
z_{m}(0) = \sum_{l=0}^{m} z_{0,l,m} \omega_l, \quad \text{where} \quad z_{0,l,m} = \langle z_0, \omega_l \rangle_{L^2}
\]

\[
\gamma_{m}(0) = \sum_{l=0}^{m} \gamma_{0,l,m} \omega_l, \quad \text{where} \quad \gamma_{0,l,m} = \langle \gamma_0, \omega_l \rangle_{L^2},
\]

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

\[
\left\{ \{ u_{l,i,m} \}_{l=0}^{m}, \{ p_{l,m} \}_{l=0}^{m}, \{ v_{i,l,m} \}_{l=0}^{m}, \{ v_{e,l,m} \}_{l=0}^{m}, \{ w_{l,m} \}_{l=0}^{m}, \{ \gamma_{l,m} \}_{l=0}^{m}, \{ z_{l,m} \}_{l=0}^{m} \right\}.
\]
To be concise, we detail in the following paragraph how the bidomain equations can be treated to obtain the ODE system. We first note that using $v_m = v_{i,m} - v_{e,m}$, we have:

$$\frac{d}{dt} \int_{\Omega} v_{i,m} \omega_l - \frac{d}{dt} \int_{\Omega} v_{e,m} \omega_l + \frac{d}{dt} \int_{\Omega} v_{i,m} \omega_l + \int_{\Omega} (M_{e}(x, \nabla u_{e,m}) \nabla v_{i,m} \cdot \nabla \omega_l)$$

$$+ I_{\text{ion}}(v_{e,m}, w_{e,m}, z_{e,m}) \omega_l) dx = \int_{\Omega} I^I_{\omega_l} dx,$$

$$\frac{d}{dt} \int_{\Omega} v_{i,m} \mu_l - \frac{d}{dt} \int_{\Omega} v_{e,m} \mu_l - \frac{d}{dt} \int_{\Omega} v_{i,m} \mu_l - \int_{\Omega} (M_{e}(x, \nabla u_{e,m}) \nabla v_{e,m} \cdot \nabla \mu_l)$$

$$+ I_{\text{ion}}(v_{e,m}, w_{e,m}, z_{e,m}) \mu_l) dx = \int_{\Omega} I^I_{\mu_l} dx,$$

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

$$(1 + \varepsilon) \sum_{r=0}^{m} \left( \int_{\Omega} \omega_r \omega_l \right) v'_{i,r,m} - \sum_{r=0}^{m} \left( \int_{\Omega} \mu_r \omega_l \right) v'_{e,r,m} + \int_{\Omega} (M_{e}(x, \nabla u_{e,m}) \nabla v_{i,m} \cdot \nabla \omega_l)
$$

$$+ I_{\text{ion}}(v_{e,m}, w_{e,m}, z_{e,m}) \omega_l) dx = \int_{\Omega} I^I_{\omega_l} dx,$$

$$\sum_{r=0}^{m} \left( \int_{\Omega} \omega_r \mu_l \right) v'_{i,r,m} - \sum_{r=0}^{m} \left( \int_{\Omega} \mu_r \mu_l \right) v'_{e,r,m} - \int_{\Omega} (M_{e}(x, \nabla u_{e,m}) \nabla v_{e,m} \cdot \nabla \mu_l)
$$

$$+ I_{\text{ion}}(v_{e,m}, w_{e,m}, z_{e,m}) \mu_l) dx = \int_{\Omega} I^I_{\mu_l} dx,$$

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

$$(1 + \varepsilon) v'_{i,r,m} - \sum_{r=0}^{m} \left( \int_{\Omega} \mu_r \omega_l \right) v'_{e,r,m} = F_i \left( \{u_{i,m} \}_{r=0}^{m}, \{v_{i,r,m} \}_{r=0}^{m}, \{v_{e,r,m} \}_{r=0}^{m}, \{w_{r,m} \}_{r=0}^{m}, \{z_{r,m} \}_{r=0}^{m} \right),$$

$$- \sum_{r=0}^{m} \left( \int_{\Omega} \omega_r \mu_l \right) v'_{i,r,m} + (1 + \varepsilon) v'_{e,i,m} = F_e \left( \{u_{i,m} \}_{r=0}^{m}, \{v_{i,r,m} \}_{r=0}^{m}, \{v_{e,r,m} \}_{r=0}^{m}, \{w_{r,m} \}_{r=0}^{m}, \{z_{r,m} \}_{r=0}^{m} \right),$$

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

$$M \begin{pmatrix} v'_{i,m} \\ v'_{e,m} \end{pmatrix} = b,$$

where

$$M = \begin{pmatrix} (1 + \varepsilon)I_{m+1} & -A \\ -A^T & (1 + \varepsilon)I_{m+1} \end{pmatrix}.$$

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

$$M = \begin{pmatrix} I_{m+1} & -A \\ -A^T & I_{m+1} \end{pmatrix} + \varepsilon \begin{pmatrix} I_{m+1} & 0 \\ 0 & I_{m+1} \end{pmatrix}.$$

It is enough to prove that the matrix $N := \begin{pmatrix} I_{m+1} & -A \\ -A^T & I_{m+1} \end{pmatrix}$ 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

$$\xi^T N \xi = \xi^T_i \xi_i - \xi^T_i A \xi_i + \xi^T_e \xi_e - \xi^T_e A^T \xi_i.$$
So we have
\[
\xi^T N \xi = \sum_{k,l} [\xi_i,k \xi_i,l] \int_{\Omega} \omega_k \omega_l - 2 \xi_i,k a_{kl} \xi_i,l + \xi_i,k \xi_i,l \int_{\Omega} \mu_k \mu_l \]
\[
= \int_{\Omega} \sum_{k,l} [\xi_i,k \xi_i,l \omega_k \omega_l - 2 \xi_i,k \xi_i,l \omega_l \mu_k + \xi_i,k \xi_i,l \mu_k \mu_l] \]
\[
= \int_{\Omega} (\sum_{i} \xi_i,\omega_i)^2 - 2 \sum_{k,l} \xi_i,k \xi_i,l \omega_l \mu_k + (\sum_{i} \xi_i,\mu_i)^2 \]
\[
= \int_{\Omega} \left[ \sum_{i} \xi_i,\omega_i - \sum_{i} \xi_i,\mu_i \right]^2 \geq 0.
\]

Thus the matrix $M$ is positive definite, hence invertible. Consequently, the whole system is well-defined and constitute approximate solutions to the regularized system (3.2). The global existence of the Faedo-Galerkin solutions is a consequence of the $m$–independent a priori estimates bounding $u_{\varepsilon,m}, v_{\varepsilon,m}, v_{\varepsilon,m}, w_{\varepsilon,m}, \gamma_{\varepsilon,m}$ and $\gamma_{\varepsilon,m}$ that are derived in the next section. For more details, consult [3].

3.2. A priori estimates. To prove global existence of the Faedo-Galerkin solutions we derive $m$–independent a priori estimates bounding $u_{\varepsilon,m}, v_{\varepsilon,m}, v_{\varepsilon,m}, u_{\varepsilon,m}, \varepsilon_{\varepsilon,m}, \varepsilon_{\varepsilon,m}, \gamma_{\varepsilon,m}$ and $\gamma_{\varepsilon,m}$ in various Banach spaces. Given some (absolutely continuous) coefficients $a_{l,\varepsilon,m}(t), b_{l,\varepsilon,m}(t), \varepsilon, e, c$ and $d_{l,\varepsilon,m}(t)$ we form the functions $\psi_{m}(t, x) := \sum_{l=1}^{m} a_{l,\varepsilon,m}(t) \psi_{l}(x), \rho_{m}(t, x) := \sum_{l=1}^{m} b_{l,\varepsilon,m}(t) \rho_{l}(x), \xi_{m}(t, x) := \sum_{l=1}^{m} b_{l,\varepsilon,m}(t) \xi_{l}(x), \mu_{m}(t, x) := \sum_{l=1}^{m} b_{l,\varepsilon,m}(t) \mu_{l}(x),$ and $\omega_{m}(t, x) := \sum_{l=1}^{m} d_{l,\varepsilon,m}(t) \omega_{l}(x)$ for $\kappa := \varepsilon, \varepsilon, e, c$. It follows that the Faedo-Galerkin solutions satisfy the following weak formulations for each fixed $t$, which will be the starting point for deriving a series of a priori estimates:

