



HAL
open science

Electromechanical coupling of the heart : modeling, mathematical analysis and numerical simulation

Fatima Mroue

► **To cite this version:**

Fatima Mroue. Electromechanical coupling of the heart : modeling, mathematical analysis and numerical simulation. Biomechanics [physics.med-ph]. École centrale de Nantes; Université Libanaise, 2019. English. NNT : 2019ECDN0039 . tel-02439254

HAL Id: tel-02439254

<https://theses.hal.science/tel-02439254v1>

Submitted on 14 Jan 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

THESE DE DOCTORAT DE

L'ÉCOLE CENTRALE DE NANTES
COMUE UNIVERSITE BRETAGNE LOIRE
ET L'UNIVERSITÉ LIBANAISE

ECOLE DOCTORALE N° 601
*Mathématiques et Sciences et Technologies
de l'Information et de la Communication*
Spécialité : *Mathématiques et leurs interactions*

Par **Fatima MROUE**

« **Couplage Électromécanique du cœur : Modélisation, analyse mathématique et simulation numérique** »

Thèse présentée et soutenue au Laboratoire de Mathématique Jean Leray, le 24 octobre 2019
Unité de recherche : Laboratoire de Mathématique Jean Leray (LMJL)

Rapporteurs avant soutenance :

Yves BOURGAULT Professeur, University of Ottawa
Catherine CHOQUET Professeur, Université de la Rochelle

Composition du Jury :

Président :	Catherine CHOQUET	Professeur, Université de la Rochelle
Rapporteurs :	Yves BOURGAULT Catherine CHOQUET	Professeur, University of Ottawa Professeur, Université de la Rochelle
Examineurs :	Mathieu COLIN Samer ISRAWI François JAUBERTEAU	MC-HDR, Université de Bordeaux Professeur, Université Libanaise Professeur, Université de Nantes

Dir. de thèse :	Mazen SAAD	Professeur, École Centrale de Nantes
Dir. de thèse :	Raafat TALHOUK	Professeur, Université Libanaise
Co-dir. de thèse :	Mostafa BENDAHMANE	MC-HDR, Université de Bordeaux



Université Libanaise

École Doctorale
Sciences et Technologies



CENTRALE
NANTES

THESE de doctorat en Cotutelle

Pour obtenir le grade de Docteur délivré par

L'Université Libanaise

L'Ecole Doctorale des Sciences et Technologie

Spécialité : Mathématiques et leurs applications

Présentée et soutenue publiquement par

MROUE Fatima

Le 24 octobre 2019

Couplage Électromécanique du Cœur : Modélisation, Analyse

Mathématique et Simulation Numérique

Directeur de thèse : **TALHOUK Raafat**

Co-encadrement de la thèse : **SAAD Mazen**

Co-encadrement de la thèse : **BENDAHMANE Mostafa**

Membres du Jury

M. Mostafa BENDAHMANE,	MC-HDR	Université de Bordeaux	Co-dir. de thèse
M. Yves BOURGAULT,	Professeur	University of Ottawa	Rapporteur
Mme Catherine CHOQUET,	Professeur	Université de la Rochelle	Rapporteur
M. Mathieu COLIN,	MC-HDR	Université de Bordeaux	Examineur
M. Samer ISRAWI,	Professeur	Université Libanaise	Examineur
M. François JAUBERTEAU,	Professeur	Université de Nantes	Examineur
M. Mazen SAAD,	Professeur	École Centrale de Nantes	Co-dir. de thèse
M. Raafat TALHOUK,	Professeur	Université Libanaise	Co-dir. de thèse

Acknowledgments

The world is a better place thanks to people who have the will to develop others. What makes it even better are people who share the gift of their time and knowledge to help others grow. What could be better than empowering others with the light of science? I would like first to express my deep gratitude to my supervisors Professor Mostafa Bendahmane, Professor Mazen Saad and Professor Raafat Talhouk. It was a pleasure to venture through this doctoral research journey endowed with your guidance, help and encouragement.

To Professor Yves Bourgault and Professor Catherine Choquet, I want to say thank you for accepting to review this PhD thesis despite your busy timetable. I greatly appreciate the time and effort spent in reading and commenting on my work.

I would also like to thank Professor Mathieu Colin, Professor Samer Israwi and Professor François Jauberteau for being committee members of the PhD thesis defense.

I would equally like to thank Dr. Françoise Foucher for the suggestions and corrections of the French introduction of this work.

My sincere thankfulness to the faculty members and staff of the department of Mathematics at the American University of Beirut for always maintaining a dynamic and competitive environment boosting our will for better achievements. Special thanks to Professor Kamal Khuri-Makdissi and Professor Bassam Shayya for their continuous support and guidance. To the soul of Professor Nazih Nahlus, you will always stay in my heart as a sacrificing teacher and a sweet heart.

Without the experiences and support from the friends and colleagues I met in Nantes and at the Mathematics Laboratory of the Lebanese University, this manuscript would not exist. Thank you to Abir, Hala, Zeinab, Maha, Hussein, Ahmad, Fakhreldine, . . .

Thank you to my parents for the unwavering nurturance: Mum who took care of my three kids for long days and Dad for your belief in my ability. I've often needed your support and it has always been there. Thanks to my caring brothers for their emotional support. Thanks to my family in law for their kindness and understanding.

I am eternally grateful to my awesome husband, Ayman. Special thanks for your patience, support, love, and encouragement during these three years. You are a rare example (in our

patriarchal societies) of men who clear the path for women to achieve. It is a special pleasure to recognize you as someone who gives his heart and soul to his family!

To my three shining stars: Mohamad, Nour and Lynn, you will always be the pump of love for my soul just as the heart is the pump of blood for the body. My life is dedicated to you and this work is nothing but a tiny part!

Abstract

This thesis is concerned with the mathematical analysis and numerical simulation of cardiac electrophysiology models.

We use the unfolding method of homogenization to rigorously derive the macroscopic bidomain equations. We consider tensorial and space dependent conductivities and physiological as well as simplified ionic models. Using the Faedo-Galerkin approach followed by compactness, we prove the existence and uniqueness of solution to the microscopic bidomain model. The convergence of a sequence of solutions of the microscopic model to the solution of the macroscopic model is then obtained. Due to the nonlinear terms on the oscillating manifold, the boundary unfolding operator is used as well as a Kolmogorov compactness argument for the simplified models and a Minty type argument for the physiological models.

Furthermore, we consider the monodomain model coupled to Beeler-Reuter's ionic model. We propose a finite volume scheme and analyze its convergence. First, we derive the corresponding discrete variational formulation and we show existence and uniqueness of its solution. By compactness, the convergence of the discrete solution is obtained. Since the two-point flux approximation (TPFA) scheme is inefficient in approximating anisotropic diffusion fluxes, we propose and analyze a nonlinear combined scheme that preserves the maximum principle. In this scheme, a Godunov approximation to the diffusion term ensures that the solutions are bounded without any restriction on the transmissibilities or on the mesh.

Finally, in view of addressing the solvability of cardiac electromechanics coupled to physiological ionic models, we considered a model 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 and the Faedo-Galerkin method followed by a compactness argument.

Keywords: Bidomain, homogenization, unfolding method, finite volumes, CVFE, electromechanical coupling, active strain.

Résumé

Cette thèse est dédiée à l'analyse mathématique et la simulation numérique des équations intervenant dans la modélisation de l'électrophysiologie cardiaque.

D'abord, nous donnons une justification mathématique rigoureuse du processus d'homogénéisation périodique à l'aide de la méthode d'éclatement périodique. Nous considérons des conductivités électriques tensorielles qui dépendent de l'espace et des modèles ioniques non linéaires physiologiques et phénoménologiques. Nous montrons l'existence et l'unicité d'une solution du modèle microscopique en utilisant une approche constructive de Faedo-Galerkin suivie par un argument de compacité dans L^2 . Ensuite, nous montrons la convergence de la suite de solutions du problème microscopique vers la solution du problème macroscopique. À cause des termes non linéaires sur la variété oscillante, nous utilisons l'opérateur d'éclatement sur la surface et un argument de compacité de type Kolmogorov pour les modèles phénoménologiques et de type Minty pour les modèles physiologiques.

En outre, nous considérons le modèle monodomaine couplé au modèle physiologique de Beeler-Reuter. Nous proposons un schéma volumes finis et nous analysons sa convergence. D'abord, nous dérivons la formulation variationnelle discrète correspondante et nous montrons l'existence et l'unicité de sa solution. Par compacité, nous obtenons la convergence de la solution discrète. Comme le schéma TPFA (two-point flux approximation) est inefficace pour approcher les flux diffusifs avec des tenseurs anisotropes, nous proposons et analysons, ensuite, un schéma combiné non-linéaire qui préserve le principe de maximum. Ce schéma est basé sur l'utilisation d'un flux numérique de Godunov pour le terme de diffusion assurant que les solutions discrètes soient bornées sans restriction sur le maillage du domaine spatial ni sur les coefficients de transmissibilité.

Enfin, dans la perspective d'étudier la solvabilité des modèles électromécaniques couplés avec des modèles ioniques physiologiques, nous considérons un modèle avec une description linéarisée de la réponse élastique passive du tissu cardiaque, une linéarisation de la contrainte d'incompressibilité et une approximation tronquée des diffusivités non linéaires intervenant dans les équations du modèle bidomaine. La preuve utilise des approximations par des systèmes non-dégénérés et la méthode Faedo-Galerkin suivie par un argument de compacité.

Mots clés: Bidomaine, homogénéisation, éclatement périodique, volumes finis, CVFE, couplage électromécanique, déformation active.

Contents

Introduction Générale	11
1 Electromechanical Modeling of the heart	35
1.1 Introduction	35
1.2 Cardiac Anatomy and Function	35
1.2.1 Macroscopic description	35
1.2.2 Microscopic description	36
1.3 Cardiac electrophysiology models	38
1.3.1 The bidomain model: Physical derivation	39
1.3.2 Ionic Models	41
1.4 Cardiac Mechanical Modeling	43
1.4.1 Nonlinear Elasticity	43
1.4.2 Constitutive Laws	45
1.4.3 Constitutive laws of the myocardium	48
1.5 Electromechanical coupling models	49
1.5.1 The active strain model	50
1.5.2 The active stress model	51
1.5.3 Mechanical to electrical coupling	52
2 Unfolding Homogenization of the Bidomain Model	55
2.1 Introduction	55
2.1.1 Homogenization Techniques	55
2.2 Formal derivation of cardiac electrophysiology model	57
2.2.1 The Microscopic Bidomain Model	57
2.2.2 Nondimensional Analysis	58
2.2.3 The Two-Scale Asymptotic Expansion	60
2.3 Mathematical Assumptions on the Microscopic Bidomain Model	62
2.3.1 Assumptions on the Domain	62
2.3.2 Assumptions on the Data	63
2.3.3 Main Results	65
2.4 Existence of solutions for the microscopic model	66
2.5 Convergence of solutions to the macroscopic problem	75
2.5.1 Energy estimates for the microscopic solutions	75
2.5.2 A new formulation of the microscopic problem	76
2.6 “Unfolding” compactness	80
2.7 Macroscopic bidomain model	90

2.8	Unfolding homogenization to physiological models	91
2.9	Conclusion	100
3	Numerical Schemes For an Electrophysiology Model	101
3.1	Introduction	101
3.2	Mathematical Assumptions	102
3.3	Numerical Analysis of a Finite Volume Scheme	104
3.3.1	Weak Formulation	104
3.3.2	Discrete Problem	105
3.3.3	Convergence of the Discrete Scheme	110
3.4	Numerical Analysis of CVFE Scheme	127
3.4.1	Mathematical Assumptions	128
3.4.2	Weak Formulation	129
3.4.3	Discrete Problem	129
3.5	Discrete properties and existence of a discrete solution	133
3.6	Compactness estimates on the family of discrete solutions	143
3.7	Identification of the limit as a weak solution	146
3.8	Numerical Results	150
3.9	Conclusion	157
4	Mathematical analysis of cardiac electromechanics	163
4.1	Introduction	163
4.2	Governing equations for the electromechanical coupling	165
4.2.1	Linearizing the elasticity equations	165
4.2.2	The problem to be solved and its weak formulation	166
4.3	Existence for a regularized problem	169
4.3.1	Faedo-Galerkin approximations for the regularized problem	169
4.3.2	A priori estimates	173
4.3.3	Compactness properties and Convergence	186
4.4	Existence of solution to the original problem	190
4.5	Conclusion	193
	Bibliography	193

Introduction Générale

Ce mémoire de thèse est consacré à la modélisation, l'étude mathématique et l'analyse numérique de phénomènes électriques et mécaniques ayant lieu dans le cœur humain.

Contexte de la thèse

Cette thèse se place dans un cadre interdisciplinaire mettant en interaction les sciences médicales et les mathématiques. En fait, la modélisation des systèmes vivants est un défi scientifique majeur qui pourra améliorer la compréhension des phénomènes physiologiques et apporter des solutions à des problèmes cliniques. De nombreuses simulations des systèmes biologiques sont aujourd'hui proposées aux médecins dans le but de les aider à faire des diagnostics (non invasifs, adaptés spécifiquement aux patients, en temps réel, ...) et à planifier les thérapies correspondantes (opérations, traitements, ...). Une première étape vers un tel objectif est de trouver des modèles mathématiques représentant ces phénomènes complexes. Une deuxième étape est de vérifier du point de vue mathématique la validité de ces modèles et par la suite vérifier leur capacité à reproduire les phénomènes biologiques sains ou perturbés. Nous citons, par exemple, la modélisation de la dynamique clonale dans le cancer du sang pour la prédiction du taux de survie après traitement [SBHMC15], et la prédiction de la rupture d'un anévrisme cérébral [Kro11].

L'objet de cette thèse est le cœur. Cet organe, ayant la taille d'un poing, est l'un des organes vitaux du corps. Il se contracte rythmiquement pour faire circuler le sang vers tous les organes. Chacun de ses battements est initié par une onde électrique qui dépolarise les cellules cardiaques et induit leur contraction. Ainsi, l'analyse mathématique des phénomènes impliqués fait intervenir trois domaines avec leurs interactions: l'électrophysiologie, la mécanique des tissus et la mécanique des fluides. La littérature liée à ces sujets est abondante. Citons, par exemple, les travaux pionniers de Peskin [Pes77] pour la modélisation de l'écoulement sanguin dans le cœur. Les premières contributions pertinentes dans le cadre de la mécanique cardiaque remontent à la thèse de Hunter en 1975 [Hun75]. En parallèle, des équations aux dérivées partielles représentant la diffusion du potentiel d'action ont été proposées par Tung [Tun78]. Ces dernières sont couplées avec des équations différentielles ordinaires modélisant le potentiel d'action à l'échelle cellulaire. La première modélisation du potentiel d'action est celle proposée par les travaux de Hodgkin et Huxley [HH52] sur l'axone géant du calamar. Ces travaux ont été suivis par de nombreuses modifications pour les appliquer à l'électrophysiologie cardiaque, citons par exemple [Nob62, BR77, LR94]. Une fois ces modèles établis, la communauté mathématique s'est intéressée à ces modèles de l'électrophysiologie. Par exemple, citons comme travaux précurseurs celui de Colli Franzone et Magenes [FM79] ainsi que celui de Panfilov et Winfree [PW85]. Par la suite, la littérature autour de l'analyse d'existence et d'unicité est abondante. Cependant les

problèmes posés sont dans leur majorité des modèles simplifiés. La seule contribution tenant compte de modèles physiologiques est celle de Veneroni [Ven09]. En outre, malgré l'abondance de références reliées aux méthodes numériques pour des modèles électromécaniques du cœur (citons par exemple [GK10, LAVH12, NP04, NNN⁺11, Tra11]), il reste encore beaucoup de problèmes ouverts concernant leur validité de point de vue mathématique. Quelques résultats d'existence ont été obtenus par Pathmanatan *et al.* [PCGW10, POK13] et par Andreianov *et al.* [ABQRB15].

Dans cette thèse, nous établissons rigoureusement le modèle bidomaine couplé aux modèles physiologiques de la membrane cellulaire, nous proposons un schéma numérique convergent qui respecte les bornes physiologiques des différentes variables et nous démontrons un résultat d'existence de solution pour un modèle électromécanique couplé avec des modèles ioniques physiologiques.

Contenu de la thèse

Les travaux effectués dans cette thèse se concentrent sur deux axes principaux, notamment l'électrophysiologie et le couplage électromécanique. Dans un premier temps, nous effectuons l'homogénéisation rigoureuse d'un modèle bidomaine microscopique. Puis nous proposons et nous étudions un schéma combiné éléments finis - volumes finis, positif non linéaire pour le modèle monodomaine couplé avec le modèle ionique physiologique de Beeler-Reuter. Finalement nous établissons l'existence de solution d'un modèle électromécanique couplé avec un modèle ionique physiologique.

Chapitre 1

Ce chapitre est composé de plusieurs parties. La première est une brève présentation du rôle du cœur et de son fonctionnement à l'échelle macroscopique et microscopique. Nous illustrons les notions physiologiques qui sont nécessaires pour la lecture de cette thèse.

Le cœur est un muscle actif formé de deux parties principales, le cœur gauche et le cœur droit, séparées par un mur musculaire, le septum. Chaque partie contient une oreillette et un ventricule (voir Figure 1).