\[
\varepsilon \int_{\Omega} \partial_t u_{\varepsilon,m} \cdot \psi_{m} + \int_{\Omega} \left( (\nabla u_{\varepsilon,m}) \sigma(x, \varepsilon_{m}) + \nabla \psi_{m} - p_{\varepsilon,m} \nabla \cdot \psi_{m} \right) \right) dx
\]
\[
+ \int_{\partial \Omega} \alpha u_{\varepsilon,m} \cdot \psi_{m} ds = \int_{\Omega} f \cdot \psi_{m} dx,
\]
\[
\varepsilon \int_{\Omega} \partial_t p_{\varepsilon,m} \rho_{m} + \int_{\Omega} \rho_{m} \nabla \cdot u_{\varepsilon,m} = 0,
\]
\[
\int_{\Omega} \partial_t v_{\varepsilon,m} \xi_{m} + \varepsilon \int_{\Omega} \partial_t v_{\varepsilon,m} \xi_{m} + \int_{\Omega} \left( \chi_{l}(x, \nabla u_{\varepsilon,m}) \nabla v_{\varepsilon,m} \cdot \nabla \xi_{m} \right) \right) dx = \int_{\Omega} I_{\varepsilon,m} \xi_{m} dx,
\]
\[
\int_{\Omega} \partial_t v_{\varepsilon,m} \mu_{m} - \varepsilon \int_{\Omega} \partial_t v_{\varepsilon,m} \mu_{m} - \int_{\Omega} \left( \chi_{l}(\nabla u_{\varepsilon,m}) \nabla v_{\varepsilon,m} \cdot \nabla \mu_{m} \right) \right) dx = \int_{\Omega} I_{\varepsilon,m} \mu_{m} dx,
\]
\[
\int_{\Omega} \partial_t w_{\varepsilon,m} \omega_{m} = \int_{\Omega} R_{j}(v_{\varepsilon,m}, w_{\varepsilon,m}) \omega_{m},
\]
\[
\int_{\Omega} \partial_t z_{\varepsilon,m} \omega_{m} = \int_{\Omega} G(v_{\varepsilon,m}, w_{\varepsilon,m}, \varepsilon_{m}) \omega_{m},
\]
\[
\int_{\Omega} \partial_t \gamma_{\varepsilon,m} \omega_{m} = \int_{\Omega} S(\gamma_{\varepsilon,m}, w_{\varepsilon,m}) \omega_{m},
\]
\[
(3.6)
\]
We Substitute

We first extend the function following Lemma, we show that the gating variables 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 $\omega_m^w \in H^1(\Omega)$:

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

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

$0 \leq w_j \leq 1$, a.e. in $\Omega_T$. \quad (3.8)

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

$$R_j(v, w_j) = \begin{cases} -\beta_j w_j & \text{if } w_j > 1, \\ \alpha_j(1 - w_j) - \beta_j w_j & \text{if } w_j \leq 1 \end{cases} \quad (3.9)$$

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

$$\frac{d}{dt}|w_j^\ast|^2 \leq 0, \text{ for } j = 1, \ldots, k.$$

Using Gronwall’s inequality, we get $w_j^\ast = 0$ and $w_j \geq 0$, for $j = 1, \ldots, k$. Similarly, substituting $\omega_m^w = (w_j - 1)^+$ in (3.7) and using (3.9), we obtain by using Gronwall’s inequality that $w_j \leq 1$, for a.e. $(t, x) \in \Omega_T$ and for $j = 1, \ldots, k$. \hfill \Box

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

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:

$$\partial_t z = G(v, w, z), \quad (3.10)$$

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

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

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

Proof. For a.e. $x \in \Omega$ fixed, we have $z(0, x) = z_0 > 0$ and the map: $t \mapsto z(t, x)$ is in $C[0, T]$. Assume that at some time $t$, $z(t, x) = 0$ and let $t_1 = \inf\{t \in (0, T) : z(t, x) = 0\}$. Using (2.24) and (2.30), we see that $G(v, w, z) \rightarrow +\infty$ as $t \rightarrow t_1$. 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 $z(t_1, x) > z(t_1 - \delta, x) > 0$ which is a contradiction. Consequently by diagonalisation and compactness of $[0, T]$, $z > 0$. \hfill \Box

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

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

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

$$\int_0^t |\partial_t z|^2 \leq C \left(1 + |z_0 \ln z_0| + |z_0|^2 + \|v\|_{L^2(0,t)}^2\right), \quad (3.13)$$

$$\int_0^t |\ln z|^2 \leq C \left(1 + |z_0 \ln z_0| + |z_0|^2 + \|v\|_{L^2(0,t)}^2\right), \quad (3.14)$$
Proof. In our proof, we follow the idea in [6].

Proof of (3.11):
 Fixing \( x \in \Omega \) and multiplying equation (3.10) by \( z \), we get

\[
z \partial_t z = a_1(a_2 - z)z - a_3 z I_{ion}(v, w, z, \ln z).
\]

Next, we use (2.25) to obtain

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

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 \( \Omega_T \), we find

\[
\frac{1}{2} \frac{d}{dt} |z(t, \cdot)|^2 \leq a_1 (a_2 + |z|) |z| + \frac{kc_1}{e} + c_1 |z||v|.
\]

By Young’s inequality, we have

\[
\frac{1}{2} \frac{d}{dt} |z(t, \cdot)|^2 \leq \frac{k c_1}{e} + a_1 (a_2 + \frac{3}{2} |z(t, \cdot)|^2) + \frac{k c_1}{2} |z(t, \cdot)|^2 + \frac{k c_1}{2} |v(t, \cdot)|^2,
\]

which can be rewritten as

\[
\frac{d}{dt} |z(t, \cdot)|^2 \leq (3a_1 + kc_1) |z(t, \cdot)|^2 + \frac{2kc_1}{e} + 2a_1 a_2^2 + kc_1 |v(t, \cdot)|^2.
\]

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

\[
|z(t, \cdot)|^2 \leq \exp \left( (kc_1 + 3a_1) t \right) \left[ |z_0(\cdot)|^2 + \int_0^t \frac{2kc_1}{e} + 2a_1 a_2^2 + kc_1 |v(s, \cdot)|^2 ds \right] \quad \forall t \in [0, T].
\]

Or equivalently, for positive constants \( c_2, c_3 \) and \( c_4 \),

\[
|z(t, \cdot)|^2 \leq e^{c_2 t} \left[ |z_0(\cdot)|^2 + c_3 t + c_4 \int_0^t |v(s, \cdot)|^2 ds \right] \quad \forall t \in [0, T].
\]

We conclude that there exists a constant \( c_5 > 0 \), dependent on \( T \) such that

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

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

\[
\frac{dz}{dt} = a_1(a_2 - z) - a_3 I_{ion}(v, w, z, \ln z).
\]

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

\[
\frac{dz}{dt} \geq c_6 - c_7 |z| - c_8 (|v| + \ln z),
\]

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

\[
\frac{dz}{dt} \geq c_6 - c_9 (1 + |z_0(\cdot)| + \|v\|_{L^2(0, T)}) - c_8 |v| - c_8 \ln z, \quad (3.15)
\]

for some constant \( c_9 > 0 \). After rearrangement of the inequality, we obtain:

\[
c_8 \ln z \geq c_6 - c_9 (1 + |z_0(\cdot)| + \|v\|_{L^2(0, T)}) - c_8 |v| - \frac{dz}{dt}, \quad (3.16)
\]

Furthermore, since \( \frac{dz}{dt} \) is continuous over \([0, T]\), it is bounded below and there exists a constant \( c_{10} \) such that:

\[
\ln z \geq c_{10} (1 + |z_0(\cdot)| + |v(t, \cdot)| + \|v\|_{L^2(0, T)}) \quad (3.17)
\]

On the other hand, knowing that \( \ln z < z \), one has by (3.11):

\[
\ln z < C (1 + |z_0(\cdot)| + \|v\|_{L^2(0, T)}) \leq C (1 + |z_0(\cdot)| + |v(t, \cdot)| + \|v\|_{L^2(0, T)}).
\]

Estimate (3.12) follows easily from (3.17) and (3.18).
Proof of (3.13):

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

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

Letting

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

and observing that

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

The above equation simplifies to

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

Therefore

$$\int_{0}^{t} \frac{1}{\Theta(s)} \left(\frac{dz}{ds}\right)^2 ds = \int_{0}^{t} \left[ a_1 (a_2 - z) - a_3 I_{\text{ion}}^{z} (v, w, z, 0) \right] \frac{dz}{ds} ds - a_3 (z \ln z - z - z_0 \ln z_0 - z_0).$$

Note that by (2.26), the mean value theorem and Lemma 3.1 there exist $\theta_1, \theta_2 > 0$ such that

$$\theta_2 \leq \Theta(t) \leq \theta_1.$$  

(3.19)