La contraction du cœur se fait d'une manière intrinsèque, c'est-à-dire qu'aucune stimulation d'origine nerveuse n'intervient. Les battements cardiaques sont sous le contrôle d'un *pace-maker* naturel, sorte de groupement de cellules du myocarde qui constituent le nœud sinusal ou nœud sino-auriculaire (SA), situé en haut de l'oreillette droite. Le nœud SA donne naissance à un signal de dépolarisation, aussi dit potentiel d'action, toutes les 0.8 secondes. Ce signal parcourt, pendant 0.1 seconde, le tissu musculaire des deux oreillettes jusqu'à ce qu'il atteigne le nœud auriculo-ventriculaire. La conduction à travers le nœud auriculo-ventriculaire (qui est la seule connexion électrique entre les oreillettes et les ventricules) se fait à une fréquence plus lente laissant le temps aux oreillettes de se contracter et expulser le sang vers les ventricules avant que le potentiel d'action arrive aux ventricules et déclenche leur contraction. L'onde d'excitation est transmise aux parois des deux ventricules via le faisceau de His puis les fibres de Purkinje. Ces dernières, ayant une conduction rapide, transmettent le courant au myocarde

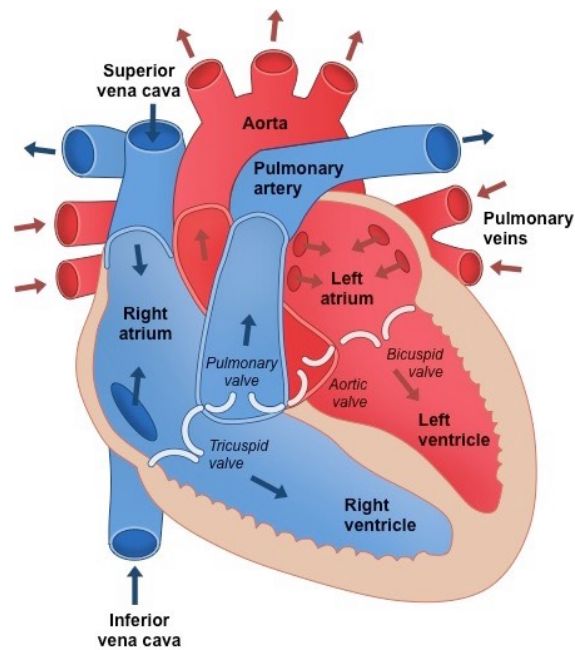


Figure 1 – L’anatomie du cœur. <https://www.drmani.com/what-is-the-heart/>

entier presque simultanément et entraînent sa contraction.

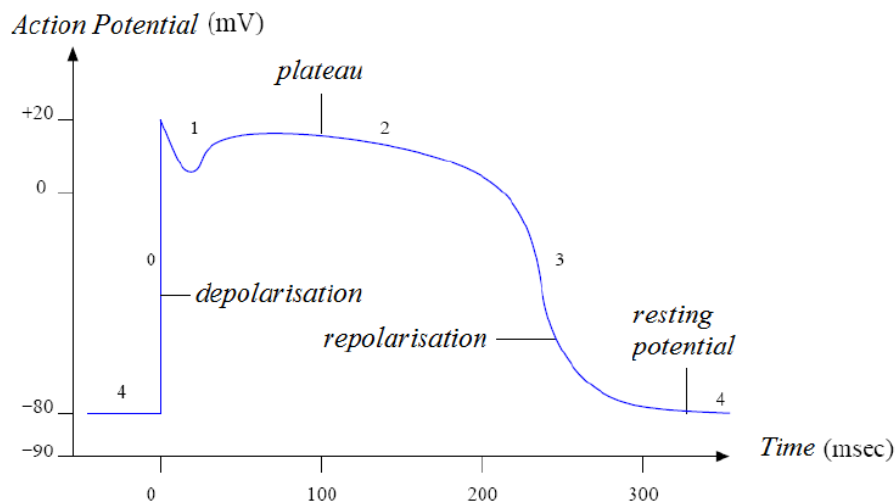


Figure 2 – Phases du potentiel d’action ventriculaire, adapté de [Kat10].

À l’échelle microscopique, la cellule cardiaque (cardiomyocyte) est polarisée et elle a un certain potentiel, appelé “potentiel de repos”, dont les modifications forment ce que l’on appelle le potentiel d’action. Le potentiel d’action dure un peu plus de 300 ms et comporte cinq phases différentes: une brutale dépolariation où la perméabilité de la membrane au sodium Na^+ augmente suivie par une courte durée de repolarisation due à la fermeture des canaux de sodium. Ensuite, un plateau est maintenu par un courant entrant de calcium Ca^{2+} . La dernière phase est celle de repolarisation. Elle est due à plusieurs courants sortants de potassium K^+ et elle remet

le potentiel à son état de repos (voir Figure 2).

D'autre part, chaque cardiomyocyte est formé par des éléments basiques, les sarcomères, responsables de la contraction cardiaque (voir Figure 3). La structure d'un sarcomère consiste en un arrangement parallèle de filaments d'actine et de myosine. Ces derniers forment des "ponts" qui causent leur glissement et conduisent à la contraction sous l'action de calcium. La libération de calcium est activée par l'excitation électrique des cardiomyocytes.

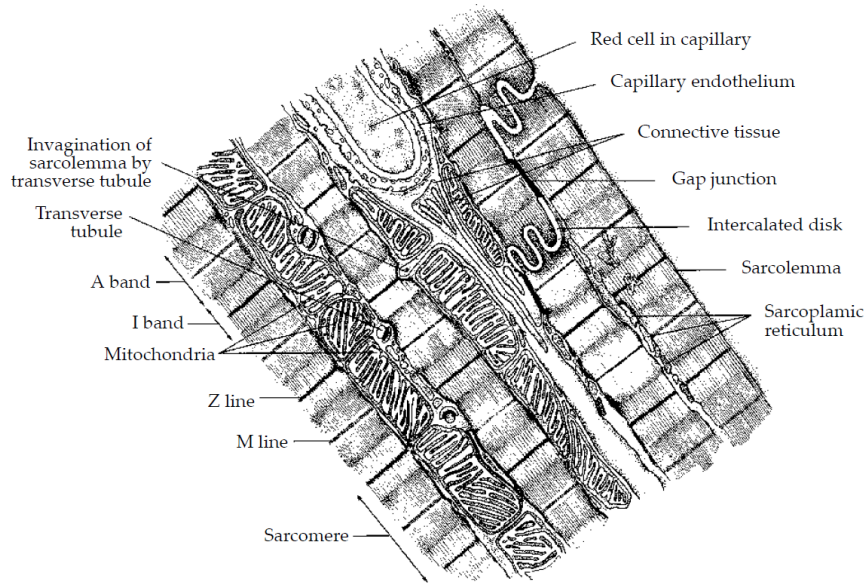


Figure 3 – Diagramme montrant la structure d'une cellule cardiaque. (Extraite de Berne et Levy, [KS09])

La deuxième partie de ce chapitre présente les modèles disponibles en électrophysiologie. Une analyse détaillée du modèle bidomaine est donnée en s'appuyant sur la littérature. De plus, nous illustrons par des exemples de modèles ioniques. Dans la troisième partie, nous présentons les éléments nécessaires pour toute modélisation en mécanique des milieux continus et ensuite nous exposons des lois de comportement du myocarde proposées dans la littérature. La dernière partie de ce chapitre présente les modèles de couplage électromécanique.

Chapitre 2

Le chapitre 2 propose une justification mathématique complète et rigoureuse du processus d'homogénéisation périodique qui mène au modèle bidomaine. Nous considérons des conductivités électriques tensorielles qui dépendent de l'espace et des modèles ioniques non linéaires physiologiques et phénoménologiques. Nous effectuons d'abord une adimensionalisation des équations bidomaine microscopiques. Ces équations forment un système d'équations elliptiques dans chacun des milieux intracellulaire $\Omega_{i,\varepsilon}$ et extracellulaire $\Omega_{e,\varepsilon}$, couplées à des équations dynamiques sur la membrane Γ_ε et des équations différentielles ordinaires représentant le modèle ionique. Elles dépendent aussi d'un paramètre adimensionnel ε représentant le rapport entre le diamètre d'une cellule et la longueur macroscopique du tissu. Ainsi les propriétés électriques du tissu sont décrites par le potentiel *intracellulaire* $u_{i,\varepsilon}$ et *extracellulaire* $u_{e,\varepsilon}$. Dans ce qui suit, les potentiels $u_{j,\varepsilon}$ sont définis de $\Omega_{j,\varepsilon}$ dans \mathbb{R} pour $j = i, e$ tandis que leur différence, $v_\varepsilon := (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} : \Gamma_\varepsilon \rightarrow \mathbb{R}$, est le potentiel *transmembranaire* qui vérifie une condition

dynamique sur Γ_ε et qui fait intervenir une fonction auxiliaire $w_\varepsilon : \Gamma_\varepsilon \rightarrow \mathbb{R}$ (nommée variable de porte).

Le système couplé réaction-diffusion suivant forme le modèle bidomaine microscopique, pour $j = i, e$ (voir, *par exemple*, [SLC⁺07, Yin05]):

$$\begin{cases} -\nabla \cdot (\mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon}) = 0 & \text{dans } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \\ \varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, w_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m & \text{sur } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \\ \mathcal{I}_m = -\mathbf{M}_{i,\varepsilon} \nabla u_{i,\varepsilon} \cdot \mu_i = \mathbf{M}_{e,\varepsilon} \nabla u_{e,\varepsilon} \cdot \mu_e & \text{sur } \Gamma_{\varepsilon,T}, \\ \partial_t w_\varepsilon - H(v_\varepsilon, w_\varepsilon) = 0 & \text{sur } \Gamma_{\varepsilon,T}. \end{cases} \quad (1)$$

Le système (1) est complété par des conditions au bord de type Neumann

$$(\mathbf{M}_j(x) \nabla u_{j,\varepsilon}) \cdot \mu_j = 0 \text{ sur } (0, T) \times (\partial\Omega_{j,\varepsilon} \setminus \Gamma_\varepsilon), \quad j \in \{e, i\}, \quad (2)$$

où les vecteurs μ_j , $j = i, e$ sont les normales unitaires (sortantes) à $\partial\Omega_{j,\varepsilon}$, pour $j = i, e$ respectivement, et $\mu_i = -\mu_e$ sur Γ_ε .

Le système est aussi complété par des conditions initiales pour le potentiel transmembranaire et la variable de porte

$$v_\varepsilon(0, \cdot) = v_{0,\varepsilon}(\cdot), \quad w_\varepsilon(0, \cdot) = w_{0,\varepsilon}(\cdot) \text{ sur } \Gamma_\varepsilon. \quad (3)$$

Nous établissons ensuite d'une manière formelle les équations macroscopiques suivant la littérature. Puis, nous démontrons l'existence et l'unicité de solutions faibles du problème (1)-(2)-(3) au sens suivant:

Définition 1 (Formulation Faible). *Une solution du problème (1)-(2)-(3) est un 4-uplet $(u_{i,\varepsilon}, u_{e,\varepsilon}, v_\varepsilon, w_\varepsilon)$ tel que $u_{i,\varepsilon} \in L^2(0, T; H^1(\Omega_{i,\varepsilon}))$, $u_{e,\varepsilon} \in L^2(0, T; H^1(\Omega_{e,\varepsilon}))$, $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon)) \cap L^r(\Gamma_{\varepsilon,T})$ ($r \in (2, +\infty)$ est précisée dans la condition (C.3) plus tard), $w_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, $\partial_t v_\varepsilon, \partial_t w_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, et satisfaisant la formulation faible suivante pour presque tout $t \in (0, T)$*

$$\begin{aligned} \int_{\Gamma_\varepsilon} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, dx \\ + \int_{\Gamma_\varepsilon} \varepsilon I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \varphi \, ds(x) = \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x), \end{aligned} \quad (4)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_\varepsilon \zeta \, ds(x) - \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon) \zeta \, ds(x) = 0, \quad (5)$$

pour tout $\varphi_j \in H^1(\Omega_{j,\varepsilon})$ avec $\varphi := (\varphi_i - \varphi_e)|_{\Gamma_\varepsilon} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$ pour $j = i, e$ et $\zeta \in L^2(\Gamma_\varepsilon)$.

Les hypothèses portant sur le système (1)-(3) sont données par:

(C.1) Le domaine Ω (le tissu cardiaque) est un ouvert borné dans \mathbb{R}^3 avec frontière régulière $\partial\Omega$. Le tissu cardiaque est composé de deux régions connexes, la région intracellulaire $\Omega_{i,\varepsilon}$ et extracellulaire $\Omega_{e,\varepsilon}$. Ces deux régions sont séparées par une membrane active $\Gamma_\varepsilon = \partial\Omega_{i,\varepsilon} \cap \partial\Omega_{e,\varepsilon}$. Suivant l'approche standard de l'homogénéisation, les cellules sont supposées être organisées d'une façon périodique.

Soit $Y := [0, 1]^3$ une représentation d'une cellule de référence dans \mathbb{R}^3 . On note par $Y_{i,e} \subset Y$, ses parties intra- et extracellulaire et par Γ leur frontière commune ($\Gamma = \partial Y_i \cap \partial Y_e$) tels que $Y_i \cup Y_e \cup \Gamma = Y$.

Les domaines physiques intra- ou extracellulaires sont des ε -dilatations des treillis de référence $Y_{i,e}$ étendus périodiquement, et définies par: pour $k \in \mathbb{Z}^3$,

$$Y_{j,k,\varepsilon} := \varepsilon k + \varepsilon Y_j = \{\varepsilon \xi : \xi \in k + Y_j\},$$

et leur frontière commune

$$\Gamma_{k,\varepsilon} := \varepsilon k + \varepsilon \Gamma = \{\varepsilon \xi : \xi \in k + \Gamma\}.$$

Donc les domaines intra- et extracellulaire $\Omega_{j,\varepsilon}$ pour $j = i, e$ peuvent être simplement

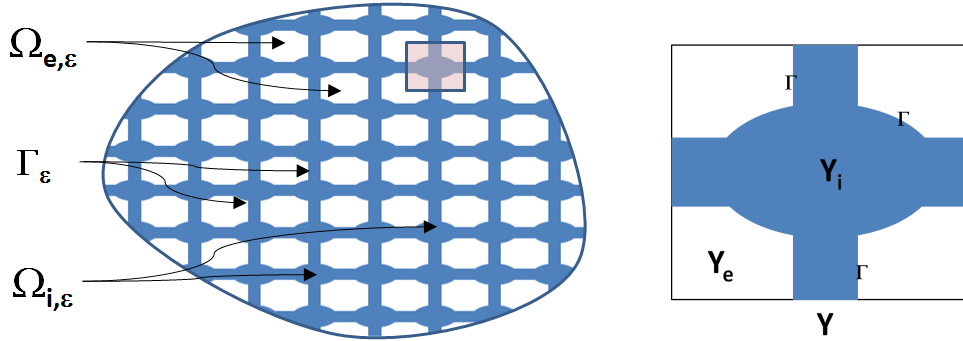


Figure 4 – Gauche: Une section 2D de l'organisation périodique des treillis. Droite: Section 2D du treillis de référence Y .

obtenus en prenant l'intersection de Ω avec $Y_{j,k,\varepsilon}$ pour $j = i, e$ (voir Figure 4), i.e.:

$$\Omega_{j,\varepsilon} = \Omega \cap \bigcup_{k \in \mathbb{Z}^3} Y_{j,k,\varepsilon}.$$

De même,

$$\Gamma_\varepsilon = \Omega \cap \bigcup_{k \in \mathbb{Z}^3} \Gamma_{k,\varepsilon}.$$

La frontière Γ est une variété régulière telle que Γ_ε est régulière et connexe. En outre, les domaines $\Omega_{j,\varepsilon}$ sont supposés être bornés et connexes dans \mathbb{R}^3 .

(C.2) La conductivité du tissu est représentée par des tenseurs symétriques Lipschitziens $\mathbf{M}_{i,\varepsilon}(x) = \mathbf{M}_i(x, x/\varepsilon)$ et $\mathbf{M}_{e,\varepsilon}(x) = \mathbf{M}_e(x, x/\varepsilon)$ vérifiant les conditions de coercivité et périodicité suivantes: Il existe des constantes $m_1, m_2 > 0$ telles que pour $j = i, e$

$$m_1 |\zeta|^2 \leq \mathbf{M}_j(x, \xi) \zeta \cdot \zeta \leq m_2 |\zeta|^2, \quad (6a)$$

$$\mathbf{M}_j(x, \xi + e_k) = \mathbf{M}_j(x, \xi), \quad (6b)$$

pour tout $(x, \xi) \in \Omega \times Y_j$ et $\zeta \in \mathbb{R}^3$.

(C.3) Le courant ionique $I_{\text{ion}}(u, w)$ est la somme de $I_{1,\text{ion}}(u)$ et $I_{2,\text{ion}}(w)$. La fonction $I_{1,\text{ion}} : \mathbb{R} \rightarrow \mathbb{R}$ est de classe C^1 , et les fonctions $I_{2,\text{ion}} : \mathbb{R} \rightarrow \mathbb{R}$ et $H : \mathbb{R}^2 \rightarrow \mathbb{R}$ sont linéaires. De

plus, nous supposons qu'il existe $r \in (2, +\infty)$ et des constantes $\alpha_1, \alpha_2, \alpha_3, L > 0, l \geq 0$ telles que

$$\begin{aligned} \frac{1}{\alpha_1} |v|^{r-1} \leq |I_{1,\text{ion}}(v)| &\leq \alpha_1 (|v|^{r-1} + 1), \\ \text{et } I_{2,\text{ion}}(w)v - \alpha_2 H(v, w)w &\geq \alpha_3 |w|^2, \end{aligned} \quad (7)$$

$$\tilde{I}_{1,\text{ion}} : z \mapsto I_{1,\text{ion}}(z) + Lz + l \quad \text{est strictement croissante sur } \mathbb{R} \quad \text{avec } \lim_{z \rightarrow 0} \tilde{I}_{1,\text{ion}}(z)/z = 0 \quad (8a)$$

$$\text{et } \forall z, s \in \mathbb{R} \quad (\tilde{I}_{1,\text{ion}}(z) - \tilde{I}_{1,\text{ion}}(s))(z - s) \geq \frac{1}{C} (1 + |z| + |s|)^{r-2} |z - s|^2. \quad (8b)$$

(C.4) Il existe une constante C indépendante de ε telle que le terme source $I_{\text{app},\varepsilon}$ vérifie:

$$\|\varepsilon^{1/2} I_{\text{app},\varepsilon}\|_{L^2(\Gamma_{\varepsilon,T})} \leq C. \quad (9)$$

De plus, I_{app} est la limite faible de la suite d'éclatement correspondante.

(C.5) Les données initiales $v_{0,\varepsilon}$ et $w_{0,\varepsilon}$ vérifient

$$\|\varepsilon^{1/r} v_{0,\varepsilon}\|_{L^r(\Gamma_\varepsilon)} + \|\varepsilon^{1/2} v_{0,\varepsilon}\|_{L^2(\Gamma_\varepsilon)} + \|\varepsilon^{1/2} w_{0,\varepsilon}\|_{L^2(\Gamma_\varepsilon)} \leq C, \quad (10)$$

pour une constante C indépendante de ε . De plus, $v_{0,\varepsilon}$ et $w_{0,\varepsilon}$ sont les traces de suites uniformément bornées dans $C^1(\bar{\Omega})$.

(C.6) Nous imposons la condition de compatibilité suivante:

$$\int_{\Omega_{e,\varepsilon}} u_{e,\varepsilon}(t, x) \, d\mathbf{x} = 0 \text{ p.p. dans } (0, T). \quad (11)$$

Nous énonçons maintenant le premier théorème démontré dans ce chapitre:

Théorème 1 (Modèle Bidomaine Microscopique). *Sous les conditions (C.1), ..., (C.6), si $v_{0,\varepsilon} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$, $w_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)$, le problème bidomaine microscopique (1)-(3) admet une solution faible unique au sens de la Définition 1.*

Il est important de noter que la preuve est constructive, basée sur la méthode Faedo-Galerkin sur des systèmes approchés suivie par la compacité dans L^2 , et sans la condition trouvée dans la littérature qui imposent que les matrices de conductivité doivent être diagonales ou avoir la même base de vecteurs propres. Le deuxième résultat est celui de l'homogénéisation, où le paramètre ε tend vers 0.

Théorème 2 (Modèle Bidomaine Macroscopique). *Une suite de solutions $(u_{i,\varepsilon}, u_{e,\varepsilon}, w_\varepsilon)_\varepsilon$ du système microscopique (1)-(3) (obtenues dans le théorème 1) converge vers une solution faible (u_i, u_e, w) avec $v = u_i - u_e$, $u_i, u_e \in L^2(0, T; H^1(\Omega))$, $v \in L^2(0, T; H^1(\Omega)) \cap L^r(\Omega)$, $\partial_t v \in L^2(0, T; (H^1(\Omega))') + L^{r/(r-1)}(\Omega)$ et $w \in C(0, T; L^2(\Omega))$, du problème macroscopique*

$$|\Gamma| \partial_t v - \nabla \cdot (\mathcal{M}_i(x) \nabla u_i) + |\Gamma| I_{\text{ion}}(v, w) = |\Gamma| I_{\text{app}} \text{ dans } \Omega_T, \quad (12a)$$

$$|\Gamma| \partial_t v + \nabla \cdot (\mathcal{M}_e(x) \nabla u_e) + |\Gamma| I_{\text{ion}}(v, w) = |\Gamma| I_{\text{app}} \text{ dans } \Omega_T, \quad (12b)$$

$$\partial_t w - H(v, w) = 0 \text{ dans } \Omega_T. \quad (12c)$$

complété par les conditions au bord, représentant un tissu cardiaque isolé

$$(\mathcal{M}_j(x)\nabla u_j) \cdot \mathbf{n} = 0 \text{ sur } \Sigma_T := \partial\Omega \times (0, T), \quad j \in \{e, i\}, \quad (13)$$

et les conditions initiales, v_0 et $w_0 \in L^2(\Omega)$, pour le potentiel transmembranaire et la variable de porte

$$v(0, x) = v_0(x), \quad w(0, x) = w_0(x). \quad (14)$$

Le vecteur \mathbf{n} désigne la normale unitaire à $\partial\Omega$ sortante de Ω et les tenseurs \mathcal{M}_i et \mathcal{M}_e sont définis, respectivement pour $j = i, e$ par

$$\mathcal{M}_j := \int_{Y_j} (\mathbf{M}_j + \mathbf{M}_j \nabla_\xi f(\xi)) d\xi, \quad (15)$$

où les composantes $f_{k,j}$ de f_j ($k = 1, 2, 3$) sont les fonctions correctrices, solutions des problèmes cellulaires

$$\begin{cases} -\nabla_y \cdot (\mathbf{M}_j \nabla_y f_{k,j}) = -\nabla_y \cdot (\mathbf{M}_j e_k) & \text{dans } Y_j, \\ \mathbf{M}_j \nabla_y f_{k,j} \cdot \mu_j = \mathbf{M}_j e_k \cdot \mu_j & \text{sur } \Gamma, \\ \int_{Y_j} f_{k,j} = 0, & f_{k,j} \text{ } Y\text{-périodique.} \end{cases}$$

En utilisant la méthode d'éclatement périodique ("unfolding" en anglais), nous montrons la convergence de la suite de solutions du problème microscopique vers la solution du problème macroscopique. À cause des termes non linéaires sur la variété, nous utilisons l'opérateur d'éclatement sur la surface et un argument de compacité de type Kolmogorov.

Dans la dernière partie de ce chapitre, nous considérons un modèle ionique physiologique et nous montrons l'existence et l'unicité d'une solution du problème microscopique. Puis, nous obtenons la solution faible du problème macroscopique par passage à la limite en ε . Dans ce modèle, l'équation différentielle ordinaire est remplacée par un système d'équations et une variable de concentration, qui apparaît comme un argument d'une fonction logarithmique, y intervient. L'hypothèse (C.3), sur le modèle ionique, est maintenant remplacée par les conditions suivantes:

(A.1) On définit la fonction \mathbf{R} par $\mathbf{R}(v, \mathbf{w}) := (R_1(v, w_1), \dots, R_k(v, w_k))$ où $R_l : \mathbb{R}^2 \rightarrow \mathbb{R}$ sont globalement Lipschitziennes et données par

$$R_l(v, \mathbf{w}) = \alpha_l(v)(1 - w_l) - \beta_l(v)w_l \quad (16)$$

où α_l et β_l , $l = 1, \dots, k$ sont des fonctions positives et rationnelles d'exponentielles en v telles que:

$$0 < \alpha_l(v), \beta_l(v) \leq C_{\alpha, \beta}(1 + |v|). \quad (17)$$

(A.2) La fonction $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty) \rightarrow \mathbb{R}$ a la forme générale suivante:

$$I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{l=1}^k I_{\text{ion}}^l(v, w_l) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \quad (18)$$

où $I_{\text{ion}}^l \in C^0(\mathbb{R} \times \mathbb{R}) \cap \text{Lip}(\mathbb{R} \times [0, 1])$ et vérifie la condition:

$$|I_{\text{ion}}^l(v, w_l)| \leq C_{1,I}(1 + |w_l| + |v|), \quad (19)$$

et I_{ion}^z est telle que:

$$I_{\text{ion}}^z \in C^1(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}^+ \times \mathbb{R}) \cap \text{Lip}(\mathbb{R} \times [0, 1]^k \times \mathbb{R}^+ \times \mathbb{R}),$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \leq C_{2,I}(1 + |v| + |w| + |z| + \ln z), \quad (20)$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3,I} \sum_{l=1}^k (|v| + w_l + w_l \ln z), \quad (21)$$

$$0 < \underline{\Theta}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(\mathbf{w}), \quad (22)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \right| \leq L(\mathbf{w}), \quad (23)$$

$$\frac{\partial}{\partial w_l} I_{\text{ion}}^z \leq C_{4,I}(1 + |v| + |\ln z|), \quad \forall l = 1, \dots, k, \quad (24)$$

$$0 \leq \frac{\partial}{\partial z} I_{\text{ion}}^z \leq C_{5,I}, \quad (25)$$

où $\underline{\Theta}$, $\bar{\Theta}$ et L appartiennent à $C^0(\mathbb{R}, \mathbb{R}^+)$ et $C_{1,I}, \dots, C_{5,I}$ sont des constantes positives.

(A.3) La fonction $G \in \text{Lip}(\mathbb{R} \times [0, 1]^k \times \mathbb{R}^+)$ est donnée par:

$$G(v, \mathbf{w}, z) = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z), \quad (26)$$

où a_1, a_2, a_3 sont des constantes positives physiologiques qui varient d'un ion à l'autre. Dans notre cas, nous considérons que z correspond à la concentration intracellulaire du calcium.

Remarque 1. Les hypothèses (A.1)-(A.3) sont vérifiées par le modèle ionique de Beeler-Reuter et Luo-Rudy I [BR77, LR94]. Dans le modèle ionique Luo-Rudy I, il y a plusieurs variables de concentration mais pour simplifier les estimations, nous avons considéré juste une seule variable.

Avec les hypothèses précédentes, le système microscopique devient:

$$-\nabla \cdot (\mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon}) = 0 \text{ dans } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \quad (27a)$$

$$\varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m \text{ sur } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \quad (27b)$$

$$\mathcal{I}_m = -\mathbf{M}_{i,\varepsilon} \nabla u_{i,\varepsilon} \cdot \mu_i = \mathbf{M}_{e,\varepsilon} \nabla u_{e,\varepsilon} \cdot \mu_e \text{ sur } \Gamma_{\varepsilon,T}, \quad (27c)$$

$$\partial_t \mathbf{w}_\varepsilon - \mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) = 0 \text{ sur } \Gamma_{\varepsilon,T}, \quad (27d)$$

$$\partial_t z_\varepsilon - G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) = 0 \text{ sur } \Gamma_{\varepsilon,T}, \quad (27e)$$

avec les conditions au bord

$$(\mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon}) \cdot \mu_j = 0 \text{ sur } (0, T) \times (\partial \Omega_{j,\varepsilon} \setminus \Gamma_\varepsilon), \quad j \in \{e, i\}, \quad (28)$$

et les conditions initiales convenables

$$v_\varepsilon(0, \cdot) = v_{0,\varepsilon}(\cdot), \quad \mathbf{w}_\varepsilon(0, \cdot) = \mathbf{w}_{0,\varepsilon}(\cdot), \quad z_\varepsilon(0, \cdot) = z_{0,\varepsilon}(\cdot) \text{ sur } \Gamma_\varepsilon, \quad (29)$$

où $v_{0,\varepsilon} \in H^{1/2}(\Gamma_\varepsilon)$, $z_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)$ et $\mathbf{w}_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)^k$ avec $z_{0,\varepsilon} > c_0 > 0$ pour une constante $c_0 > 0$ et $0 \leq w_{l,0,\varepsilon} \leq 1$ pour $l = 1, \dots, k$.

Par analogie au modèle microscopique avec la dynamique de FitzHugh-Nagumo généralisée, on obtient le résultat d'existence et d'unicité suivant.

Théorème 3. *Supposons que les conditions (A.1)-(A.3), (C.1), (C.2), et (C.4)-(C.6) sont vérifiées. Si $v_{0,\varepsilon} \in H^{1/2}(\Gamma_\varepsilon)$, $z_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)$ et $\mathbf{w}_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)^k$ avec $z_{0,\varepsilon} > c_0 > 0$ pour une constante $c_0 > 0$ et $0 \leq w_{l,0,\varepsilon} \leq 1$ pour $l = 1, \dots, k$, le problème microscopique (27),(28),(29) admet une solution faible unique définie comme: $u_{i,\varepsilon} \in L^2(0, T; H^1(\Omega_{i,\varepsilon}))$, $u_{e,\varepsilon} \in L^2(0, T; H^1(\Omega_{e,\varepsilon}))$, avec $\int_{\Omega_{e,\varepsilon}} u_{e,\varepsilon} = 0$, $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} \in L^2(\Gamma_{\varepsilon,T})$, $\mathbf{w}_\varepsilon \in (L^2(\Gamma_{\varepsilon,T}))^k$, $z_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, $\partial_t v_\varepsilon, \partial_t z_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, et $\partial_t \mathbf{w}_\varepsilon \in (L^2(\Gamma_{\varepsilon,T}))^k$ telles que*

$$\begin{aligned} \iint_{\Gamma_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, d\mathbf{x} \, dt \\ + \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \varphi \, ds(x) \, dt = \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt, \end{aligned} \quad (30)$$

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t w_{l,\varepsilon} \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} R_l(v_\varepsilon, \mathbf{w}_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (31)$$

pour $l = 1, \dots, k$ et

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t z_\varepsilon \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (32)$$

pour tout $\varphi_j \in L^2(0, T; H^1(\Omega_{j,\varepsilon}))$ avec $\varphi := (\varphi_i - \varphi_e)|_{\Gamma_\varepsilon} \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon))$, $j = i, e$ et $\phi \in L^2(\Gamma_{\varepsilon,T})$.

Finalement, par passage à la limite quand ε tend vers 0, nous avons le résultat suivant:

Théorème 4 (Modèle Bidomaine Macroscopique Physiologique). *Il existe une suite de solutions $(u_{i,\varepsilon}, u_{e,\varepsilon}, \mathbf{w}_\varepsilon, z_\varepsilon)_\varepsilon$ du système microscopique (27)-(29) (obtenues dans le théorème 3) qui converge vers une solution faible $(u_i, u_e, \mathbf{w}, z)$ avec $v = u_i - u_e$, $u_i, u_e \in L^2(0, T; H^1(\Omega))$, $v \in L^2(0, T; H^1(\Omega))$, $\partial_t v \in L^2(0, T; (H^1(\Omega))')$, $\mathbf{w} \in C(0, T; L^2(\Omega))^k$ et $z \in C(0, T; L^2(\Omega))$ du problème macroscopique*

$$|\Gamma| \partial_t v - \nabla \cdot (\mathcal{M}_i(x) \nabla u_i) + |\Gamma| I_{\text{ion}}(v, \mathbf{w}) = |\Gamma| I_{\text{app}} \text{ dans } \Omega_T, \quad (33a)$$

$$|\Gamma| \partial_t v + \nabla \cdot (\mathcal{M}_e(x) \nabla u_e) + |\Gamma| I_{\text{ion}}(v, \mathbf{w}) = |\Gamma| I_{\text{app}} \text{ dans } \Omega_T, \quad (33b)$$

$$\partial_t \mathbf{w} - \mathbf{R}(v, \mathbf{w}) = 0 \text{ dans } \Omega_T, \quad (33c)$$

$$\partial_t z - G(v, \mathbf{w}, z) = 0 \text{ dans } \Omega_T, \quad (33d)$$

avec les conditions au bord

$$(\mathcal{M}_j(x) \nabla u_j) \cdot \mathbf{n} = 0 \text{ sur } \Sigma_T := \partial\Omega \times (0, T), \quad j \in \{e, i\}, \quad (34)$$

et les conditions initiales, $v_0, z_0 \in L^2(\Omega)$ et $\mathbf{w}_0 \in L^2(\Omega)^k$, pour le potentiel transmembranaire, la variable de concentration et les variables de portes

$$v(0, x) = v_0(x), \quad z(0, x) = z_0(x), \quad \text{et } \mathbf{w}(0, x) = \mathbf{w}_0(x), \quad (35)$$

où \mathbf{n} est la normale unitaire sortante de $\partial\Omega$ et les tenseurs \mathcal{M}_i et \mathcal{M}_e sont définis respectivement pour $j = i, e$ par (15).

Pour démontrer ce dernier théorème, on utilise (comme pour le cas des modèles phénoménologiques) la méthode d'éclatement périodique. Par contre, pour les termes non linéaires, nous recourons à l'utilisation d'un argument de type Minty parce que des estimations sur les translatés en espace des variables \mathbf{w} et z semblent hors de portée.