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

$$\int_{0}^{t} \frac{1}{\Theta(s)} \left(\frac{dz}{ds}\right)^2 ds \leq \frac{1}{\theta_2} \int_{0}^{t} \left[ a_1 a_2 + a_1 |z| + a_3 C(1 + |v| + |z|) \right] \left| \frac{dz}{ds} \right| ds + a_3 (1 + z_0 \ln z_0 - z_0).$$

By (3.19), there holds

$$\frac{1}{\theta_1} \int_{0}^{t} \left(\frac{dz}{ds}\right)^2 ds \leq \frac{1}{\theta_2} \int_{0}^{t} \left[ a_1 a_2 + a_1 |z| + a_3 C(1 + |v| + |z|) \right] \left| \frac{dz}{ds} \right| ds + a_3 (1 + z_0 \ln z_0 - z_0).$$

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

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

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

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

Consequently,

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

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

$$\int_{0}^{t} \left(\frac{dz}{ds}\right)^2 ds \leq c_{11} \left( 1 + |z_0 \ln z_0 - z_0| + |z_0| \right)^2 + ||v(x)||_{L^2(0, t)}^2, \forall t \in (0, T),$$

(3.20)

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

4
Lemma 3.5. There exist constants \( C_1, C_2, C_3 > 0 \) independent of \( \varepsilon \) and \( m \) such that

\[
\max_{t \in [0,T]} \left( \left\| v_{\varepsilon,m}(t) \right\|_{L^2(\Omega)} + \sum_{j=1}^{k} \left\| \sqrt{\varepsilon} v_{j,\varepsilon,m}(t) \right\|_{L^2(\Omega)} \right) \leq C_1, \tag{3.23}
\]

\[
\sum_{j=1}^{k} \left\| v_{j,\varepsilon,m} \right\|_{L^2(0,T;H^1(\Omega))} + \left\| v_{\varepsilon,m} \right\|_{L^2(0,T;H^1(\Omega^c))} \leq C_2, \tag{3.24}
\]

\[
\left\| \partial_t (v_{\varepsilon,m} + \varepsilon v_{i,\varepsilon,m}) \right\|_{L^2(0,T;H^1(\Omega^c))} + \left\| \partial_t (v_{\varepsilon,m} - \varepsilon v_{i,\varepsilon,m}) \right\|_{L^2(0,T;H^1(\Omega^c))} \leq C_3. \tag{3.25}
\]

Proof of Lemma 3.5.

We have by (2.16) and (2.30)

\[
I^z_{\text{ion}}(v, w, z, \ln z) = \frac{1}{a_4} \left[ a_1(a_2 - z) - \frac{dz}{dt} \right].
\]

We rewrite it as:

\[
\left( I^z_{\text{ion}}(v, w, z, \ln z) - I^z_{\text{ion}}(v, w, z, 0) \right) \ln z = \frac{1}{a_4} \left[ a_1(a_2 - z) - \frac{dz}{dt} \right] - I^z_{\text{ion}}(v, w, z, 0).
\]

After squaring both sides, we obtain:

\[
\Theta^2(\ln z)^2 \leq \frac{3}{a_3^2} \left( \frac{a_1^2(a_2 - z)^2}{a_3^2} + \frac{1}{a_3^2} \left( \frac{dz}{dt} \right)^2 + I^z_{\text{ion}}(v, w, z, 0)^2 \right).
\]

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

\[
\int_0^t \Theta^2(\ln z)^2 ds \leq 3 \int_0^t \left( \frac{a_1^2(a_2 - z)^2}{a_3^2} + \frac{1}{a_3^2} \left( \frac{dz}{dt} \right)^2 + I^z_{\text{ion}}(v, w, z, 0)^2 \right) ds.
\]

Therefore, by (3.11), (3.20) and (2.4) we find

\[
\int_0^t (\ln z(s))^2 ds \leq c_{12} \left( 1 + |z_0 \ln z_0 - z_0| + |z_0|^2 + \|v\|_{L^2(0,T)}^2 \right),
\]

for some constant \( c_{12} > 0 \).

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

\[
\| I_{\text{ion}}(v, w, z, \ln(z)) \|_{L^2(\Omega)} \leq C(1 + \|v\|_{L^2(\Omega^c)}^2).
\]

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

\[
|I_{\text{ion}}(v, w, z, \ln(z))|^2 \leq C \left( \sum_{j=1}^{k} (1 + |v|^2) + |v|^2 + |z|^2 + |\ln z|^2 \right) \quad (C \text{ is a generic constant}).
\]

Using (3.11) and (3.12), one obtains

\[
|I_{\text{ion}}(v, w, z, \ln(z))|^2 \leq C(1 + |z_0|^2 + |v|^2 + \|v\|_{L^2(0,T)}^2) \tag{3.22}
\]

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

Lemma 3.5. There exist constants \( C_1, C_2, C_3 > 0 \) independent of \( \varepsilon \) and \( m \) such that
1 Proof.
Proofs of \(3.23\) and \(3.24\):
First, we make use of the relation \(v_{e,m} = v_{i,e,m} - v_{e,e,m}\). We take \(\xi_m := v_{i,e,m}\) and \(\mu_m := -v_{e,e,m}\) as test functions in \(3.6\) to get

\[
\int_{\Omega} v_{i,e,m} \partial_t v_{i,e,m} + \varepsilon \int_{\Omega} v_{i,e,m} \partial_t v_{i,e,m} + \int_{\Omega} \left( M_i(x, \nabla u_{e,m}) \nabla v_{i,e,m} \cdot \nabla v_{i,e,m} + I_{i\text{on}}(v_{e,m}, \mathbf{w}_{e,m}, \mathbf{z}_{e,m}) v_{i,e,m} \right) dx = \int_{\Omega} I^+_s v_{i,e,m} dx, \tag{3.26}
\]

\[
- \int_{\Omega} v_{e,e,m} \partial_t v_{e,e,m} + \varepsilon \int_{\Omega} v_{e,e,m} \partial_t v_{e,e,m} + \int_{\Omega} \left( M_s(x, \nabla u_{e,m}) \nabla v_{e,e,m} \cdot \nabla v_{e,e,m} - I_{i\text{on}}(v_{e,m}, \mathbf{w}_{e,m}, \mathbf{z}_{e,m}) v_{e,e,m} \right) dx = - \int_{\Omega} I^+_s v_{e,e,m} dx. \tag{3.27}
\]

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

\[
\int_{\Omega} \left( I_{i\text{on}}(v_{e,m}, \mathbf{w}_{e,m}, \mathbf{z}_{e,m}) v_{e,m} + \sum_{j=i,e} M_j(x, \nabla u_{e,m}) \nabla v_{j,e,m} \cdot \nabla v_{j,e,m} \right) + \frac{1}{2} \int_{\Omega} |\partial_t v_{e,m}|^2 + \frac{1}{2} \sum_{k=1,e} \int_{\Omega} |v_{k,e,m}(s, \cdot)|^2 = \int_{\Omega} (I^+_s v_{i,e,m} - I^+_s v_{e,e,m}). \tag{3.28}
\]

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

\[
\int_{0}^{s} \int_{\Omega} \left( I_{i\text{on}}(v_{e,m}, \mathbf{w}_{e,m}, \mathbf{z}_{e,m}) v_{e,m} + \sum_{j=i,e} M_j(x, \nabla u_{e,m}) \nabla v_{j,e,m} \cdot \nabla v_{j,e,m} \right)
\]

\[
+ \frac{1}{2} \int_{\Omega} |\partial_t v_{e,m}(s, \cdot)|^2 + \frac{1}{2} \sum_{k=1,e} \int_{\Omega} |v_{k,e,m}(s, \cdot)|^2 dx = \int_{\Omega} (I^+_s v_{i,e,m} - I^+_s v_{e,e,m}). \tag{3.29}
\]

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

\[
\frac{1}{c} \sum_{j=i,e} \|\nabla v_{j,e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}(s)\|^2_{L^2(\Omega)} + \frac{1}{2} \sum_{j=i,e} \|\nabla v_{j,e,m}\|^2_{L^2(\Omega)} \leq \left( \varepsilon + \frac{1}{2} \right) \|v_{0,e,m}\|^2_{L^2(\Omega)} + \|I^+_s\|_{L^2(\Omega)} \|v_{e,m}\|_{L^2(\Omega)} + \sum_{j=i,e} \|I^+_s\|_{L^2(\Omega)} \|v_{e,m}\|_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}\|^2_{L^2(\Omega)}
\]

\[
+ \frac{1}{2} \|I_{i\text{on}}(v_{e,m}, \mathbf{w}_{e,m}, \mathbf{z}_{e,m})\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}\|^2_{L^2(\Omega)} \leq \left( \varepsilon + \frac{1}{2} \right) \|v_{0,e,m}\|^2_{L^2(\Omega)} + \|I^+_s\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}\|^2_{L^2(\Omega)} + \sum_{j=i,e} \|I^+_s\|^2_{L^2(\Omega)} + \frac{1}{2} \|\nabla v_{e,m}\|^2_{L^2(\Omega)}
\]

\[
+ \frac{c}{2} \|1 + \|v_{e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|\nabla v_{e,m}\|^2_{L^2(\Omega)}
\]

\[
\leq \left( \varepsilon + \frac{1}{2} \right) \|v_{0,e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}(s)\|^2_{L^2(\Omega)} + \frac{1}{2} \|v_{e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|\nabla v_{e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|\nabla v_{e,m}\|^2_{L^2(\Omega)} + \frac{c}{2} \|1 + \|v_{e,m}\|^2_{L^2(\Omega)} + \frac{1}{2} \|\nabla v_{e,m}\|^2_{L^2(\Omega)}
\]

\[
+ \left( \frac{C}{2} + 1 \right) \|v_{e,m}\|^2_{L^2(\Omega)} + \frac{C}{2}.
\]
where $C > 0$ is the constant of estimate (3.21). Or equivalently:

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

(3.30)

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

$$
\|v_{e,m}(t)\|_{L^2(\Omega)}^2 \leq c_{15}\int_0^t \|v_{e,m}(t)\|_{L^2(\Omega)}^2 dt \leq c_{16},
$$

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

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

Hence, one obtains

$$
\operatorname{max}_{\epsilon \in [0, T]} \|v_{e,m}(t)\|_{L^2(\Omega)}^2 \leq c_{17},
$$

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

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

(3.31)

for some constants $c_{18}, c_{19} > 0$. The last inequality implies the bound on $v_{i,e,m}$, $v_{e,e,m}$ and $v_{e,m}$ in $L^2(0, T; H^1(\Omega))$ (recall that $v_{e,m} = v_{i,e,m} - v_{e,e,m}$). The proof of estimate (3.24) is thus achieved.

Proof of (3.25):

In order to prove (3.25), we introduce the sequences $U_{i,e,m} = v_{e,m} + \epsilon v_{i,e,m}$ and $U_{e,e,m} = v_{e,m} - \epsilon v_{e,e,m}$. Indeed, $\partial_t U_{i,e,m}$ and $\partial_t U_{e,e,m}$ are bounded (independent of $\epsilon$) 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)

$$
\int_0^T \left| \langle \partial_t U_{i,e,m}, \varphi \rangle_{H^1(\Omega)'}, H^1(\Omega) \right| dt = \int_0^T \left| \langle \partial_t U_{i,e,m}, \varphi \rangle_{L^2(\Omega)} \right| dt
$$

$$
\quad = \int_0^T \left| -\langle M_i(x, \nabla u_{e,m}) \nabla v_{i,e,m}, \nabla \varphi \rangle_{L^2(\Omega)} + \langle -I_{ion} + I_s, \varphi \rangle_{L^2(\Omega)} \right| dt
$$

$$
\leq \int_0^T \left( \|M_i(x, \nabla u_{e,m}) \|_{L^2(\Omega)} \|\nabla v_{i,e,m}\|_{L^2(\Omega)} \|\nabla \varphi\|_{L^2(\Omega)} + \| -I_{ion} + I_s \|_{L^2(\Omega)} \|\varphi\|_{L^2(\Omega)} \right) dt
$$

$$
\leq c_{20} \left( \|\nabla v_{i,e,m}\|_{L^2(\Omega)} + \|I_{ion}\|_{L^2(\Omega)} + \|I_s\|_{L^2(\Omega)} \right) \|\varphi\|_{L^2(\Omega)}
$$

(3.32)

for some constants $c_{20}, c_{21} > 0$. This implies that $\partial_t U_{i,e,m}$ is uniformly bounded in $L^2(0, T; (H^1(\Omega))')$. The bound of $\partial_t U_{e,e,m}$ in $L^2(0, T; (H^1(\Omega))')$ follows by a similar argument.

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

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

$$
\|w_{e,m}\|_{L^2(\Omega; T; H^1(\Omega)^*)} + \|z_{e,m}\|_{L^2(\Omega; T; H^1(\Omega))} + \|\gamma_{e,m}\|_{L^2(\Omega; T; H^1(\Omega))} \leq C_4,
$$

(3.32)

$$
\|\partial_t w_{e,m}\|_{L^2(\Omega; T; H^1(\Omega)^*)} + \|\partial_t z_{e,m}\|_{L^2(\Omega; T; H^1(\Omega))} + \|\partial_t \gamma_{e,m}\|_{L^2(\Omega; T; H^1(\Omega))} \leq C_5.
$$

(3.33)
Proof. 
Proof of (3.32):
We turn now to the gating variables \(w_{j,z,m}\) (recall that \(0 \leq w_{j,z,m} \leq 1\)). Observe that by differentiation of equation (2.15) with respect to \(z\) and by the chain rule, one has

\[
\partial_t \nabla w_{j,z,m} = \frac{d\alpha_j}{dv} \nabla v, m (1 - w_{j,z,m}) - (\alpha_j + \beta_j) \nabla w_{j,z,m} - \frac{d\beta_j}{dv} \nabla v, m w_{j,z,m}.
\]

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

\[
\frac{1}{2} \partial_t |\nabla w_{j,z,m}|^2 \leq \frac{d\alpha_j}{dv} \nabla v, m \nabla w_{j,z,m} + \frac{d\beta_j}{dv} \nabla v, m \nabla w_{j,z,m} \leq \frac{d\alpha_j}{dv} |\nabla v, m|^2 + \frac{d\beta_j}{dv} (v, m)^2 + |\nabla w_{j,z,m}|^2,
\]

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

\[
\| \nabla w_{j,z,m}(t) \|_{L^2(\Omega)} \leq C(T, \Omega, \| \nabla w_{j,0} \|_{L^2(\Omega)}),
\]

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

\[
\int_{\Omega} |z_{e,m}(x,t)|^2 \leq c_{22} \left(1 + \|z_0\|_{L^2(\Omega)} + \|v, m\|^2_{L^2(\Omega_T)}\right), \quad \forall t \in [0, T].
\]

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

\[
\partial_t \nabla z_{e,m} = -a_1 \nabla z_{e,m} - a_3 \left(\frac{\partial I_{ion}^z}{\partial v} \nabla v, m + \sum_{j=1}^k \frac{\partial I_{ion}^z}{\partial v_{1,j}} \nabla w_{1,j,m} + \frac{\partial I_{ion}^z}{\partial v_{ion}} \nabla w_{ion,m} + \frac{\partial I_{ion}^z}{\partial \zeta} \frac{\nabla z_{e,m}}{\nabla z_{ion,m}} \right).
\]

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

\[
\frac{1}{2} \partial_t |\nabla z_{e,m}|^2 = -a_1 |\nabla z_{e,m}|^2 - a_3 \left(\frac{\partial I_{ion}^z}{\partial v} \nabla v, m \cdot \nabla z_{e,m} + \sum_{j=1}^k \frac{\partial I_{ion}^z}{\partial v_{1,j}} \nabla w_{1,j,m} \cdot \nabla z_{e,m} \right)

\leq -a_3 \left(\frac{\partial I_{ion}^z}{\partial v} \nabla v, m \cdot \nabla z_{e,m} + \sum_{j=1}^k \frac{\partial I_{ion}^z}{\partial v_{1,j}} \nabla w_{1,j,m} \cdot \nabla z_{e,m} \right)

\leq a_3 \left(\frac{\partial I_{ion}^z}{\partial v} \nabla v, m \cdot \nabla z_{e,m} + \sum_{j=1}^k \frac{\partial I_{ion}^z}{\partial v_{1,j}} \nabla w_{1,j,m} \cdot \nabla z_{e,m} \right)

\leq a_3 \left(\frac{\partial I_{ion}^z}{\partial v} \nabla v, m \right)^2 + a_3 \left(\frac{\partial I_{ion}^z}{\partial v_{1,j}} \nabla w_{1,j,m} \right)^2 + \frac{k a_3}{2} |\nabla z_{e,m}|^2.
\]

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

\[
\partial_t |\nabla z_{e,m}|^2 \leq c_{24} \left(1 + |\nabla z_{e,m}|^2 + |\nabla v, m|^2 + |v, m|^2 + |\ln z_{e,m}|^2 + \sum_{j=1}^k |\nabla w_{1,j,m}|^2 \right),
\]

for some constant \(c_{24} > 0\). Using Gronwall’s inequality, we get

\[
|\nabla z_{e,m}(t)|^2 \leq e^{c_{24} t} \left(|\nabla z_0|^2 + c_{24} \int_0^t \left(|\nabla v, m|^2 + |v, m|^2 + |\ln z_{e,m}|^2 + \sum_{j=1}^k |\nabla w_{1,j,m}|^2 + 1\right) ds\right).
\]
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 of $w_{j,\varepsilon,m}$ in $L^2(H^1)$ for $j = 1, \ldots, k$.