Chapitre 3

Dans ce chapitre, nous nous sommes intéressés au modèle monodomaine de l'électrophysiologie cardiaque couplé avec le modèle ionique Beeler-Reuter. Le modèle monodomaine est une simplification du modèle bidomaine, obtenue dans le cas particulier où les rapports d'anisotropie dans les milieux intra- et extra-cellulaires sont égaux. Le modèle ionique Beeler-Reuter est l'un des premiers modèles physiologiques décrivant l'électrophysiologie des myocytes ventriculaires chez les mammifères. Plus précisément, nous considérons le système suivant:

$$\left\{ \begin{array}{ll} \frac{\partial v}{\partial t} = \nabla \cdot (\Lambda \nabla v) - I_{\text{ion}}(v, \mathbf{w}, c), & \text{p.p. dans } \Omega_T, \\ \frac{\partial w_j}{\partial t} = \alpha_j(v)(1 - w_j) - \beta_j(v)w_j, & \text{p.p. dans } \Omega_T \text{ et pour } j = 1, \dots, 6, \\ \frac{\partial c}{\partial t} = 0.07(10^{-4} - c) - 10^{-4}I_s(v, f, r, c), & \text{p.p. dans } \Omega_T, \\ v(0, x) = v_0(x), & \text{p.p. dans } \Omega, \\ \mathbf{w}(0, x) = \mathbf{w}_0(x), & \text{p.p. dans } \Omega, \\ c(0, x) = c_0(x), & \text{p.p. dans } \Omega, \\ \Lambda(x)\nabla v \cdot \mathbf{n} = 0 & \text{p.p. sur } \partial\Omega \times (0, T). \end{array} \right. \quad (36)$$

L'objectif est de proposer un schéma numérique robuste et convergent du système (36) avec des solutions vérifiant les bornes physiologiques. La difficulté principale se manifeste quand la conductivité dans le terme diffusif est anisotrope. Dans la première partie de ce chapitre, nous utilisons la méthode des volumes finis classique sous la condition d'isotropie du milieu. Cette méthode, qui conserve les flux, est inefficace pour approcher les flux diffusifs avec des tenseurs anisotropes. Néanmoins, comme la méthode des éléments finis permet une discrétisation simple pour approcher les flux de diffusion, nous introduisons, dans la deuxième partie du chapitre, un schéma combiné non-linéaire qui préserve le principe de maximum (les bornes physiologiques). Le domaine occupé par le cœur est toujours noté Ω , un ensemble ouvert, borné, connexe et polygonal de \mathbb{R}^d , $d = 2, 3$. Le bord de Ω est noté $\partial\Omega$, le temps final est fixé à $T > 0$, et nous notons $\Omega_T = (0, T) \times \Omega$. La variable c représente la concentration intracellulaire de calcium ($c = 10^3[Ca^{++}]_i$) et les composantes du vecteur des variables de porte $\mathbf{w} : \Omega_T \rightarrow \mathbb{R}^6$ sont m, o, l, f, r, z et désignent w_j , $j = 1, \dots, 6$, respectivement. Nous donnons également les hypothèses portant sur la conductivité, les fonctions ioniques et les données initiales:

(H.1) Sous la condition d'isotropie, la conductivité Λ est représentée par le tenseur $\lambda(x)\mathbf{I}$ où \mathbf{I} est la matrice identité de dimensions $d \times d$ et $\lambda(x) \in L^\infty(\Omega)$ telle que

$$\lambda : \Omega \rightarrow \mathbb{R}^+, \quad \text{et } \exists m_0, \text{ telle que } \lambda(x) \geq m_0 > 0, \text{ p.p. dans } \Omega. \quad (37)$$

(H.2) Les fonctions α_j et β_j qui représentent respectivement le taux d'ouverture et de clôture des différents canaux ioniques, sont lipschitziennes et données par

$$\alpha_j(v) = \frac{c_{1,j}e^{c_{2,j}(v+c_{3,j})} + c_{4,j}(v + c_{5,j})}{e^{c_{6,j}(v+c_{3,j})} + c_{7,j}},$$

et

$$\beta_j(v) = \frac{d_{1,j}e^{d_{2,j}(v+d_{3,j})} + d_{4,j}(v + d_{5,j})}{e^{d_{6,j}(v+d_{3,j})} + d_{7,j}},$$

où $c_{i,j}$ et $d_{i,j}$, $i = 1, \dots, 7$, $j = 1, \dots, 6$ sont des constantes telles que

$$\alpha_j(v), \beta_j(v) > 0. \quad (38)$$

(H.3) La fonction $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^6 \times \mathbb{R}^+ \rightarrow \mathbb{R}$ est la collection des courants transmembranaires, contenant quatre courants. La direction de deux parmi ceux-ci, I_{Pot} et I_z , représentant le flux des ions de potassium (K^+), est vers l'extérieur de la cellule. Aussi, deux courants sont dirigés vers l'intérieur: le courant de sodium Na^+ , noté I_{Na} , et le courant lent de calcium, noté I_s . Les expressions de ces fonctions sont détaillées dans le chapitre 1. L'expression du courant ionique total est donnée par:

$$I_{\text{ion}}(v, \mathbf{w}, [Ca^{++}]) = I_{Pot}(v) + I_z(v, z) + I_{Na}(v, m, o, l) + I_s(v, f, r, c).$$

(H.4) Les données initiales (v_0, \mathbf{w}_0, c_0) , sont supposées vérifier

$$\begin{aligned} v_m \leq v_0 \leq v_M & \quad \text{p.p. dans } \Omega, \\ c_m \leq c_0 \leq c_M & \quad \text{p.p. dans } \Omega, \\ 0 \leq w_{0,j} \leq 1 & \quad \text{p.p. dans } \Omega, \text{ pour } j = 1, \dots, 6 \end{aligned} \quad (39)$$

où $v_m = -85$, $v_M = 127.69$, $c_m = 10^{-4}$ et $c_M = 0.0187$ sont des constantes données.

Schéma Volumes Finis

Dans la première partie du Chapitre 3, nous définissons d'abord la solution faible du système (36):

Définition 2. *Sous les hypothèses, (H.1)-(H.4), un vecteur $\mathbf{U} = (v, \mathbf{w}, c)$ est dit solution faible du système (36), s'il vérifie:*

$$\begin{aligned} v \in L^\infty(\Omega_T) \cap L^2(0, T; H^1(\Omega)), \mathbf{w} \in L^\infty(\Omega_T)^6 \text{ et } c \in L^\infty(\Omega_T), \\ v_m \leq v \leq v_M, c_m \leq c \leq c_M \text{ et } 0 \leq w_j \leq 1 \text{ pour presque tout } (t, x) \in \Omega_T, \text{ pour } \\ j = 1, \dots, 6 \end{aligned}$$

et pour tout φ et $\xi \in \mathcal{D}([0, T) \times \bar{\Omega})$

$$- \int_{\Omega} v_0(x) \varphi(0, x) dx + \iint_{\Omega_T} (-v \partial_t \varphi + \lambda \nabla v \cdot \nabla \varphi) dx dt = \iint_{\Omega_T} -I_{\text{ion}}(v, \mathbf{w}, c) \varphi dx dt, \quad (40)$$

$$- \int_{\Omega} w_{0,k}(x) \xi(0, x) dx + \iint_{\Omega_T} -w_k \partial_t \xi dx dt = \iint_{\Omega_T} (\alpha_k(v)(1 - w_k) - \beta_k(v)w_k) \xi dx dt, \quad (41)$$

pour $k = 1, \dots, 6$ et

$$- \int_{\Omega} c_0(x) \xi(0, x) dx + \iint_{\Omega_T} -c \partial_t \xi dx dt = \iint_{\Omega_T} (0.07(10^{-4} - c) - 10^{-4} I_s(v, f, d, c)) \xi dx dt. \quad (42)$$

Nous utilisons, ensuite, la méthode de volumes finis pour discrétiser les équations du système (36) afin d'obtenir un schéma vérifiant le principe de maximum. Nous décrivons d'abord les discrétisations en espace et en temps (voir [EGGH98]) pour écrire la discrétisation de (36) en volumes finis.

Discrétisation en espace On rappelle que le domaine Ω est un ouvert borné polygonal et connexe de bord $\partial\Omega$ et qu'il est inclu dans \mathbb{R}^d ($d = 2$ ou $d = 3$). On considère un maillage admissible \mathcal{T}_h du domaine Ω (au sens de [EGH00]), formé de polygones K ouverts et connexes nommés "volumes de contrôle" et une famille $\mathcal{P} = (x_K)_{K \in \mathcal{T}_h}$, où x_K est le centre du volume K tel que $\overline{x_K x_L} \perp \sigma_{K,L}$ où $\sigma_{K,L}$ est l'interface commune entre deux volumes de contrôle voisins. Dans le cas d'une triangularisation, on prend x_K comme étant le centre du cercle circonscrit de K . Nous utilisons les notations suivantes:

- \mathcal{E} est l'ensemble des arêtes ou faces notées σ du maillage, pour $d = 2, 3$ respectivement.
- Pour tout $K \in \mathcal{T}_h$, \mathcal{E}_K est le sous-ensemble de \mathcal{E} tel que $\partial K = \bigcup_{\sigma \in \mathcal{E}_K} \sigma$.
- \mathcal{E}_{int} est l'ensemble des interfaces intérieures du maillage et $\mathcal{E}_{ext} = \{\sigma \in \mathcal{E}; \sigma \subset \partial\Omega\}$.
- $N(K) = \{L \in \mathcal{T}_h; \exists \sigma \in \mathcal{E}_K, \bar{\sigma} = \bar{K} \cap \bar{L}\}$ est l'ensemble des volumes de contrôle voisins de K .
- $\mathbf{n}_{K,L}$ est la normale à $\sigma_{K,L}$ (le côté commun entre les volumes K et L) sortant de K .
- Le coefficient de transmissibilité à travers $\sigma_{K,L}$ est donné par

$$\tau_{K,L} = \frac{|\sigma_{K,L}|}{d_{K,L}},$$

où $d_{K,L}$ est la distance entre les centres x_K et x_L de K et L respectivement.

- $T_{K,L}$ est le diamant convexe construit en reliant deux centres voisins x_K et x_L aux sommets de l'interface commune $\sigma_{K,L}$ (voir Figure 5). Quand $\sigma \in \partial K \cap \partial\Omega$, le demi-diamant $T_{K,\sigma}$ est construit en reliant le centre x_K au sommets de l'interface σ .

Discrétisation en temps La discrétisation de l'intervalle de temps $[0, T]$ est donnée par un pas de temps Δt et un entier positif N tels que $N\Delta t = T$. On note $t_n = n\Delta t$ pour $n \in \{0, \dots, N\}$.

Discrétisation de Ω_T Une discrétisation admissible \mathcal{D} de Ω_T est définie par

$$\mathcal{D} = \left(\mathcal{T}, \mathcal{E}, (x_K)_{K \in \mathcal{T}}, N, (t_n)_{n \in \{0, \dots, N\}} \right)$$

où $(\mathcal{T}, \mathcal{E}, (x_K)_{K \in \mathcal{T}})$ est un maillage admissible de Ω et $N, (t_n)_{n \in \{0, \dots, N\}}$ est la discrétisation de $(0, T)$.

Fonctions Discrètes Sur un maillage admissible \mathcal{T}_h , une fonction discrète u est définie par un ensemble $\{u_K\}_{K \in \mathcal{T}_h}$ et est identifiée à une fonction u_h constante par morceaux telle que: $u_h|_K = u_K, \forall K \in \mathcal{T}_h$. Étant donné deux fonctions discrètes w_h et u_h , le produit scalaire et la norme dans $L^2(\Omega)$ sont définis par:

$$(u_h, w_h)_{L^2(\Omega)} = \sum_{K \in \mathcal{T}_h} |K| w_K u_K, \quad \|w_h\|_{L^2(\Omega)}^2 = \sum_{K \in \mathcal{T}_h} |K| |w_K|^2.$$

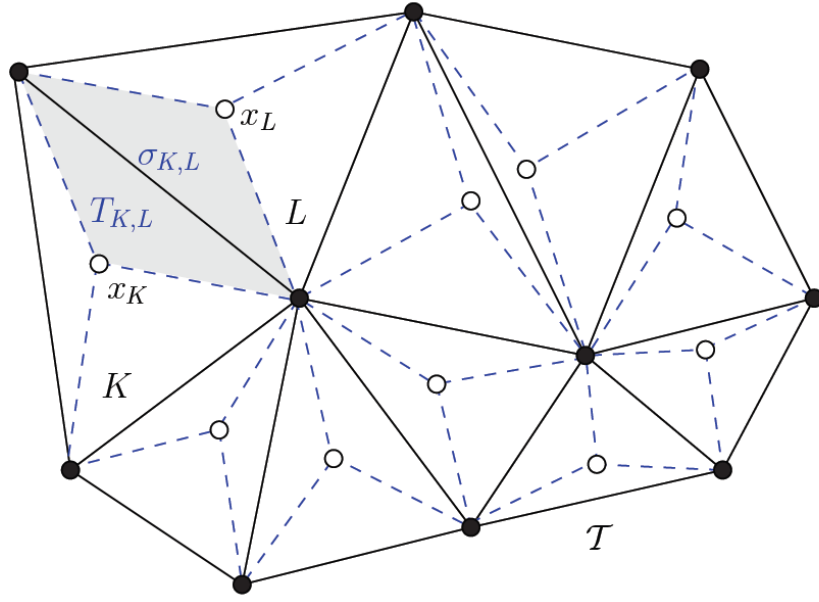


Figure 5 – Volumes de contrôle, centres et diamants (en lignes détachées).

Le gradient discret $\nabla_h u_h$ d'une fonction u_h , constante par volume de contrôle, est défini sur le maillage dual comme une fonction constante par diamant $T_{K,L}$:

$$\nabla_h u_h(x) = \begin{cases} d \frac{u_L - u_K}{d_{K,L}} \mathbf{n}_{K,L} & \text{si } x \in T_{K,L}, \\ 0 & \text{si } x \in T_{K,\sigma}. \end{cases}$$

Pour une fonction u_h , constante par volume de contrôle, la semi-norme H^1 discrète est définie par:

$$|u_h|_{1,\mathcal{T}_h} = \left(d \sum_{\sigma_{K,L} \in \mathcal{E}} \tau_{K,L} (u_L - u_K)^2 \right)^{1/2}.$$

Comme le problème considéré dépend du temps, nous définissons aussi des fonctions sur la discrétisation \mathcal{D} du cylindre espace-temps $(0, T) \times \Omega$. Nous utilisons l'indice \mathcal{D} pour représenter les fonctions constantes par sous-intervalle de temps et volume de contrôle et les indices K et n pour leurs valeurs en (t_n, x_K) :

$$u_{\mathcal{D}}(t, x) = u_K^{n+1}, \text{ pour presque tout } (t, x) \in (t_n, t_{n+1}] \times K, \forall K \in \mathcal{T}_h, \forall n \in \{0, \dots, N-1\}.$$

Schéma Numérique En utilisant une discrétisation Euler semi-implicite en temps, on peut écrire le schéma volumes finis suivant, ayant comme inconnues $(v_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$, $(\mathbf{w}_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$ et $(c_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$: $\forall K \in \mathcal{T}_h$,

$$v_K^0 = \frac{1}{|K|} \int_K v_0(x) dx, \mathbf{w}_K^0 = \frac{1}{|K|} \int_K \mathbf{w}_0(x) dx, \text{ et } c_K^0 = \frac{1}{|K|} \int_K c_0(x) dx \quad (43)$$

et $\forall n \in \{0, \dots, N-1\}, \forall K \in \mathcal{T}_h$,

$$\frac{|K|}{\Delta t}(v_K^{n+1} - v_K^n) + \sum_{\sigma \in \mathcal{E}_K \cap \mathcal{E}_{int}} F_{K,\sigma}^{n+1} = -|K| \left(I_{Pot}(v_K^n) + I_z(v_K^n, z_K^{n+1}) \right) \quad (44)$$

$$+ I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n),$$

$$w_{j,K}^{n+1} - w_{j,K}^n = \Delta t \left(\alpha_j(v_K^n)(1 - w_{j,K}^{n+1}) - \beta_j(v_K^n)w_{j,K}^{n+1} \right), \text{ pour } j = 1, \dots, 6, \quad (45)$$

$$c_K^{n+1} - c_K^n = \Delta t \left(0.07(10^{-4} - c_K^{n+1}) - g_s 10^{-4} f_K^n r_K^n (v_K^{n+1} - 7.7 + 13.0287 \ln(c_K^{n+1})) \right), \quad (46)$$

où $F_{K,\sigma}^{n+1}$ est une approximation de $\int_{\sigma} -\lambda(x) \nabla v(t_{n+1}, x) \cdot \mathbf{n}_{K,\sigma} d\gamma$ qui garantit la conservation des flux et qui tient compte de la condition au bord de type Neumann. On définit cette approximation comme suit:

$$F_{K,\sigma}^{n+1} = 0, \quad \forall K \in \mathcal{T}_h, \forall \sigma \in \mathcal{E}_K \cap \mathcal{E}_{ext}.$$

$$F_{K,\sigma}^{n+1} = -\tau_{\sigma}(v_L^{n+1} - v_K^{n+1}), \text{ si } \sigma \in \mathcal{E}_{int}, \sigma = \sigma_{K,L}, \text{ où}$$

$$\tau_{\sigma} = |\sigma| \frac{\lambda_K \lambda_L}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}},$$

avec $\lambda_K = \frac{1}{|K|} \int_K \lambda(x) dx$ et $d_{K,\sigma}$ la distance de x_K à l'interface σ , pour $K \in \mathcal{T}_h$ et $\sigma \in \mathcal{E}_K$.

Résultat Principal Le résultat principal de cette partie est donné par le théorème suivant dont la preuve repose sur plusieurs lemmes et propositions détaillées dans la première partie du chapitre 3.