Now, we substitute $\omega_{\varepsilon,m}^T := \gamma_{\varepsilon,m}$ into the equation satisfied by $\gamma$ 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))

$$
\frac{1}{2} \| \gamma_{\varepsilon,m}(s) \|^2_{L^2(\Omega)} + \beta \eta_0 \int_0^s \| \gamma_{\varepsilon,m}(t) \|^2_{L^2(\Omega)} \, dt 
= \frac{1}{2} \| \gamma_{\varepsilon,m}(0) \|^2_{L^2(\Omega)} + \beta \sum_{j=1}^k \eta_j \int_0^s \int_{\Omega} \gamma_{\varepsilon,m} w_{j,\varepsilon,m} \, dx \, dt 
\leq \frac{1}{2} \| \gamma_{\varepsilon,m}(0) \|^2_{L^2(\Omega)} + \frac{k \beta \eta_0}{2} \int_0^s \| \gamma_{\varepsilon,m}(t) \|^2_{L^2(\Omega)} \, dt + \beta \eta \sum_{j=1}^k \int_0^s \| w_{j,\varepsilon,m}(t) \|^2_{L^2(\Omega)} \, dt.
$$

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

$$
\| \gamma_{\varepsilon,m}(s) \|^2_{L^2(\Omega)} \leq (k \beta \eta - 2 \beta \eta_0) \int_0^s \| \gamma_{\varepsilon,m}(t) \|^2_{L^2(\Omega)} \, dt + \| \gamma_{\varepsilon,m}(0) \|^2_{L^2(\Omega)}
+ \beta \eta \sum_{j=1}^k \int_0^s \| w_{j,\varepsilon,m} \|^2_{L^2(\Omega)} \, dt 
\leq c_25 \int_0^s \| \gamma_{\varepsilon,m}(t) \|^2_{L^2(\Omega)} \, dt + \| \gamma(0) \|^2_{L^2(\Omega)} + \beta \eta k c_26,
$$

where $c_25 = -2 \beta \eta_0 + k \beta \eta$ and $c_26 > 0$. Let $\tilde{C} = \| \gamma(0) \|^2_{L^2(\Omega)} + \beta \eta k c_26$, by Gronwall’s lemma, we obtain

$$
\| \gamma_{\varepsilon,m}(t) \|^2_{L^2(\Omega)} \leq \tilde{C}(1 + c_25 t e^{c_25 t}) < c_27,
$$

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 $\mathbf{x}$ and multiplying by $\nabla \gamma_{\varepsilon,m}$, we get

$$
\frac{1}{2} \partial_t |\nabla \gamma_{\varepsilon,m}|^2 \leq \beta \sum_{j=1}^k \eta_j |\nabla \gamma_{\varepsilon,m} \cdot \nabla w_{j,\varepsilon,m}| + \beta \eta |\nabla \gamma_{\varepsilon,m}|^2 
\leq \left( \frac{3 \beta \eta}{2} + \beta \eta_0 \right) |\nabla \gamma_{\varepsilon,m}|^2 + \frac{\beta \eta}{2} |\nabla w_{\varepsilon,m}|^2.
$$

An application of Gronwall’s inequality, we deduce

$$
|\nabla \gamma_{\varepsilon,m}|^2 \leq e^{(3 \beta \eta + 2 \beta \eta_0) t} |\nabla \gamma(0)|^2 + \beta \eta \int_0^t |\nabla w_{\varepsilon,m}|^2 \, ds.
$$

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

**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

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

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

$$
\| \partial_t w_{j,\varepsilon,m} \|^2_{L^2(\Omega_T)} \leq c_{28}(T).
$$
Now the $L^2(\Omega_T)$ uniform estimate on $\partial_t z_{\epsilon, m}$ 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

$$|\partial_t z_{\epsilon, m}|^2 \leq 4a_1^2(a_2^2 + z_{\epsilon, m}^2) + 2a_3^2(f_{ion})^2$$

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

$$|\partial_t z_{\epsilon, m}|^2 \leq C \left(1 + |z_{\epsilon, m}|^2 + |v_{\epsilon, m}|^2 + \|z_{\epsilon, m}\|^2\right).$$

Integrating the above inequality over $\Omega_T$ and exploiting the estimates of Lemma 3.3 along with estimate (3.23), we obtain (3.33) for $T$. Integrating the above inequality over $\Omega$ and let $v \in (H^1(\Omega))^3$ and a subsequence $v_{n_k}$ in $(H^1(\Omega))^3$ such that

$$v_{n_k} \rightarrow v \quad \text{in} \quad (L^2(\Omega))^3$$

Next, we define the continuous bilinear form

$$a(u, v) = \int \nabla u \cdot \nabla v \, dx + \int \alpha \cdot u \cdot v \, ds.$$
and
\[ \nabla v_{n_k} \to \nabla v \text{ in } D'(\Omega). \]
Now using (3.36), we deduce that \( \nabla v = 0 \), hence \( v = C \), since \( \Omega \) is connected.
Also, using (3.36) and the convergence of \( v_{n_k} \) to \( C \) in \( (L^2(\Omega))^3 \), we obtain
\[ v_{n_k} \to C \text{ in } (H^1(\Omega))^3 \]
which implies by the continuity of the trace map \( \gamma_0 \) that
\[ \gamma_0 v_{n_k} \to C \text{ in } (L^2(\partial \Omega))^3. \]
On the other hand, by (3.37), we have \( v_{n_k} \to 0 \) in \( (L^2(\partial \Omega))^3 \). So \( C = 0 \), hence we obtain a contradiction since \( \|v_{n_k}\|_{(H^1(\Omega))^3} = 1 \).

By the coercivity of the bilinear form \( a \) and Young's inequality, we have
\[ \frac{1}{2} \frac{d}{dt} \left( \|\sqrt{\varepsilon} u_{\varepsilon,m}\|^2_{L^2(\Omega)} + \|\sqrt{\varepsilon} \rho_{\varepsilon,m}\|^2_{L^2(\Omega)} \right) + \frac{c}{2} \|u_{\varepsilon,m}\|^2_{H^1(\Omega)} \leq \frac{1}{2c_0} \|f\|^2_{L^2(\Omega)}. \]
Integrating (3.38) over \((0, t)\) with \(0 < t \leq T\), noting that \( u_{\varepsilon,m}(0) = 0\) and \( \|\rho_{\varepsilon,m}\|_{L^2(\Omega)} \leq \|\rho_0\|_{L^2(\Omega)}\), we obtain
\[ \|\sqrt{\varepsilon} u_{\varepsilon,m}(t)\|^2_{L^2(\Omega)} + \|\sqrt{\varepsilon} \rho_{\varepsilon,m}(t)\|^2_{L^2(\Omega)} \leq c_{28} \left( \|f\|^2_{L^2(\Omega)} + \varepsilon \|\rho_0\|^2_{L^2(\Omega)} \right). \]
Hence,
\[ \max_{t \in [0, T]} \left( \|\sqrt{\varepsilon} u_{\varepsilon,m}\|^2_{L^2(\Omega)} + \|\sqrt{\varepsilon} \rho_{\varepsilon,m}\|^2_{L^2(\Omega)} \right) \leq c_{29}. \]
We also have upon integration of (3.38)
\[ c \int_0^T \|u_{\varepsilon,m}(t)\|^2_{H^1(\Omega)} \leq c_{30}(T) \left( \|f\|^2_{L^2(\Omega)} + \varepsilon \|\rho_0\|^2_{L^2(\Omega)} \right). \]
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
\[ \int_0^T \left| \langle \varepsilon \partial_t \rho_{\varepsilon,m}, \psi \rangle_{(H^1)'(\Omega)} \right|^2 dt = \int_0^T |(\partial_t \rho_{\varepsilon,m}, \psi)_{L^2}|^2 dt \]
\[ = \int_0^T |(\psi, \nabla \cdot u_{\varepsilon,m})_{L^2}|^2 dt \]
\[ \leq \int_0^T \|\psi\|^2_{L^2} \|\nabla \cdot u_{\varepsilon,m}\|^2_{L^2} dt \]
\[ \leq \|u_{\varepsilon,m}\|^2_{L^2(0, T; H^1(\Omega))} \|\psi\|^2_{L^2(0, T; H^1(\Omega))} \]
\[ \leq C_6 \|\psi\|^2_{L^2(0, T; H^1(\Omega))}. \]
Similarly, we get
\[ \int_0^T \left| \langle \varepsilon \partial_t u_{\varepsilon,m}, \psi \rangle_{(H^1)'(\Omega)} \right|^2 dt \leq C'_6 \|\psi\|^2_{L^2(0, T; H^1(\Omega))}, \]
for some constant \( C'_6 > 0 \). Therefore, estimate (3.35) follows directly.

Remark 3.1. We note that one can exploit the structure of the equations to obtain upper bounds 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 functions in \( H_0^1(0, T) \) along with the Ladyzhenskaya-Babuška-Brezzi condition, we can bound \( p_{\varepsilon,m} \)
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 solutions (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 $\varepsilon > 0$.

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

In view of Lemma 3.5, we can construct subsequences of $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $w_{\varepsilon,m}$, $\gamma_{\varepsilon,m}$, $z_{\varepsilon,m}$, $u_{\varepsilon,m}$, $p_{\varepsilon,m}$ which we do not bother to relabel, such that:

- $v_{\varepsilon,m} \to v_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$,
- $w_{\varepsilon,m} \to w_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\partial_tw_{\varepsilon,m} \to \partial_tw_{\varepsilon}$ weakly in $(L^2(\Omega_T))^k$,
- $\gamma_{\varepsilon,m} \to \gamma_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\partial_t\gamma_{\varepsilon,m} \to \partial_t\gamma_{\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $z_{\varepsilon,m} \to z_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\partial_tz_{\varepsilon,m} \to \partial_tz_{\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $v_{i,\varepsilon,m} \to v_{i,\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\nabla v_{i,\varepsilon,m} \to \nabla v_{i,\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $v_{e,\varepsilon,m} \to v_{e,\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\nabla v_{e,\varepsilon,m} \to \nabla v_{e,\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $u_{\varepsilon,m} \to u_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega)\times H^1(\Omega))$ and $\nabla u_{\varepsilon,m} \to \nabla u_{\varepsilon}$ weakly in $L^2(\Omega_T)^3 \times 3$,
- and $p_{\varepsilon,m} \to p_{\varepsilon}$ weak star in $L^\infty(0,T;L^2(\Omega))$ and weakly in $L^2(\Omega_T)$.

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

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

Moreover, knowing that $\partial_tU_{i,\varepsilon,m}$ and $\partial_tU_{e,\varepsilon,m}$ 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 $\Omega_T$,
- $U_{e,\varepsilon,m} \to U_{e,\varepsilon} = v_{\varepsilon} - \varepsilon v_{e,\varepsilon}$ in $L^2(\Omega_T)$ and a.e. in $\Omega_T$.

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 $\Omega_T$. Hence, $v_{\varepsilon,m} \to v_{\varepsilon}$ in $L^2(\Omega_T)$ and a.e. in $\Omega_T$.

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

- $w_{\varepsilon,m} \to w_{\varepsilon}$ strongly in $L^2(\Omega_T)^k$ and a.e. in $\Omega_T$,
- $\gamma_{\varepsilon,m} \to \gamma_{\varepsilon}$ strongly in $L^2(\Omega_T)$ and a.e. in $\Omega_T$,
- $z_{\varepsilon,m} \to z_{\varepsilon}$ strongly in $L^2(\Omega_T)$ and a.e. in $\Omega_T$,

where $w_{\varepsilon} \in L^2(0,T;H^1(\Omega)^\times)$, $v_{\varepsilon} \in L^\infty(0,T;L^2(\Omega) \cap L^2(0,T;H^1(\Omega)))$, $w_{\varepsilon,m} \in L^\infty(\Omega_T)^k \cap L^2(0,T;H^1(\Omega)^k)$, $\gamma_{\varepsilon,m} \in L^2(0,T;H^1(\Omega))$, $z_{\varepsilon,m} \in L^2(0,T;H^1(\Omega))$, and $p_{\varepsilon,m}$, in $L^\infty(0,T;L^2(\Omega))$. For $l \geq 1$ fixed, $j = 1, \cdots, k$ and $\phi \in D(0,T)$, naturally have

$$\varepsilon \int_0^T \int_\Omega \partial_t w_{\varepsilon,m} \psi_j \phi = -\varepsilon \int_0^T \int_\Omega u_{\varepsilon,m} \psi_j \phi' - \varepsilon \int_0^T \int_\Omega u_{\varepsilon} \psi_j \phi',$$

$$\varepsilon \int_0^T \int_\Omega \partial_t p_{\varepsilon,m} \psi_j \phi = -\varepsilon \int_0^T \int_\Omega p_{\varepsilon,m} \psi_j \omega_t' - \varepsilon \int_0^T \int_\Omega p_{\varepsilon} \omega_t \phi'. $$

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

$$\varepsilon \int_\Omega \int_0^T \partial_t w_{\varepsilon,m} \psi_j \to \varepsilon \int_\Omega \int_0^T \partial_t w_{\varepsilon} \psi_j \text{ and } \varepsilon \int_\Omega \int_0^T \partial_t p_{\varepsilon,m} \omega_l \to \varepsilon \int_\Omega \int_0^T \partial_t p_{\varepsilon} \omega_l. $$

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

We have $w_{\varepsilon,m} \to w_{\varepsilon}$ and $\gamma_{\varepsilon,m} \to \gamma_{\varepsilon}$ a.e. in $\Omega_T$ and $S$ is continuous, so that $S(\gamma_{\varepsilon,m}, w_{\varepsilon,m}) \to S(\gamma_{\varepsilon}, w_{\varepsilon})$ a.e. in $\Omega_T$; and $S(\gamma_{\varepsilon,m}, w_{\varepsilon,m}) \to S(\gamma_{\varepsilon}, w_{\varepsilon})$ 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 $\textbf{R}(v_{\varepsilon,m},w_{\varepsilon,m})$ 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 $\textbf{R}(v_{\varepsilon,m},w_{\varepsilon,m}) \to \textbf{R}(v_{\varepsilon},w_{\varepsilon})$ in $L^2(\Omega_T)^k$.

Similarly, by continuity of $G(v_{\varepsilon,m},w_{\varepsilon,m},z_{\varepsilon,m})$ and its boundedness in $L^2(\Omega_T)$ (as a result of (3.14), and (3.23)), we obtain the weak convergence $G(v_{\varepsilon,m},w_{\varepsilon,m},z_{\varepsilon,m}) \to G(v_{\varepsilon},w_{\varepsilon},z_{\varepsilon})$ in $L^2(\Omega_T)$.
The strong $L^2(\Omega_T)$ and a.e. $\Omega_T$ convergence of $\gamma_{\varepsilon,m}$ implies the strong and a.e. convergence of the uniformly bounded family of tensors $\sigma(x, \gamma_{\varepsilon,m})$, due to assumptions (A.1) and (A.2).

With this information, we can write for all $\varphi \in \mathcal{D}(0,T)$:

$$
\int_0^T \langle \nabla u_{\varepsilon,m}(x, \gamma_{\varepsilon,m}), \nabla \psi_l \rangle_{L^2(\Omega), L^2(\Omega)} \varphi \; dt = \int_0^T \langle \nabla u_{\varepsilon,m}(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon}), \nabla \psi_l \rangle \varphi \; dt + \int_0^T \langle \nabla u_{\varepsilon,m}(x, \gamma_{\varepsilon}), \nabla \psi_l \rangle \varphi \; dt
$$

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

$$
\int_0^T \langle \nabla u_{\varepsilon,m}(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon}), \nabla \psi_l \rangle \varphi \; dt 
\leq \int_0^T \| \nabla u_{\varepsilon,m} \|_{L^2(\Omega)} \| (\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})) \nabla \psi_l \|_{L^2(\Omega)} \| \varphi \| \; dt 
\leq C \int_0^T \| (\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})) \nabla \psi_l \|_{L^2(\Omega)} \| \varphi \| \; dt.
$$

Knowing that $(\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})) \nabla \psi_l \to 0$ a.e. in $\Omega$ and a.e. in $(0,T)$ and that $||(\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})) \nabla \psi_l||_{L^2(\Omega)}$ is (due to assumption (A.1)) bounded by a constant multiple of $||\nabla \psi_l||_{L^2(\Omega)}$ for a.e. $t \in (0,T)$, we can apply Lebesgue’s dominated convergence theorem to obtain $||\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon}) ||_{L^2(\Omega)} \to 0$ 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 $\Omega_T$. Furthermore, by assumption (A.8) and estimate (3.32) we get:

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

In order to pass to the limit in the electrical part of the system, the strong $L^2$ convergence of the gradients $\nabla u_{\varepsilon,m}$ is needed. Indeed, since the limit $u$ solves the limit equation of (3.2), using the Minty-Browder trick (see, e.g. [38, 37, 39]), we are able to assert that $\nabla u_{\varepsilon,m} \to \nabla u$, 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

$$\frac{1}{\varepsilon} \left\| u_{\varepsilon,m} - u_{\varepsilon} \right\|_{L^2(0,T; H^1(\Omega)^3)}^2 \leq \int_0^T a(u_{\varepsilon,m} - u_{\varepsilon}, u_{\varepsilon,m} - u_{\varepsilon}) \, dt$$

$$= - \int_0^T \langle \partial_t u_{\varepsilon,m} - u_{\varepsilon}, u_{\varepsilon,m} - u_{\varepsilon} \rangle \, dt + \varepsilon \| p_{\varepsilon,m}(T) - p_0 \|^2_{L^2(\Omega_T)}$$

$$- \int_{\Omega_T} \nabla u_{\varepsilon} [\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})] : \nabla(u_{\varepsilon,m} - u_{\varepsilon}) \, dx \, dt$$

$$- \int_{\Omega_T} [f(x, \gamma_{\varepsilon,m}) - f(x, \gamma_{\varepsilon})] \cdot (u_{\varepsilon,m} - u_{\varepsilon}) \, dx \, dt$$

$$\leq - \int_0^T \langle \partial_t u_{\varepsilon,m} - u_{\varepsilon}, u_{\varepsilon,m} - u_{\varepsilon} \rangle \, dt + \varepsilon \| p_{\varepsilon,m}(0) - p_0 \|^2_{L^2(\Omega_T)}$$

$$- \int_{\Omega_T} \nabla u_{\varepsilon} [\sigma(x, \gamma_{\varepsilon,m}) - \sigma(x, \gamma_{\varepsilon})] : \nabla(u_{\varepsilon,m} - u_{\varepsilon}) \, dx \, dt$$

$$- \int_{\Omega_T} [f(x, \gamma_{\varepsilon,m}) - f(x, \gamma_{\varepsilon})] \cdot (u_{\varepsilon,m} - u_{\varepsilon}) \, dx \, dt.$$ 

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, $\nabla u_{\varepsilon,m} \to \nabla u_{\varepsilon}$ strongly in $L^2(\Omega_T)^3$. 

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

$$\int_0^T \int_{\Omega} M_k(x, \nabla u_{\varepsilon,m}) \nabla v_k, \varepsilon_m \cdot \nabla \phi(t) \to \int_0^T \int_{\Omega} M_k(x, \nabla u_{\varepsilon}) \nabla v_k, \varepsilon \cdot \nabla \phi(t).$$

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

$$\int_0^T \int_{\Omega} I_{\text{ion}}(v_{\varepsilon,m}, u_{\varepsilon,m}, z_{\varepsilon,m}) \omega(t) \to \int_0^T \int_{\Omega} I_{\text{ion}}(v, u, z) \omega(t), \quad \forall \phi \in D(0,T).$$

Gathering all these results, the functions $u_{\varepsilon}, p_{\varepsilon}, v_{\varepsilon}, v_{i,e}, v_{k,e}, \gamma_{\varepsilon}, u_{\varepsilon}, \varepsilon_{m, k}, \gamma_{\varepsilon,m}$ verify in the space of distributions $D'(0,T)$, for all functions $\psi \in H^1(\Omega)^3, \rho \in L^2(\Omega), \phi \in H^1(\Omega)$ and $\mu \in H^{1,0}(\Omega)$:

$$\langle \varepsilon \partial_t u_{\varepsilon}, \psi \rangle + \int_{\Omega} (\nabla u_{\varepsilon}) \sigma(x, \gamma_{\varepsilon}) \cdot \nabla \psi - p_{\varepsilon} \nabla \cdot \psi \, dx + \int_{\Omega} \alpha u_{\varepsilon} \cdot \psi \, dx = \int_{\Omega} f \cdot \psi \, dx$$

$$\langle \varepsilon p_{\varepsilon}, \rho \rangle + \int_{\Omega} \rho \nabla \cdot u_{\varepsilon} = 0$$

$$\langle \partial_t v_{\varepsilon} + \varepsilon \partial_t v_{i,e}, \omega \rangle + \int_{\Omega} (M_1(x, \nabla u_{\varepsilon}) \nabla v_{i,e} \cdot \nabla \omega + I_{\text{ion}}(v, u_{\varepsilon}, z_{\varepsilon}) \omega) \, dx = \int_{\Omega} I^v_1 \omega \, dx$$

$$\langle \partial_t v_{\varepsilon} - \varepsilon \partial_t v_{k,e}, \mu \rangle - \int_{\Omega} (M_2(x, u_{\varepsilon}) \nabla v_{k,e} \cdot \nabla \mu + I_{\text{ion}}(v, u_{\varepsilon}, z_{\varepsilon}) \mu) \, dx = \int_{\Omega} I^v_2 \mu \, dx$$ (3.40)

$$\forall j = 1, \ldots, k, \quad \int_{\Omega} \partial_t w_{j,e} \omega = \int_{\Omega} R_j(v_{e}, w_{e}) \omega$$

$$\int_{\Omega} \partial_t z_{\varepsilon} \omega = \int_{\Omega} G(v_{e}, u_{e}, \varepsilon) \omega$$

$$\int_{\Omega} \partial_t \gamma_{\varepsilon} \omega = \int_{\Omega} S(\gamma_{\varepsilon}, u_{\varepsilon}, \varepsilon) \omega.$$ 

Finally, having $u_{\varepsilon} \in L^2(0,T; H^1(\Omega)^3), U_{i,e}, \gamma_{\varepsilon}, z_{\varepsilon} \in L^2(0,T; H^1(\Omega)), w_{\varepsilon} \in L^2(0,T; H^1(\Omega)^k)$ and $p_{\varepsilon} \in L^\infty(0,T; L^2(\Omega)), \gamma_{\varepsilon}, z_{\varepsilon} \in L^2(0,T; H^1(\Omega)^3)$, their weak derivatives $\partial_t u_{\varepsilon} \in L^2(0,T; (H^1(\Omega)^3)), \partial t U_{i,e} \in L^2(0,T; (H^1(\Omega)^3)), \partial t w_{\varepsilon} \in L^2(\Omega_T)^k$ and $\partial t \gamma_{\varepsilon}, \partial t z_{\varepsilon}$ in $L^2(\Omega_T)^k$, it is deduced from a classical result, that the functions $u_{\varepsilon} : t \in [0,T] \mapsto u_{\varepsilon}(t) \in H^1(\Omega)^3, U_{i,e} : t \in [0,T] \mapsto U_{i,e}(t) \in H^1(\Omega), w_{\varepsilon} : t \in [0,T] \mapsto w_{\varepsilon}(t) \in L^2(\Omega)^k, \gamma_{\varepsilon} : t \in [0,T] \mapsto \gamma_{\varepsilon}(t) \in L^2(\Omega), \text{ and } z_{\varepsilon} : t \in [0,T] \mapsto z_{\varepsilon}(t) \in L^2(\Omega)$ are continuous. For $p_{\varepsilon}$, it only proves that they are weakly continuous in $H^1(\Omega)$.

Furthermore, since $u_{\varepsilon,m}(0) \to u_0, p_{\varepsilon,m}(0) \to p_0, v_{\varepsilon,m}(0) \to v_0, v_{k,e,m}(0) \to v_{k,0,k = i, e,}$
This lemma will be used to prove the following result.

Now we recall the following standard lemma (see for instance Theorem IV.3.1 p 245 in [40], see also [3]).