Théorème 5. Soient $v_0 \in L^\infty(\Omega)$, $\mathbf{w}_0 \in H^1(\Omega)^6$ et $c_0 \in H^1(\Omega)$, vérifiant les inégalités (39). Étant donné les hypothèses (H.1)-(H.4), le schéma (44)-(46) admet une solution unique $\mathbf{U}_{\mathcal{D}}$ qui converge vers $\mathbf{U} = (v, \mathbf{w}, c)$ quand $h, \Delta t \rightarrow 0$. Le vecteur \mathbf{U} est une solution faible de (36) au sens de la définition (2). De plus, les fonctions limites v et c sont dans l'espace $L^2(0, T; H^1(\Omega))$ et $\mathbf{w} \in L^2(0, T; H^1(\Omega)^6)$.

Schéma CVFE Positif

Cette partie du chapitre est centrée sur l'analyse numérique d'un schéma combiné éléments finis-volumes finis de type CVFE (control volume finite element) positif, non linéaire approchant le système (36) avec un tenseur pour le terme diffusif. Le but est d'obtenir un schéma numérique convergent sans restriction sur le maillage du domaine spatial ni sur les coefficients de transmissibilité. Plus précisément, nous considérons le système (36) avec les mêmes hypothèses (H.2)-(H.4) qui sont énumérées dans la première partie. L'hypothèse (H.1) est remplacée par l'hypothèse plus générale suivante:

(H.1)' Sous la condition d'anisotropie, la conductivité est représentée par le tenseur symétrique $\Lambda(x)$, $\Lambda : \Omega \rightarrow \mathbb{R}^{d \times d}$, tel que:

$$\forall \xi \in \mathbb{R}^d, \exists m_0, M_0 / 0 < m_0 |\xi|^2 \leq \Lambda \xi \cdot \xi \leq M_0 |\xi|^2, \text{ pour presque tout } x \in \Omega. \quad (47)$$

Le maillage de CVFE Nous nous plaçons dans le cas où Ω est un domaine ouvert, borné, connexe et polygonal de \mathbb{R}^d , $d = 2$, avec bord $\partial\Omega$. Nous construisons une triangulation conforme \mathcal{T} de Ω au sens des éléments finis. La discrétisation \mathcal{T} est un recouvrement du domaine Ω , c'est-à-dire $\bigcup_{T \in \mathcal{T}} \bar{T} = \bar{\Omega}$. Nous notons par \mathcal{V} l'ensemble des sommets (localisés aux positions $(x_K)_{K \in \mathcal{V}}$) et par \mathcal{E} l'ensemble des arêtes de la triangulation \mathcal{T} . Pour chaque triangle $T \in \mathcal{T}$, \mathcal{E}_T représente le sous ensemble des arêtes σ tels que $\bigcup_{\sigma \in \mathcal{E}_T} \sigma = \partial T$ et $\mathcal{E} = \bigcup_{T \in \mathcal{T}} \mathcal{E}_T$. Pour chaque triangle $T \in \mathcal{T}$, x_T est le centre de gravité du triangle T , h_T le diamètre du triangle T , et ρ_T le diamètre du cercle circonscrit au triangle T . La taille h et la régularité $\theta_{\mathcal{T}}$ du maillage sont définies par

$$h = \max_{T \in \mathcal{T}} h_T, \quad \theta_{\mathcal{T}} = \max_{T \in \mathcal{T}} \frac{h_T}{\rho_T}.$$

Pour $K \in \mathcal{V}$, nous notons par \mathcal{T}_K l'ensemble de tous les triangles de \mathcal{T} admettant K comme sommet et par \mathcal{E}_K l'ensemble des arêtes admettant K comme extrémité. Le sous-ensemble \mathcal{V}_K de \mathcal{V} est composé des sommets L qui partagent une arête commune σ_{KL} avec K .

Une fois le maillage triangulaire primal construit, nous construisons un maillage dual barycentrique \mathcal{M} de Ω . À chaque sommet $K \in \mathcal{V}$, on associe un volume de contrôle ω_K (de mesure m_K) dont les sommets sont les centres de gravité x_T des triangles $T \in \mathcal{T}_K$ et les milieux des arêtes $\sigma \in \mathcal{E}_K$.

Discrétisation en temps Nous utilisons une discrétisation uniforme en temps de l'intervalle $(0, T)$. Le pas de temps est noté $\Delta t = T/N$ où N est un entier positif. Nous fixons $t_n = n\Delta t$ pour $n \in \{0, \dots, N\}$.

Espaces Discrets Nous utilisons deux espaces fonctionnels discrets correspondant au maillage primal et dual. Le premier est l'espace usuel des éléments finis c'est-à-dire l'espace \mathbb{P}_1 -discret noté par:

$$V_{\mathcal{T}} = \{f \in C(\Omega); f|_T \in \mathbb{P}_1(\mathbb{R}^d), \forall T \in \mathcal{T}\}.$$

Nous notons par $(e_K)_{K \in \mathcal{V}}$ la base canonique de $V_{\mathcal{T}}$, caractérisée par $e_K(x_L) = \delta_{KL}$, pour tout $K \in \mathcal{V}$. Le deuxième est l'espace discret de volumes finis $X_{\mathcal{M}}$ formé de fonctions constantes par morceaux sur le maillage dual

$$X_{\mathcal{M}} = \{f : \Omega \rightarrow \bar{\mathbb{R}} \text{ mesurable}; f|_{\omega_K} \in \mathbb{P}_0(\mathbb{R}^d), \forall K \in \mathcal{V}\}.$$

Nous définissons aussi les espaces discrets spatio-temporels par $V_{\mathcal{T}, \Delta t}$ et $X_{\mathcal{M}, \Delta t}$ comme des espaces de fonctions constantes par morceaux en temps à valeurs dans $V_{\mathcal{T}}$ et $X_{\mathcal{M}}$ respectivement, i.e.:

$$f \in V_{\mathcal{T}, \Delta t} \Leftrightarrow f(t, x) = f(t_{n+1}, x) \in V_{\mathcal{T}}, \quad \forall t \in (t_n, t_{n+1}],$$

et

$$f \in X_{\mathcal{M}, \Delta t} \Leftrightarrow f(t, x) = f(t_{n+1}, x) \in X_{\mathcal{M}}, \quad \forall t \in (t_n, t_{n+1}].$$

Pour un vecteur donné $(v_K^{n+1})_{n \in \{0, \dots, N-1\}, K \in \mathcal{V}} \in \mathbb{R}^{N \text{Card}(\mathcal{V})}$, nous notons par $v_{\mathcal{T}, \Delta t} \in V_{\mathcal{T}, \Delta t}$ et $v_{\mathcal{M}, \Delta t} \in X_{\mathcal{M}, \Delta t}$, les éléments uniques tels que

$$v_{\mathcal{T}, \Delta t}(t, x_K) = v_{\mathcal{M}, \Delta t}(t, x_K) = v_K^{n+1}, \quad \forall K \in \mathcal{V}, \forall t \in (t_n, t_{n+1}].$$

Pour chaque couple $(K, L) \in \mathcal{V}^2$, nous définissons le coefficient de transmissibilité Λ_{KL} par

$$\Lambda_{KL} = - \int_{\Omega} \Lambda(x) \nabla e_K(x) \cdot \nabla e_L(x) dx = \Lambda_{LK}. \quad (48)$$

Schéma Numérique Afin de discrétiser la première équation du système (36) et d'obtenir des solutions qui vérifient les bornes physiologiques, nous sommes amenés à introduire les fonctions suivantes:

$$\begin{aligned}\eta(v) &= \begin{cases} v(1-v), & \text{si } 0 \leq v \leq 1, \\ 0, & \text{si } v < 0 \text{ ou } v > 1, \end{cases} \\ p(v) &= \ln\left(\frac{v}{1-v}\right), \text{ si } 0 < v < 1, \\ \Gamma(v) &= v \ln(v) + (1-v) \ln(1-v) + 1, \text{ si } 0 < v < 1, \\ \phi(v) &= 2 \arcsin \sqrt{v}, \text{ si } 0 \leq v \leq 1. \end{aligned}$$

En utilisant ces fonctions, nous obtenons le schéma CVFE non linéaire, semi-implicite en temps suivant:

Les vecteurs $(v_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$, $(\mathbf{w}_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$, et $(c_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$ sont les solutions du système non linéaire: $\forall K \in \mathcal{V}$,

$$v_K^0 = \frac{1}{m_K} \int_{\omega_K} v_0(x) dx, \quad \mathbf{w}_K^0 = \frac{1}{m_K} \int_{\omega_K} \mathbf{w}_0(x) dx \text{ et } c_K^0 = \frac{1}{m_K} \int_{\omega_K} c_0(x) dx. \quad (49)$$

$\forall n \in \{0, \dots, N-1\}, \forall K \in \mathcal{V}$,

$$\begin{aligned} \frac{m_K}{\Delta t} (v_K^{n+1} - v_K^n) + \sum_{\sigma_{KL} \in \mathcal{E}_K} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) \\ = -m_K \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_{Na}(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_s(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right) \end{aligned} \quad (50)$$

$$w_{j,K}^{n+1} - w_{j,K}^n = \Delta t \left(\alpha_j(v_K^n)(1 - w_{j,K}^{n+1}) - \beta_j(v_K^n) w_{j,K}^{n+1} \right), \text{ pour } j = 1, \dots, 6, \quad (51)$$

$$c_K^{n+1} - c_K^n = \Delta t \left(0.07(10^{-4} - c_K^{n+1}) - g_s 10^{-4} f_K^{n+1} r_K^{n+1} (v_K^{n+1} - 7.7 + 13.0287 \ln(c_K^{n+1})) \right), \quad (52)$$

où, notant par $J_{KL}^{n+1} = [\min(v_K^{n+1}, v_L^{n+1}), \max(v_K^{n+1}, v_L^{n+1})]$, nous avons fixé

$$\eta_{KL}^{n+1} = \begin{cases} \max_{s \in J_{KL}^{n+1}} \eta(s) & \text{si } \Lambda_{KL} \geq 0, \\ \min_{s \in J_{KL}^{n+1}} \eta(s) & \text{si } \Lambda_{KL} < 0. \end{cases} \quad (53)$$

Remarque 2. Les fonctions Γ et ϕ sont utilisées pour obtenir des estimations d'entropie et quelques propriétés discrètes des solutions.

Résultat Principal Soit $(\mathcal{T}_m)_{m \geq 1}$ une suite de triangulations de Ω telle que

$$h_m = \max_{T \in \mathcal{T}_m} \text{diam}(T) \rightarrow 0 \text{ quand } m \rightarrow \infty.$$

Une suite de maillages barycentriques duals $(\mathcal{M}_m)_{m \geq 1}$ est aussi construite. En outre, pour une suite croissante d'entiers naturels $(N_m)_{m \geq 1}$, nous définissons la suite de pas de temps $(\Delta t_m)_{m \geq 1}$ correspondante, telle que $\Delta t_m \rightarrow 0$ quand $m \rightarrow \infty$. Le but principal de cette partie est de démontrer le résultat suivant.

Théorème 6. *Il existe une suite $(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m})_m$ de solutions du schéma (50)-(51)-(52), telle que $0 \leq v_{\mathcal{M}_m, \Delta t_m} \leq 1$, $0 \leq w_{j, \mathcal{M}_m, \Delta t_m} \leq 1$ pour $j = 1, \dots, 6$, $c_m \leq c_{\mathcal{M}_m, \Delta t_m} \leq c_M$ et*

$$v_{\mathcal{M}_m, \Delta t_m} \rightarrow v, \quad \mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w} \text{ et } c_{\mathcal{M}_m, \Delta t_m} \rightarrow c \text{ p.p. dans } \Omega_T \text{ quand } m \rightarrow \infty,$$

où le triplet (v, \mathbf{w}, c) est une solution faible du système (36) au sens de la définition 2.

La preuve de ce théorème constitue le corps de cette partie. Quelques propriétés discrètes, le principe de maximum discret, quelques estimations a priori et l'existence de solutions du schéma sont obtenus. Un argument de compacité est utilisé pour passer, par la suite, à la limite et identifier finalement les fonctions limites comme une solution faible du système (36).

La dernière partie de ce chapitre présente plusieurs tests numériques montrant l'efficacité du schéma proposé.

Chapitre 4

Ce chapitre concerne l'analyse mathématique d'un système elliptique-parabolique modélisant l'interaction entre la propagation du potentiel d'action et la contraction mécanique du tissu cardiaque. Pour le modèle de propagation des ondes électriques, nous utilisons le modèle bidomaine couplé avec un modèle ionique physiologique. Le couplage entre la contraction musculaire, les réactions biochimiques et l'activité électrique est introduit par le modèle de déformation active. Le gradient de déformation \mathbf{F} est donc factorisé en un facteur actif \mathbf{F}_a (dépendant de l'électrophysiologie) et un facteur élastique passif \mathbf{F}_p : $\mathbf{F} = \mathbf{F}_p \mathbf{F}_a$.

Le tissu cardiaque occupe, dans la configuration de référence, un domaine ouvert, borné et connexe Ω_R de \mathbb{R}^3 avec un bord $\partial\Omega_R$ régulier. Il est considéré comme un matériau homogène, hyperélastique et incompressible. D'où le premarqueier tenseur de contraintes de Piola-Kirchhoff est donné par:

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

où $\mathcal{W} = \mathcal{W}(\mathbf{X}, \mathbf{F})$, est l'énergie de déformation qui dépend du point matériel \mathbf{X} et de la déformation. En outre, $\text{Cof}(\cdot)$ est la matrice cofacteur et p est le multiplicateur de Lagrange associé à la contrainte d'incompressibilité: $\det(\mathbf{F}) = 1$ et interprété comme la pression hydrostatique. Les équations d'équilibre s'écrivent dans la configuration de référence comme:

$$\begin{cases} \nabla \cdot \mathbf{P}(\mathbf{F}, p) = \mathbf{g} & \text{dans } \Omega_R, \\ \det(\mathbf{F}) = 1 & \text{dans } \Omega_R, \\ \mathbf{P}\mathbf{n} = -\alpha\phi & \text{sur } \partial\Omega_R, \end{cases} \quad (54)$$

où ϕ est la fonction de déformation, \mathbf{g} est une force volumique prescrite, \mathbf{n} est le vecteur unitaire normal à $\partial\Omega_R$ sortant de Ω_R , et $\alpha > 0$ est une constante. Le choix des conditions au bord de type Robin dans (54) est lié au fait qu'elles peuvent être réglées pour imiter le mouvement global du muscle cardiaque [RLRB⁺14].

Évidemment, pour obtenir une expression précise de la premarqueière équation du système (54), nous avons besoin d'une loi de comportement particulière définissant l'énergie \mathcal{W} . Nous considérons, dans ce chapitre, le cas de matériau Néo-Hookéen donc l'énergie \mathcal{W} est définie par:

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

où μ représente le module de cisaillement. Bien que simplifiée, cette description de la réponse passive du muscle comporte, jusque là, une relation non-linéaire entre la déformation et les contraintes résultant de la contrainte d'incompressibilité. Dans la suite, une autre forme de non-linéarité apparaîtra en raison de l'anisotropie obtenue du couplage électromécanique avec l'approche de déformation active.

Pour résumer, la formulation de déformation active de l'activité électromécanique du cœur est donnée par le système suivant [NQRB12]:

$$\left\{ \begin{array}{ll} -\nabla \cdot (a(\mathbf{x}, \gamma, \mathbf{F}, p)) = \mathbf{g} & \text{dans } Q_T, \\ \det(\mathbf{F}) = 1 & \text{dans } Q_T \\ \partial_t v + \nabla \cdot (\mathbf{M}_e(\mathbf{x}, \mathbf{F}) \nabla v_e) + I_{\text{ion}} = I_s^e & \text{dans } Q_T, \\ \partial_t v - \nabla \cdot (\mathbf{M}_i(\mathbf{x}, \mathbf{F}) \nabla v_i) + I_{\text{ion}} = I_s^i & \text{dans } Q_T, \\ v_i - v_e = v & \text{dans } Q_T, \\ \partial_t \mathbf{w} - \mathbf{R}(v, \mathbf{w}) = 0 & \text{dans } Q_T, \\ \partial_t z - G(v, \mathbf{w}, z) = 0 & \text{dans } Q_T, \\ \partial_t \gamma - S(\gamma, \mathbf{w}) = 0 & \text{dans } Q_T, \end{array} \right. \quad (55)$$

où le cylindre temps-espace est donné par $Q_T := (0, T) \times \Omega_R$. Dans ce système, les inconnues sont la déformation ϕ , la pression p , le potentiel transmembranaire v , les potentiels intra- et extra-cellulaires v_i et v_e respectivement, le vecteur de variables de porte \mathbf{w} , la variable de concentration z et la variable d'activation γ . Le terme $a(\mathbf{x}, \gamma, \mathbf{F}, p)$, dont l'expression est obtenue dans le chapitre 1, est donné par

$$a(\mathbf{x}, \gamma, \mathbf{F}, p) := \mu \mathbf{F} \mathbf{C}_a^{-1}(\mathbf{x}, \gamma) - p \text{Cof}(\mathbf{F}), \quad (56)$$

où $C_a^{-1} := \det \mathbf{F}_a \mathbf{F}_a^{-1} \mathbf{F}_a^{-T}$. Les conductivités \mathbf{M}_k , $k = i, e$, dépendent du gradient de déformation \mathbf{F} par la relation suivante:

$$\mathbf{M}_k(\mathbf{x}, \mathbf{F}) := (\mathbf{F})^{-1} \mathbf{K}_k(\mathbf{x}) (\mathbf{F})^{-T}, \quad k \in \{i, e\}, \quad (57)$$

où les tenseurs orthotropes

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

représentent la conductivité électrique du tissu et $\sigma_k^s = \sigma_k^s(\mathbf{x}) \in C^1(\mathbb{R}^3)$, $k \in \{e, i\}$, $s \in \{l, t, n\}$, sont les conductivités intra- and extracellulaires le long, transverses, et normales à la direction des fibres donnée par $\mathbf{d}_s = \mathbf{d}_s(\mathbf{x})$, $s \in \{l, t, n\}$ ('l': le long, 't': transverse, 'n': normale). Le système d'équations (55) est complété par des conditions initiales pour v , \mathbf{w} , γ , z et des conditions au bord sur les potentiels v_k , $k = i, e$ et le flux élastique $a(\cdot, \cdot, \cdot, \cdot)$.