Lemma 4.1. There exist constants $C_1, \ldots, C_6$ independent of $\varepsilon$ such that

$$
\max_{t \in [0, T]} \|v_{\varepsilon}(t)\|_{L^2(\Omega)}^2 + \sum_{j=1}^3 \|\sqrt{\varepsilon}v_{j,\varepsilon}\|_{L^2(\Omega)}^2 \leq C_1, \quad \forall t \in [0, T],
$$

(4.1)

$$
\left( \sum_{j=1}^3 \|v_{i,\varepsilon}\|_{L^2(0,T;H^1(\Omega))}^2 + \|v_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))}^2 \right) \leq C_2,
$$

(4.2)

$$
\|\partial_t (v_{\varepsilon} + \varepsilon v_{i,\varepsilon})\|_{L^2(0,T;H^1(\Omega))} + \|\partial_t (v_{\varepsilon} - \varepsilon v_{i,\varepsilon})\|_{L^2(0,T;H^1(\Omega))} \leq C_3,
$$

(4.3)

$$
\|w_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))}^2 + \|z_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))}^2 + \|\gamma_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))} \leq C_4,
$$

(4.4)

$$
\|\partial_t u_{\varepsilon}\|_{L^2(\Omega_T)^3} + \|\partial_t z_{\varepsilon}\|_{L^2(\Omega_T)} + \|\partial_t \gamma_{\varepsilon}\|_{L^2(\Omega_T)} \leq C_5,
$$

(4.5)

$$
\max_{t \in [0, T]} \left( \|\sqrt{\varepsilon}u_{i,\varepsilon}\|_{L^2(\Omega)}^2 + \|\sqrt{\varepsilon}p_{i,\varepsilon}\|_{L^2(\Omega)}^2 + \|u_{\varepsilon}\|_{L^2(0,T;H^1(\Omega))}^2 \right) \leq C_6.
$$

(4.6)

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

- $v_{i,\varepsilon} \to v$ strongly in $L^2(\Omega_T)$ and a.e. in $\Omega_T$ and weakly in $L^2(0,T;H^1(\Omega))$,
- $v_{i,\varepsilon} \to v_i$ weakly in $L^2(0,T;H^1(\Omega))$, $v_{i,\varepsilon} \to v_{\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$,
- $w_{\varepsilon} \to w$ strongly in $L^2(\Omega_T)^k$ and a.e. in $\Omega_T$,
- $\gamma_{\varepsilon} \to \gamma$ strongly in $L^2(\Omega_T)$ and a.e. in $\Omega_T$,
- $z_{\varepsilon} \to z$ strongly in $L^2(\Omega_T)$ and a.e. in $\Omega_T$,
- $u_{\varepsilon} \to u$ weakly in $L^2(0,T;H^1(\Omega))$ and $\nabla u_{\varepsilon} \to \nabla u$ in $L^2(\Omega_T)^{3 \times 3}$.

We briefly note that in the distribution sense

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

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

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

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

Remark 4.1. Recuperation of $p$

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

Now we recall the following standard lemma (see for instance Theorem IV.3.1 p 245 in [40], see also [1], [22]).

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

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 $v \in (H^1(\Omega))^3$

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

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

$$\varepsilon (\partial_t u_{\varepsilon}, v) + \int_{\Omega} (\nabla u_{\varepsilon}) \sigma(x, \gamma_{\varepsilon}) : \nabla v \, dx = \int_{\Omega} \sigma \cdot v \, dx$$

Passing to the limit in $\varepsilon$ we get

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

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, $p \in D'(\Omega)$ such that

$$\nabla \cdot (\nabla u) \sigma(x, \gamma) + f = \nabla p$$

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 $u \in (H^1(\Omega))^3$. Hence, $p \in L^2(\Omega_T)$.

Now we have, for all $v \in (H^1_0(\Omega))^3$,

$$\int_{\Omega} p_{\varepsilon} \nabla \cdot v \, dx = \varepsilon \int_{\Omega} \partial_t u_{\varepsilon} \cdot v + \int_{\Omega} (\nabla u_{\varepsilon}) \sigma(x, \gamma_{\varepsilon}) : \nabla v \, dx - \int_{\Omega} \sigma \cdot v \, dx$$

and

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

Subtracting these two equations, we obtain

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

Consequently, we get, for all $v \in (H^1_0(\Omega))^3$,

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

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:

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

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

By Equation (4.7), we have

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

In other words,

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

So in order to obtain $\int_{\Omega} (p_{\varepsilon} - p) q \, dx \rightarrow 0$, it is sufficient to show $\int_{\Omega} (p_{\varepsilon} - p) \, dx \rightarrow 0$.

In fact, by the first equation of (3.40) we have for all $v \in (H^1(\Omega))^3$,

$$\lim_{\varepsilon \to 0} \int_{\Omega} p_{\varepsilon} \nabla \cdot v \, dx = \int_{\Omega} (\nabla u) \sigma(x, \gamma) : \nabla v + \int_{\Omega} \alpha u \cdot v \, ds - \int_{\Omega} f \cdot v \, dx.$$
In particular, we can consider the test function \( \mathbf{v}_1 = (x_1, 0, 0) \) which is in \((H^1(\Omega))^3\) and verifies \( \nabla \cdot \mathbf{v}_1 = 1 \). Thus we obtain

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

Since by De Rham’s Lemma, \( p \) is found up to an additive constant, then we choose it so that we have \( \int_\Omega p \, dx = \tilde{C} \). Therefore, we have

\[
\lim_{\varepsilon \to 0} \int_\Omega p_{\varepsilon} \, dx = \tilde{C} = \int_\Omega p \, dx.
\]

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

\[
\lim_{\varepsilon \to 0} \int_\Omega (p_{\varepsilon} - p) q \, dx = 0.
\]

Therefore, according to all of the preceding convergence results, and repeating some of the arguments of the previous section, we have for all \( \psi \in H^1(\Omega)^3 \), \( \rho \in L^2(\Omega) \), \( \mu \in H^{1,0}(\Omega) \) (given as in Definition 2.1) and \( \omega \) in \( H^1(\Omega) \):

\[
\int_\Omega (\nabla \mathbf{u}) \sigma(\mathbf{x}, \gamma) : \nabla \psi - p \nabla \cdot \psi \, dx + \int_{\partial \Omega} \alpha \mathbf{u} \cdot \psi \, ds = \int_\Omega \mathbf{f} \cdot \psi \, dx
\]

\[
\int_\Omega p \nabla \cdot \mathbf{u} = 0
\]

\[
\langle \partial_t \mathbf{v}, \omega \rangle + \int_\Omega (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla \mathbf{v}_1 \cdot \nabla \omega + I_{\text{ion}}(\mathbf{v}, \mathbf{w}, z) \omega) \, dx = \int_\Omega I^*_e \omega \, dx
\]

\[
\langle \partial_t \mathbf{w}, \mu \rangle - \int_\Omega (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla \mathbf{v}_c \cdot \nabla \mu + I_{\text{ion}}(\mathbf{v}, \mathbf{w}, z) \mu) \, dx = \int_\Omega I^*_c \mu \, dx
\]

\[
\forall j = 1, \ldots, k, \int_\Omega \partial_{t,j} \mathbf{v} \cdot \omega = \int_\Omega R_{\varepsilon,j}(\mathbf{v}, \mathbf{w}) \omega
\]

\[
\int_\Omega \partial_t z \omega = \int_\Omega G(\mathbf{v}, \mathbf{w}, z) \omega
\]

\[
\int_\Omega \partial_t \gamma \omega = \int_\Omega S(\gamma, \mathbf{w}, z) \omega.
\]

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

5. Concluding remarks

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

[1] L. Tung, A bi-domain model for describing ischemic myocardial D–C potentials. PhD thesis, MIT, 1978.
[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 bidomain model of cardiac tissue. Netw. Heterog. Media, 1(1):185–218, 2006.
[4] Y. Bourgault, Y. Coudière, and C. Pierre. Existence and uniquness 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. Aris, M. Vázquez, and G. Houzeaux. Coupled electromechanical model of the heart: Parallel finite element formulation. Int. J. Numer. Methods Biomed. Engng., 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.
[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(3):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. Lasila, 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. J. Elasticity, 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 framework 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. Engng., 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., 64(3):375–399, 2010.
[26] P. Pathmanathan, C. Ortiz, 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.
CARDIAC ELECTROMECHANICS WITH PHYSIOLOGICAL IONIC MODEL

[31] J. Sundnes, G.T. Lines, X. Cai, B.F. Nielsen, K.-A. Mardal, and A. Tveito. *Computing the electrical activity in the heart*, volume 1 of Monographs in Computational Science and Engineering. Springer-Verlag, Berlin, 2006.

[32] D.M. Bers. Cardiac excitation-contraction coupling. *Nature*, 415(6868):198–205, 2002.

[33] R. Ruiz-Baier, A. Gizzi, S. Rossi, C. Cherubini, A. Laadhari, S. Filippi, and A. Quarteroni. Mathematical modeling of active contraction in isolated cardiomyocytes. *Math. Medicine Biol.*, 31:259–283, 2014.

[34] R. Ruiz-Baier, D. Ambrosi, S. Pozzuto, 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.

[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 \( \text{div} y = f \) 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 d'un 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.

[47] Jindrich Nečas. Sur les normes équivalentes dans \( W^{1,p}_0(\omega) \) et sur la coercivité des formes formellement positives. *Les presses de l'Université de Montréal*, 1966.

[48] Jindrich Nečas. *Direct methods in the theory of elliptic equations*. Springer Science & Business Media, 2011.

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