Problème Posé Afin de simplifier l'analyse mathématique, nous commençons par une linéarisation de la condition d'incompressibilité et du flux dans les équations d'équilibre. Après certaines manipulations détaillées dans le chapitre 4, le système auquel on s'intéresse s'écrit sous

la forme:

$$-\nabla \cdot (\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma)) + \nabla p = \mathbf{f}(t, \mathbf{x}, \gamma), \quad \text{dans } \Omega, \text{ p.p. dans } (0, T), \quad (58)$$

$$\nabla \cdot \mathbf{u} = 0 \quad \text{dans } \Omega, \text{ p.p. dans } (0, T), \quad (59)$$

$$\partial_t v - \nabla \cdot (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}) \nabla v_i) + I_{\text{ion}}(v, \mathbf{w}, z) = I_s^i(t, \mathbf{x}) \quad \text{dans } \Omega_T, \quad (60)$$

$$\partial_t v + \nabla \cdot (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}) \nabla v_e) + I_{\text{ion}}(v, \mathbf{w}, z) = I_s^e(t, \mathbf{x}) \quad \text{dans } \Omega_T, \quad (61)$$

$$v = v_i - v_e \quad \text{dans } \Omega_T, \quad (62)$$

$$\partial_t \mathbf{w} = \mathbf{R}(v, \mathbf{w}, z) \quad \text{dans } \Omega_T, \quad (63)$$

$$\partial_t z = G(v, \mathbf{w}, z) \quad \text{dans } \Omega_T, \quad (64)$$

$$\partial_t \gamma = S(\gamma, \mathbf{w}) \quad \text{dans } \Omega_T. \quad (65)$$

Le système (58)-(60)-(61) est complété par les conditions au bord:

$$\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma) \mathbf{n} - p \mathbf{n} = -\alpha \mathbf{u} \quad \text{sur } \partial \Omega, \text{ p.p. dans } (0, T), \quad (66)$$

pour une constante donnée $\alpha > 0$ et

$$(\mathbf{M}_k(\mathbf{x}, \nabla \mathbf{u}) \nabla v_k) \cdot \mathbf{n} = 0 \quad \text{sur } (0, T) \times \partial \Omega, \quad k = i, e. \quad (67)$$

Comme les équations (58)-(65), avec le choix des conditions de type Neumann (67), sont invariantes sous la modification de v_i et v_e en $v_i + k$ et $v_e + k$ pour tout $k \in \mathbb{R}$, une condition de compatibilité est aussi imposée (voir (79) plus loin). Les conditions initiales sont:

$$v(0, \cdot) = v_0, \quad \mathbf{w}(0, \cdot) = \mathbf{w}_0, \quad z(0, \cdot) = z_0, \quad \gamma(0, \cdot) = \gamma_0 \quad \text{dans } \Omega. \quad (68)$$

Les hypothèses portant sur le modèle (58)–(65) et (66)–(68) sont données par:

(A.1) $(\sigma(\mathbf{x}, \gamma))_{x \in \Omega, \gamma \in \mathbb{R}}$ est une famille de tenseurs symétriques, uniformément bornés et définis positifs:

$$\exists c > 0 : \text{ pour presque tout } x \in \Omega, \forall \gamma \in \mathbb{R} \quad \forall \mathbf{M} \in \mathbb{M}_{3 \times 3}$$

$$\frac{1}{c} |\mathbf{M}|^2 \leq (\sigma(\mathbf{x}, \gamma) \mathbf{M}) : \mathbf{M} \leq c |\mathbf{M}|^2;$$

(A.2) la fonction $\sigma(\cdot, \cdot)$ est de classe $C^1(\bar{\Omega} \times \mathbb{R})$;

(A.3) $(\mathbf{M}_{i,e}(\mathbf{x}, \mathbf{M}))_{x \in \Omega, \mathbf{M} \in \mathbb{M}_{3 \times 3}}$ est une famille de matrices symétriques, uniformément bornées et définies positives:

$$\exists c > 0 : \text{ pour presque tout } x \in \Omega, \forall \mathbf{M} \in \mathbb{M}_{3 \times 3} \quad \forall \xi \in \mathbb{R}^3$$

$$\frac{1}{c} |\xi|^2 \leq (\mathbf{M}_{i,e}(\mathbf{x}, \mathbf{M}) \xi) \cdot \xi \leq c |\xi|^2;$$

(A.4) les applications $\mathbf{M} \mapsto \mathbf{M}_{i,e}(\cdot, \mathbf{M})$ sont uniformément lipschitziennes;

(A.5) la fonction S est donnée par $S(\gamma, \mathbf{w}) = \beta(\sum_{j=1}^k \eta_j w_j - \eta_0 \gamma)$, où $\beta, \eta_j, j = 0, 1, \dots, k$ sont des paramètres physiologiques positifs;

(A.6) les fonctions \mathbf{R} , G et I_{ion} sont données par la cinématique d'un modèle ionique physiologique général et il est possible de vérifier que les hypothèses, énumérées en bas, sont satisfaites par plusieurs variables de porte et de concentration dans les modèles ioniques de Beeler-Reuter ou Luo-Rudy.

Nous supposons que les fonctions $\mathbf{R}(v, \mathbf{w}) := (R_1(v, w_1), \dots, R_k(v, w_k))$ où $R_j : \mathbb{R}^2 \rightarrow \mathbb{R}$ sont localement lipschitziennes et définies par

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

où α_j et β_j , $j = 1, \dots, k$ sont des fonctions rationnelles d'exponentielles en v telles que:

$$\begin{aligned} 0 < \alpha_j(v), \beta_j(v) &\leq C_{\alpha, \beta}(1 + |v|), \\ \frac{d\alpha_j}{dv} \text{ et } \frac{d\beta_j}{dv} &\text{ sont uniformément bornées,} \end{aligned} \quad (69)$$

pour des constantes $C_{\alpha, \beta} > 0$.

La fonction $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty) \rightarrow \mathbb{R}$ a la forme générale:

$$I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{j=1}^k I_{\text{ion}}^j(v, w_j) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \quad (70)$$

où les fonctions I_{ion}^j sont de classe $C^0(\mathbb{R} \times \mathbb{R})$ et elles vérifient la condition:

$$|I_{\text{ion}}^j(v, w_j)| \leq C_{1, I}(1 + |w_j| + |v|). \quad (71)$$

La fonction I_{ion}^z est telle que:

$$\begin{aligned} I_{\text{ion}}^z &\in C^1(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}^+ \times \mathbb{R}), \\ I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) &\leq C_{2, I}(1 + |v| + |w| + |z| + \ln z), \end{aligned} \quad (72)$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3, I} \sum_{j=1}^k (|v| + w_j + w_j \ln z), \quad (73)$$

$$0 < \underline{\Theta}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(\mathbf{w}), \quad (74)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \right| \leq L(\mathbf{w}), \quad (75)$$

$$\frac{\partial}{\partial w_j} I_{\text{ion}}^z \leq C_{4, I}(1 + |v| + |\ln z|), \quad \forall j = 1, \dots, k, \quad (76)$$

$$0 \leq \frac{\partial}{\partial z} I_{\text{ion}}^z \leq C_{5, I}, \quad (77)$$

où $\underline{\Theta}$, $\bar{\Theta}$ et L sont de classe $C^0(\mathbb{R}^k, \mathbb{R}^+)$ et $C_{1, I}, \dots, C_{5, I}$ sont des constantes positives. Finalement, la fonction G est donnée par:

$$G(v, \mathbf{w}, z) = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z), \quad (78)$$

où a_1 , a_2 et a_3 sont des constantes positives et physiologiques qui varient d'un ion à l'autre. Dans notre cas, nous considérons seulement que z correspond à la concentration intracellulaire du calcium.

(A.7) Les conditions suivantes sont vérifiées

$$\int_{\Omega} I_s^i = \int_{\Omega} I_s^e \text{ et } \int_{\Omega} v_e(\mathbf{x}, t) d\mathbf{x} = 0 \text{ pour presque tout } t \in (0, T). \quad (79)$$

(A.8) Les données v_0, w_0, γ_0, z_0 sont dans l'espace $H^1(\Omega)$ avec $z_0 \geq c_0 > 0$ (c_0 est une constante positive) tandis que $\mathbf{g} \in L^2(\Omega_T)^3$ et $I_s^{i,e} \in L^2(\Omega_T)$.

Notons que, en pratique, on commence par une configuration non-déformée, c'est-à-dire, avec $\gamma \equiv 0$. Grâce aux propriétés (A.1)–(A.8), nous énonçons la formulation faible du problème (58)–(68) au sens suivant.

Définition 3. Une solution faible du système (58)–(68) est un vecteur $U = (\mathbf{u}, p, v_i, v_e, v, \mathbf{w}, \gamma, z)$ qui vérifie:

- (i) $\mathbf{u} \in L^2(0, T; H^1(\Omega)^3)$, $p \in L^2(\Omega_T)$, $v_i \in L^2(0, T; H^1(\Omega))$;
 $v_e \in L^2(0, T; H^{1,0}(\Omega))$ où $H^{1,0}(\Omega) := \{v_e \in H^1(\Omega); \int_{\Omega} v_e d\mathbf{x} = 0\}$;
 $v \in E := L^2(0, T; H^1(\Omega))$ avec $\partial_t v \in E' := L^2(0, T; (H^1(\Omega))')$;
 $\gamma, z \in C([0, T]; L^2(\Omega))$ et $\mathbf{w} \in C([0, T]; L^2(\Omega)^k)$;
 $z(t, x) > 0$ et $0 \leq w_j(t, x) \leq 1$ pour presque tout $(t, x) \in \Omega_T$ et pour $j = 1, \dots, k$;
- (ii) Pour presque tout $t \in (0, T)$, pour tout $\mathbf{v} \in H^1(\Omega)^3$:

$$\int_{\Omega} (\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma) : \nabla \mathbf{v} - p \nabla \cdot \mathbf{v}) d\mathbf{x} = \int_{\Omega} \mathbf{f} \cdot \mathbf{v} d\mathbf{x} - \int_{\partial\Omega} \alpha \mathbf{u} \cdot \mathbf{v} ds. \quad (80)$$

Pour tout $q \in L^2(\Omega)$

$$\int_{\Omega} q(\nabla \cdot \mathbf{u}) d\mathbf{x} = 0. \quad (81)$$

- (iii) Pour presque tout $t \in (0, T)$, pour tout $\xi \in H^1(\Omega)$, $\mu \in H^{1,0}(\Omega)$,

$$\langle \partial_t v, \xi \rangle + \int_{\Omega} (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}) \nabla v_i \cdot \nabla \xi + I_{\text{ion}}(v, \mathbf{w}, z) \xi) = \int_{\Omega} I_s^i \xi, \quad (82)$$

$$\langle \partial_t v, \mu \rangle - \int_{\Omega} (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}) \nabla v_e \cdot \nabla \mu + I_{\text{ion}}(v, \mathbf{w}, z) \mu) = \int_{\Omega} I_s^e \mu, \quad (83)$$

avec $v = v_i - v_e$ p.p. dans Ω_T et $v(0, \cdot) = v_0$ p.p. dans Ω .

- (iv) Pour presque tout $t \in (0, T)$ les équations (63), (65), (64) sont vérifiées dans $L^2(\Omega)$, et $\mathbf{w}(0, \cdot) = \mathbf{w}_0$, $\gamma(0, \cdot) = \gamma_0$, $z(0, \cdot) = z_0$ p.p. dans Ω .

Le résultat principal de ce chapitre est le théorème suivant:

Théorème 7. Étant donné (A.1)–(A.8). Si $v_0 \in L^2(\Omega)$, $\mathbf{w}_0 \in H^1(\Omega)^k$, $\gamma_0, z_0 \in H^1(\Omega)$, avec $z_0 \geq c_0 > 0$, $\mathbf{g} \in L^2(\Omega_T)^3$, $I_s^{i,e} \in L^2(\Omega_T)$, il existe une solution faible $U = (\mathbf{u}, p, v_i, v_e, v, \mathbf{w}, \gamma, z)$ du système (58)–(65) avec les conditions au bord et les données initiales précisées dans (66)–(68).

Pour démontrer le théorème d'existence, nous introduisons tout d'abord des systèmes approchés non-dégénérés contenant une condition de compressibilité artificielle. Nous montrons l'existence de solutions aux systèmes approchés (pour un ε fixé) en utilisant la méthode de Faedo-Galerkin et un argument de compacité. Une fois l'existence pour les systèmes approchés établie, nous passons à la limite en ε pour obtenir une solution au problème de départ. La convergence est obtenue par un argument de compacité. Nous notons que le passage à la limite dans le terme de pression n'est pas simple à cause de la condition de compressibilité artificielle et de conditions au bord de type Navier.

Contributions Principales

Articles

Plusieurs publications sont issues de ce travail:

deux articles publiés dans des revues internationales:

M. Bendahmane, F. Mroue, M. Saad and R. Talhouk, Mathematical analysis of cardiac electromechanics with physiological ionic model, *DCDS-B*, 22 (2019), 1-35.

M. Bendahmane, F. Mroue, M. Saad and R. Talhouk, Unfolding homogenization method applied to physiological and phenomenological bidomain models in electrocardiology, *Nonlinear Analysis: Real-World Applications*, 50 (2019), 413-447.

et un article soumis:

M. Bendahmane, F. Mroue and M. Saad, A positive cell vertex Godunov scheme for a Beeler-Reuter based model of cardiac electrical activity.

Développement de code

Pour les simulations du Chapitre 3, la contribution était dans l'implémentation, sous MATLAB, des schémas CVFE et CVFE positif. D'autre part, pour comparer avec les résultats obtenus par la méthode des éléments finis, FreeFem++ a été utilisé [PHLHM13].

Electromechanical Modeling of the heart

1.1 Introduction

Ischaemic heart disease leading to heart attack is the top world's killer, as announced by the World Health Organization report in 2016 [WHO16]. Most of these deaths are caused by electrical activity disorders, visible through the mechanical deficiency of the heart. This muscular organ, which contracts to pump oxygenated blood to the organs, cannot stop even for a short period of time. A profound understanding of cardiac functionality is crucial to formulate adapted models and obtain realistic simulations. We present in this chapter all the elements needed for the understanding of the next chapters: a short description of the physiology and the functionality of the heart; the definition of the Action Potential; the mathematical models used to represent cardiac electrical and mechanical activity. In the last section, we give an overview of the different approaches to coupling the electrical and mechanical cardiac models.

1.2 Cardiac Anatomy and Function

1.2.1 Macroscopic description

The heart is a hollow muscle whose role is to pump blood to the body's organs through blood vessels. It is situated near the centre of the chest cavity between the right and left lungs, and is supported inside a membranous structure, the pericardial sac. It is divided into two halves (left and right) by the interventricular septal wall. It consists of four major chambers (two in each half) which are the left and right ventricles and the left and right atria (see Figure 1 and see [Kat10] for more information). Mechanical contraction of the heart is caused by the electrical activation of myocardial cells. The beats are initiated by the heart itself on a regular basis. In other words, the heart is self-contained and can continue to beat even after being removed from the body, for instance for a transplantation. Actually, the initiation of electrical activity is accomplished by the pacemaker cells which exist in various locations throughout the heart. The sinoatrial (SA) node contains the pacemaker cells with fastest rate of electrical activity. Hence

they control the activity of the entire heart. Electrical signals called *action potentials*, generated in the SA node, propagate from cell to cell firstly through the right atrium then closely to the left atrium, until they reach the atrioventricular (AV) node. The slower conduction rate in the AV node gives enough time for the atria to contract and pump blood into the ventricles. From the AV node the electrical propagation continues through the bundle of His which divides into left and right bundle branches. The branches continue to subdivide into a complex network of Purkinje fibers spreading through the ventricular myocardium. The bundle and the Purkinje fibers are fast conducting so that the entire myocardium is excited simultaneously (see Figure 1.1).

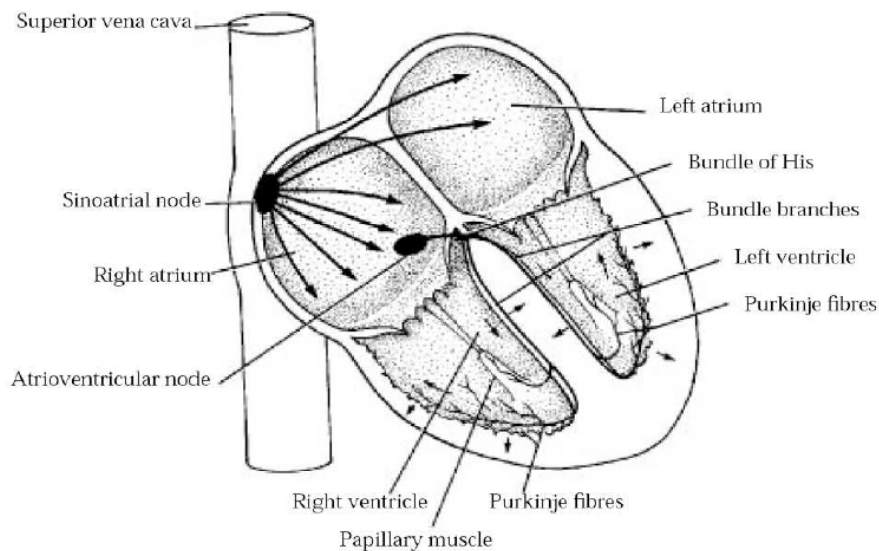


Figure 1.1 – Schematic of the activation sequence (Berne and Levy [KS09]).

1.2.2 Microscopic description

Myocardial cells, or cardiomyocytes, are cable-like roughly cylindrical, very small, typically 10-20 μm wide and 60-100 μm long, and are bounded by the cell membrane or *sarcolemma*. They have the property of being both excitable and contractile (see Figure 1.2).

Contractile property

Each cardiomyocyte is composed of contractile units, the sarcomeres (1.6-2.5 μm in length) that are the basic elements responsible of cardiac contraction. The structure of a sarcomere consists in a parallel arrangement of actin and myosin filaments that are capable to produce a force in their longitudinal direction. The generation of this force is controlled by calcium concentration $[\text{Ca}^{2+}]$. The liberation of calcium ions is activated by the electrical excitation of the myocardial cells. Calcium acts on the sarcomeres in order for actin-myosin bridges to form and for actin and myosin filaments to slide over each other leading to contraction. Each cardiomyocyte has specialized connections with its neighboring cells, mainly in end-to-end fashion giving the fiber structure of the heart. The opposing cell membranes form the *intercalated disk* structure. There are places in the end-to-end cell membranes called *junctions*

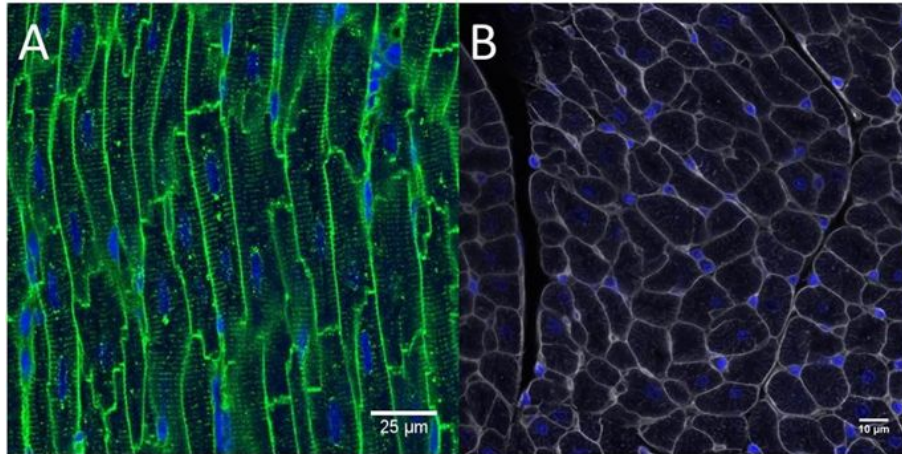


Figure 1.2 – (A): Cardiomyocytes in long section, (B): Cardiomyocytes in cross-section [BDMHB16].

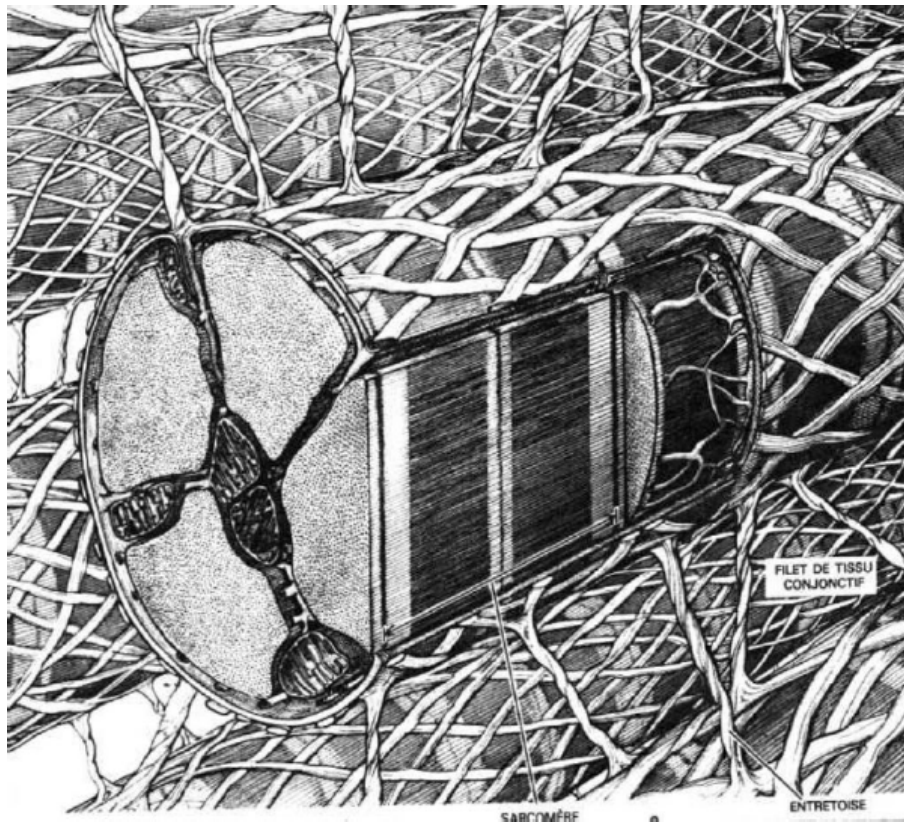


Figure 1.3 – A cardiomyocyte surrounded by an extracellular matrix of collagen and connected to other myocytes [RFS86].

where the pre- and post-junctional membranes are fused together. The mechanical adhesion of cells is provided by *tight junctions* while the electrical coupling is provided by *gap junctions* [CP08].

The myocardial fibers are surrounded by an extracellular matrix of collagen and elastin that protects the cells from excessive elongation and transfers the active force throughout the tissue [RFS86].

Electrical activation

The cell membrane is a phospholipid bilayer in which are immersed some proteins. It separates the intracellular and the extracellular electrolytic solutions and serves as a permeability barrier that allows the cell to maintain an interior composition different from the composition of the extracellular fluid. While the membrane acts as an insulator, the embedded protein channels selectively permit the flow of charged ions under some conditions [CP08, KS98]. Hence, it is possible to describe the cellular membrane as an **RC** circuit, that is, as a capacitor connected in parallel with several resistances, acting for the ionic channels. The potential difference across the membrane is known as the transmembrane potential v . Changes in this quantity are given by

$$C_m \frac{dv}{dt} = -I_{\text{ion}}$$

where C_m is the membrane capacitance, and I_{ion} are the various ionic currents flowing across the membrane. The latter are mainly caused by the flow of sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) through individual ion channels in the membrane. These channels have been profoundly studied by molecular biologists and mathematical models have been formulated. The first description of ion channels was developed by Hodgkin and Huxley [HH52] for the squid axon. In the resting state, the transmembrane potential is about -80mV . This is the phase during which the heart is passively filling with blood. Once activated, the cell membrane becomes rapidly depolarized (phase 0) due to the opening of sodium channels and the resulting inward sodium current. Then a short period of repolarization (phase 1), largely due to the closure of sodium channels, is followed by a plateau (phase 2) which in turn is maintained by the inward calcium current. Finally, the potential decreases again (repolarization - phase 3) until the resting state is achieved. This sequence of changes in potential from the activation point to the resting state constitutes the action potential (see Figure 2). Clearly, the action potential is due to the superposition of many ionic currents.

1.3 Cardiac electrophysiology models

Cardiac electrophysiology is the study of the electrical wave which precedes cardiac contraction. In this section, we introduce mathematical models largely used in cardiac electrophysiology. More specifically, we present the most used model for the propagation of cardiac electric potential: the so-called bidomain equations. The concepts leading to the bidomain model were first proposed by Schmitt [Sch69] who suggested that two interpenetrating domains could be used to describe cardiac tissue. A mathematical formulation of this proposal was constructed in several theses and papers by Tung [Tun78], Plonsey and Barr [PB84], Miller and Geselowitz [MG78] and others. The bidomain model has been widely adopted by researchers due to its convenience and simplicity. The most substantial mathematical description of the bidomain model is found in the review paper by Henriquez [Hen93], which presents a formal definition of the model from its origins in the core conductor model. The derivation presented in the next section follows the steps in this review with small changes in the notation.

1.3.1 The bidomain model: Physical derivation

The bidomain model describes the electric current flow through the cell membrane in a volume averaged approach. It considers the cardiac tissue as a continuum (due to gap junctions) and assumes the coexistence of two domains at each material point: the intracellular domain (subscript ‘ i ’) and the extracellular domain (subscript ‘ e ’). We denote by $\Omega \subset \mathbb{R}^3$ the set of all material points. At a point, the volume-averaged intracellular and extracellular potentials (unit mV) are denoted by v_i and v_e , respectively. The transmembrane potential v , being the potential difference across the cell membrane, is given by:

$$v(t, \mathbf{x}) := v_i - v_e, \quad (1.1)$$

where $\mathbf{x} \in \Omega$ represents the space variable and $t > 0$ represents the time variable.

The anatomy of the heart is composed of several layers of fibers [LSC⁺95, JMM⁺07]. From the fiber structure of the myocardium, there is a local material coordinate system defined at every point with axes aligned with each of the local fiber (‘ l ’: along the fiber), cross-fiber (‘ t ’: transverse) and cross-sheet (‘ n ’: normal) directions. These axes define the principal directions of propagation at every point and they are defined to be orthogonal in the undeformed configuration. In such a coordinate system, the electrical conductivity of the tissue (unit $(\Omega\text{m})^{-1}$) is represented by the orthotropic tensors:

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

where $\sigma_k^s = \sigma_k^s(\mathbf{x}) \in C^1(\mathbb{R}^3)$, $k \in \{e, i\}$, $s \in \{l, t, n\}$, are the intra- and extracellular conductivities along, transversal, and normal to the fibers’ direction given by $\mathbf{d}_s = \mathbf{d}_s(\mathbf{x})$, $s \in \{l, t, n\}$. Since the two media can be assimilated to passive conductors in the quasi-static state, the electric current densities (unit Am^{-1}) are derived by Ohm’s law as:

$$\mathbf{J}_i = -\mathbf{K}_i \nabla v_i \quad (1.2)$$

$$\mathbf{J}_e = -\mathbf{K}_e \nabla v_e. \quad (1.3)$$

Let $V \subset \Omega$ be a subdomain of Ω and S its surface. Using the assumption that there are no sources or sinks in the medium and no build-up of charges at any point, the total current entering a small volume must be equal to the total leaving current. Thus, using the conservation of electrical fluxes between the two domains, one has:

$$-\int_S \mathbf{n} \cdot (\mathbf{J}_i + \mathbf{J}_e) dS = 0.$$

Here \mathbf{n} is the outward unit normal to S .

Applying the divergence theorem to this last equation, we get:

$$-\int_V \nabla \cdot (\mathbf{J}_i + \mathbf{J}_e) dV = 0.$$

Since this relation holds for all volumes V , the integrand must be zero:

$$\nabla \cdot (\mathbf{J}_i + \mathbf{J}_e) = 0.$$

Substituting the values (1.2)-(1.3) of \mathbf{J}_i and \mathbf{J}_e , gives:

$$\nabla \cdot (-\mathbf{K}_i \nabla v_i) + \nabla \cdot (-\mathbf{K}_e \nabla v_e) = 0.$$

Further inserting $v_i = v + v_e$, collecting the v_e terms and multiplying by -1 , we get one of the equations of the bidomain model:

$$\nabla \cdot (\mathbf{K}_i \nabla v) + \nabla \cdot ((\mathbf{K}_i + \mathbf{K}_e) \nabla v_e) = 0. \quad (1.4)$$

On the other hand, the current density across the membrane χI_m , where χ (units m^{-1}) is the surface-to-volume ratio and I_m (units Am^{-2}) is the transmembrane current density per unit area, is equal to the change in current density in each domain. Hence, one obtains the following current density conservation equations

$$\begin{aligned} \nabla \cdot (\mathbf{K}_i \nabla v_i) &= \chi I_m, \\ \nabla \cdot (\mathbf{K}_e \nabla v_e) &= -\chi I_m. \end{aligned} \quad (1.5)$$

Moreover, since the membrane acts as a capacitor, the transmembrane current is a sum of a capacitive current given by the change in transmembrane potential and an ionic current governed by a membrane model for cardiac tissue

$$I_m = C_m \frac{dv}{dt} + I_{\text{ion}}, \quad (1.6)$$

where C_m is the membrane capacitance per unit area and I_{ion} is a nonlinear function representing the sum of all the ionic currents. Using equations (1.6), (1.5) and (1.1), we obtain the second equation of the bidomain model:

$$\chi \left(C_m \frac{\partial v}{\partial t} + I_{\text{ion}} \right) = \nabla \cdot (\mathbf{K}_i \nabla v) + \nabla \cdot (\mathbf{K}_i \nabla v_e). \quad (1.7)$$

Another formulation of the bidomain equations is given by:

$$\chi C_m \partial_t v - \nabla \cdot (\mathbf{K}_i \nabla v_i) + \chi I_{\text{ion}} = 0, \quad (t, \mathbf{x}) \in (0, T) \times \Omega, \quad (1.8)$$

$$\chi C_m \partial_t v - \nabla \cdot (\mathbf{K}_e \nabla v_e) + \chi I_{\text{ion}} = 0, \quad (t, \mathbf{x}) \in (0, T) \times \Omega. \quad (1.9)$$

The two formulations are actually equivalent. The first one (1.4)-(1.7) can be obtained from the second (1.8)-(1.9) by replacing v_i by $v + v_e$ in (1.8) to get:

$$\chi C_m \partial_t v - \nabla \cdot (\mathbf{K}_i \nabla v) - \nabla \cdot (\mathbf{K}_i \nabla v_e) + \chi I_{\text{ion}}(v, w) = 0, \quad (t, \mathbf{x}) \in (0, T) \times \Omega. \quad (1.10)$$

Now subtract (1.9) from (1.10), to get the elliptic equation, see [BCP09]:

$$\nabla \cdot (\mathbf{K}_i \nabla v) + \nabla \cdot ((\mathbf{K}_i + \mathbf{K}_e) \nabla v_e) = 0.$$

At the cellular level, it has been observed that the intracellular current does not exit the heart [Pag62]. Moreover, one can assume that the heart is electrically isolated. Consequently, on the boundary of the heart, one can impose the following boundary condition:

$$\mathbf{K}_i \nabla v_i \cdot \mathbf{n} = \mathbf{K}_e \nabla v_e \cdot \mathbf{n} = 0, \quad \text{on } \partial\Omega. \quad (1.11)$$

The Monodomain Model

The monodomain model assumes that cardiac tissue is one excitable medium with diffusion of electrical potential. It can be also obtained from the bidomain model under the assumption that the extracellular space is highly conducting (\mathbf{K}_e is effectively infinite) or the extracellular and intracellular domain have equal anisotropy ratio [CP08]. In this case, one obtains from (1.8)-(1.9) the following equation:

$$\chi C_m \frac{dv}{dt} + \chi I_{\text{ion}} = \nabla \cdot (\mathbf{K} \nabla v), \quad (1.12)$$

where $\mathbf{K} = \mathbf{K}_i$, supplemented with the boundary condition:

$$\mathbf{K} \nabla v \cdot \mathbf{n} = 0. \quad (1.13)$$

1.3.2 Ionic Models

The framework of the bidomain model is based on the existence of mathematical models describing the flow of ionic currents across the membrane. Ideally, these models would describe each of the individual ionic currents whose sum defines the ionic current I_{ion} . There are two main approaches to the construction of an ionic current model. The first is to build a *physiological* model which attempts to describe specific actions within the cell membrane. Such exact models are derived either by fitting the parameters of an equation to match experimental data or by defining equations that were confirmed by later experiments. Moreover, they are based on the cell membrane formulation developed by Hodgkin and Huxley for nerve fibers [San96, CP08]. The second approach consists of producing simpler models, known as *phenomenological* models, which replicate certain key features of activation and recovery. They can be used in large problems because they are typically small and fast to solve, although they are less flexible in their response to variations in cellular properties such as concentrations or cell size. We describe in this section one model of each category: the Beeler-Reuter model and the Fitzhugh-Nagumo model.

Beeler-Reuter model

The Beeler-Reuter model [BR77] is one of the first mathematical models describing mammalian cardiac myocytes' electrophysiology. In fact, it is classified in the first-generation models which have been extensively used for studies of ventricular fibrillation, and which provide a good balance between numerical efficiency and biophysically important details [CP08]. Although it may be considered simple compared to more recent models, it is able to realistically describe cell dynamics due to the presence of calcium concentration which is crucial for cardiac contraction. The function $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^6 \times \mathbb{R}^+ \rightarrow \mathbb{R}$ is the collection of membrane currents, and the charge flow through the membrane is assumed to include four individual currents [BR77, KS98]. The direction of two of these, representing the flow of potassium (K^+) ions, points out of the cell:

$$I_{Pot}(v) = 1.4 \frac{e^{0.04(v+85)} - 1}{e^{0.08(v+53)} + e^{0.04(v+53)}} + 0.07 \frac{v + 23}{1 - e^{-0.04(v+23)}}, \quad (1.14)$$

and

$$I_z(v, z) = 0.8z \frac{e^{0.04(v+77)} - 1}{e^{0.04(v+35)}}. \quad (1.15)$$

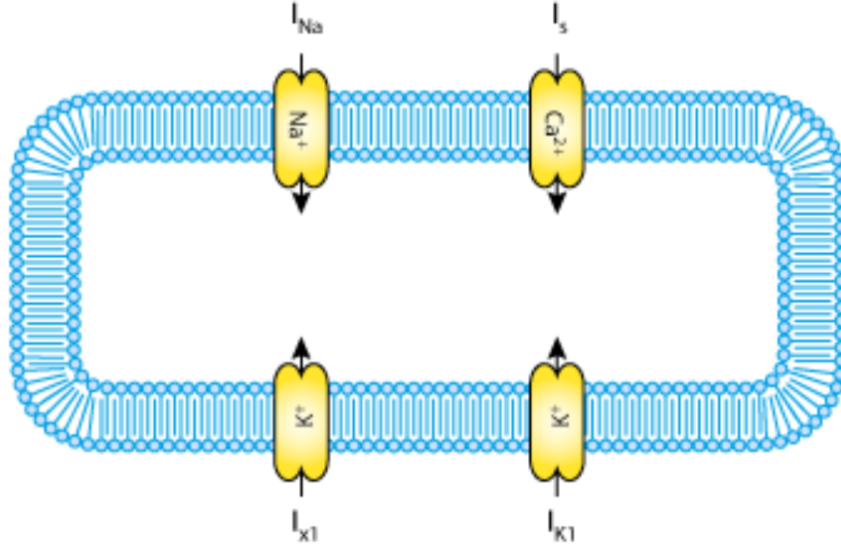


Figure 1.4 – A schematic diagram describing the current flows across the cell membrane that are captured in the BR model. http://models.cellml.org/e/23a/beeler_reuter_1977.cellml/

There are also two inward currents; the first is the inward current of sodium (Na^+) ions:

$$I_{Na}(v, m, o, l) = (g_{Na}m^3ol + g_{NaC})(v - E_{Na}), \quad (1.16)$$

where $E_{Na} = 50$ is the equilibrium potential of sodium, $g_{Na} = 4$ is the membrane conductivity of the sodium current and $g_{NaC} = 0.003$ is the membrane conductivity of the sodium-calcium exchanger current [BR77]. The second inward current is the slow inward current given by:

$$I_s(v, f, r, [Ca^{++}]_i) = g_s fr(v + 82.3 + 13.0287 \ln([Ca^{++}]_i)). \quad (1.17)$$

The latter is carried primarily but not exclusively by calcium ions across the membrane and $g_s = 0.09$ is the conductivity related to the slow inward current. As a result, the total ionic current is given by:

$$I_{ion}(v, \mathbf{w}, [Ca^{++}]_i) = I_{Pot}(v) + I_z(v, z) + I_{Na}(v, m, o, l) + I_s(v, f, r, [Ca^{++}]_i). \quad (1.18)$$

FitzHugh-Nagumo

One of the most popular simple models of activation-recovery was developed by FitzHugh and Nagumo and it has become known as the FHN model [Fit61, NAY62]. In this model, the transmembrane potential is normalized using the relation

$$u = \frac{V_m - V_{rest}}{V_{plateau} - V_{rest}}, \quad (1.19)$$

where u is the normalized potential, V_{rest} is the potential at rest (-80mV), $V_{plateau}$ is the plateau potential and V_m is the transmembrane potential.

The ionic current is given by

$$I_{ion}(u, w) = c_1 u(u - \alpha)(1 - u) - c_2 w, \quad (1.20)$$

where c_1 and c_2 are the excitation rate and excitation decay constants respectively, α is the activation threshold value ($0 < \alpha \leq 1/2$). The recovery variable is governed by the equation

$$\frac{dw}{dt} = b(u - dw), \quad (1.21)$$

where b and d are the recovery rate and recovery decay constants respectively [Fit61, NAY62]. Other models have evolved from the FHN model in order to represent more realistic shape of the cardiac ventricular action potential, we mention for example Rogers-McCulloch model and Aliev-Panfilov model [AP96, RM94].

1.4 Cardiac Mechanical Modeling

The appropriate context for mechanically modeling most organs, such as the myocardium, is continuum mechanics. In this section, we describe the theory underpinning the mechanical modeling of organs by first introducing the different tensors describing the deformation of a continuous material and stating the equilibrium equations. Then we present different constitutive laws that express the relation between strains and stresses. Finally, we give an overview of the constitutive laws of the myocardium available in the literature in the context of finite strain theory. For further details on this section, we refer the reader for instance to [Cia87, Gur82, Ogd03].

1.4.1 Nonlinear Elasticity

Kinematic

Let $\Omega_R \subset \mathbb{R}^3$, be an open, connected and bounded domain with smooth boundary Γ_R . We denote by $\bar{\Omega}_R \subset \mathbb{R}^3$ the *reference configuration* of the continuous medium, where $\bar{\Omega}_R$ is the closure of Ω_R . A material point P is represented by the coordinates of its position \mathbf{X} in the reference configuration.

Definition 1.4.1. A *deformation field* is a sufficiently smooth, one-to-one vector field

$$\phi : \bar{\Omega}_R \rightarrow \mathbb{R}^3,$$

such that

$$\det \nabla_{\mathbf{X}} \phi > 0, \text{ on } \Omega_R.$$

The function ϕ maps \mathbf{X} to its current position

$$\mathbf{x} = \phi(\mathbf{X}).$$

The set $\bar{\Omega} := \phi(\bar{\Omega}_R)$ is the *deformed configuration* which is assumed to be a compact subset of \mathbb{R}^3 such that

$$\phi(\bar{\Omega}_R) = \overline{\phi(\Omega_R)}, \quad \phi(\partial\Omega_R) = \partial\left(\phi(\Omega_R)\right), \text{ and } \phi^\circ(\bar{\Omega}_R) = \Omega_R.$$

Remark 1. The requirement that the tissue does not penetrate itself after deformation is expressed by the assumption that ϕ is one-to-one.

Definition 1.4.2. The displacement field associated to the deformation field ϕ is the function $\mathbf{u} : \bar{\Omega}_R \rightarrow \mathbb{R}^3$ defined by

$$\mathbf{u}(\mathbf{X}) = \mathbf{x} - \mathbf{X},$$

and the displacement gradient $\nabla_{\mathbf{X}}\mathbf{u}$ satisfies the following relation:

$$\nabla_{\mathbf{X}}\mathbf{u} = \nabla_{\mathbf{X}}\phi - \mathbf{I},$$

where \mathbf{I} is the identity tensor:

Furthermore, we introduce the following tensors:

- $\mathbf{F} := \nabla_{\mathbf{X}}\phi$ is the deformation gradient.
- $\mathbf{C} := \mathbf{F}^T\mathbf{F}$ is the right Cauchy strain tensor.
- $\mathbf{B} := \mathbf{F}\mathbf{F}^T$ is the left Cauchy strain tensor.
- $\mathbf{E} := \frac{1}{2}(\mathbf{C} - \mathbf{I}) = \frac{1}{2}(\nabla\mathbf{u}^T + \nabla\mathbf{u} + \nabla\mathbf{u}^T\nabla\mathbf{u})$ is the Green-St Venant strain tensor.

The right Cauchy strain tensor \mathbf{C} is symmetric and positive definite. Hence, it has three strictly positive eigenvalues denoted by $(\lambda_i^2(\mathbf{C}))_{i=1,2,3}$.

Definition 1.4.3. A function $f : \mathbb{M}_3 \rightarrow \mathbb{R}$ is said to be an invariant of a tensor \mathbf{A} if and only if for all $\mathbf{Q} \in \mathcal{O}_3$, there holds $f(\mathbf{Q}\mathbf{A}\mathbf{Q}^T) = f(\mathbf{A})$.

The tensor \mathbf{C} has mainly three invariants given by

$$\begin{aligned} I_1(\mathbf{C}) &= \text{tr}(\mathbf{C}), \\ I_2(\mathbf{C}) &= \frac{1}{2} \left((\text{tr}(\mathbf{C}))^2 - \text{tr}(\mathbf{C}^2) \right) = \text{tr}(\text{Cof}(\mathbf{C})), \\ I_3(\mathbf{C}) &= \det(\mathbf{C}) = (\det(\mathbf{F}))^2, \end{aligned} \quad (1.22)$$

where $\text{tr}(\mathbf{C})$ and $\text{Cof}(\mathbf{C})$ denote the trace of \mathbf{C} and its cofactor matrix respectively. These invariants are expressed in terms of the eigenvalues of \mathbf{C} as follows

$$\begin{cases} I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2, \\ I_2 = \lambda_1^2\lambda_2^2 + \lambda_2^2\lambda_3^2 + \lambda_1^2\lambda_3^2, \\ I_3 = \lambda_1^2\lambda_2^2\lambda_3^2. \end{cases} \quad (1.23)$$

Quasi-Static Equilibrium Equations

Theorem 1.4.4. *Cauchy's Theorem - Steady State Equations in the Deformed Configuration.* [Cia87, Gur82] If the forces are regular enough, a solid satisfies the following equations at equilibrium:

$$\begin{cases} -\nabla_{\mathbf{x}} \cdot (\boldsymbol{\sigma}(\mathbf{x})) = \mathbf{f}^\phi & \forall \mathbf{x} \in \Omega \\ \boldsymbol{\sigma}(\mathbf{x})\mathbf{n}(\mathbf{x}) = \mathbf{g}^\phi & \forall \mathbf{x} \in \partial\Omega, \end{cases}$$

where $\mathbf{f}^\phi : \Omega \rightarrow \mathbb{R}^3$ are the volume forces, $\mathbf{g}^\phi : \partial\Omega \rightarrow \mathbb{R}^3$ are the surface forces and the divergence operator is the divergence with respect to the Eulerian variable \mathbf{x} . The tensor $\boldsymbol{\sigma} : \bar{\Omega} \rightarrow \mathbb{M}_3$ is called the Cauchy stress tensor and \mathbf{n} is the outward unit normal to $\partial\Omega$.

Assuming the functions are regular enough and using Green's theorem, the variational formulation of system (1.24) can be written as

$$\int_{\Omega} \boldsymbol{\sigma} : \nabla_{\mathbf{x}}\mathbf{v} \, d\mathbf{x} = \int_{\Omega} \mathbf{f}^\phi \cdot \mathbf{v} \, d\mathbf{x} + \int_{\partial\Omega} \mathbf{g}^\phi \cdot \mathbf{v} \, ds, \quad \forall \mathbf{v} : \bar{\Omega} \rightarrow \mathbb{R}^3. \quad (1.24)$$

Piola-Kirchhoff Stress Tensors - Steady State Equations in the Reference Configuration

Since the mapping ϕ is unknown, we need to rewrite the equilibrium equations in the reference configuration. By a change of variables in (1.24) using $\mathbf{x} = \phi(\mathbf{X})$, one can get the variational formulation of steady state equations in the reference configuration:

$$\int_{\Omega_R} \mathbf{P} : \nabla_{\mathbf{X}} \mathbf{v} \, d\mathbf{X} = \int_{\Omega_R} \mathbf{f} \cdot \mathbf{v} \, d\mathbf{X} + \int_{\partial\Omega_R} \mathbf{g} \cdot \mathbf{v} \, ds, \quad \forall \mathbf{v} : \bar{\Omega}_R \rightarrow \mathbb{R}^3, \quad (1.25)$$

where

$$\mathbf{P}(\mathbf{X}) = \det(\mathbf{F}(\mathbf{X})) \boldsymbol{\sigma}(\phi(\mathbf{X})) \mathbf{F}^{-T}(\mathbf{X}), \quad (1.26)$$

is the first Piola-Kirchhoff stress tensor representing forces acting on a surface element of the deformed configuration measured per unit undeformed surface. Moreover, we have used

$$\mathbf{f}(\mathbf{X}) = \det(\mathbf{F}(\mathbf{X})) \mathbf{f}^\phi(\phi(\mathbf{X})), \quad \mathbf{g}(\mathbf{X}) \, ds(\mathbf{X}) = \mathbf{g}^\phi(\phi(\mathbf{X})) \, ds(\mathbf{x}) \text{ and } \mathbf{v}(\mathbf{X}) = \mathbf{v}(\phi(\mathbf{X})).$$

Indeed, one can show that under enough regularity condition, the first Piola-Kirchhoff stress tensor verifies the following boundary value problem

$$\begin{cases} -\nabla_{\mathbf{X}} \cdot (\mathbf{P}(\mathbf{X})) = \mathbf{f} & \forall \mathbf{X} \in \Omega_R \\ \mathbf{P}(\mathbf{X}) \mathbf{N}(\mathbf{X}) = \mathbf{g} & \forall \mathbf{X} \in \partial\Omega_R \end{cases}$$

Unlike the Cauchy stress tensor, the first Piola-Kirchhoff stress tensor is not necessarily symmetric. It is convenient to introduce a symmetric stress tensor on the reference configuration. That's why, one may define the second Piola-Kirchhoff stress tensor as

$$\mathbf{S}(\mathbf{X}) = \mathbf{F}^{-1}(\mathbf{X}) \mathbf{P}(\mathbf{X}). \quad (1.27)$$

The tensor \mathbf{S} is a symmetric tensor representing the forces acting on an undeformed surface element measured on a unit undeformed surface element. One has the following relations between the three stress tensors:

$$\begin{aligned} \mathbf{P} &= \mathbf{F} \mathbf{S} = (\det \mathbf{F}) \boldsymbol{\sigma} \mathbf{F}^{-T}, \\ \mathbf{S} &= \mathbf{F}^{-1} \mathbf{P} = (\det \mathbf{F}) \mathbf{F}^{-1} \boldsymbol{\sigma} \mathbf{F}^{-T}, \\ \boldsymbol{\sigma} &= (\det \mathbf{F})^{-1} \mathbf{P} \mathbf{F}^T = (\det \mathbf{F})^{-1} \mathbf{F} \mathbf{S} \mathbf{F}^T. \end{aligned} \quad (1.28)$$

1.4.2 Constitutive Laws

Since the steady state equations do not take into consideration the material properties of the body, the problem is still incomplete from a mathematical as well as physical points of view. Some extra assumptions are required to describe those properties. These assumptions can be translated in terms of a relationship between the stress and the strain tensors. This relationship is called the constitutive law of the material.

Definition 1.4.5. (Elasticity): A material is said to be elastic if and only if at each point the Cauchy stress tensor is a function of the material point $\mathbf{X} \in \Omega_R$ and the deformation tensor \mathbf{F} i.e. $\forall \mathbf{X} \in \Omega_R, \boldsymbol{\sigma} = \mathcal{S}(\mathbf{X}, \mathbf{F})$.

Definition 1.4.6. (Homogeneity): A material is said to be homogeneous if its density and its constitutive law are independent of the material point \mathbf{X} . In the case of a homogeneous elastic material, the Cauchy stress tensor is written as $\boldsymbol{\sigma} = \mathcal{S}(\mathbf{F})$.

Proposition 1. (Material Objectivity- Frame Indifference): The constitutive law does not depend on the reference frame in which the deformations are observed. So the Cauchy stress tensor $\boldsymbol{\sigma}$ is such that:

$$\mathcal{S}(\mathbf{X}, \mathbf{QF}) = \mathbf{Q}\mathcal{S}(\mathbf{X}, \mathbf{F})\mathbf{Q}^T, \quad \forall \mathbf{Q} \in \mathcal{O}_3, \mathbf{F} \in \mathbb{M}_3^+.$$

The isotropy properties of a material are local properties related to a material point and are interpreted by the invariance of the constitutive law with respect to some changes in the reference configuration.

Definition 1.4.7. (Material Symmetry): A tensor $\mathbf{G} \in \mathcal{O}_3$ is a material symmetry in a point \mathbf{X} if for all $\mathbf{F} \in \mathbb{M}_3^+$, there holds

$$\mathcal{S}(\mathbf{X}, \mathbf{F}) = \mathcal{S}(\mathbf{X}, \mathbf{FG}). \quad (1.29)$$

Proposition 2. The set $\mathcal{G} = \{\mathbf{G} \in \mathcal{O}_3, \mathbf{G} \text{ is a material symmetry}\}$ is a subgroup of \mathcal{O}_3 [Gur82].

Definition 1.4.8. (Orthotropy): A material is said to be orthotropic if there exist at least two orthogonal planes of material symmetry, where the properties of the material are independent of the directions in each plane.

Definition 1.4.9. (Transverse Isotropy): A special class of orthotropic materials are those having the same properties in one plane and different properties in the normal direction to this plane, their properties are therefore invariant under local rotation of the body around this privileged direction. Such materials are called transverse isotropic.

Definition 1.4.10. (Isotropy): The material is called isotropic when its properties are independent of all directions, they are invariant for any local rotation of the body. In particular, equation (1.29) is verified for all rotation $\mathbf{G} \in SO_3$.

An important characteristic of biological tissues is the anisotropy in their mechanical properties. This is indeed related to the variation of fiber orientation and to the distribution of collagen fibers in the extracellular matrix entailing some properties in privileged directions. For instance, in the myocardium, the privileged direction is the direction of the cardiac fibers.

Definition 1.4.11. (Hyperelasticity): An elastic material is said to be hyperelastic if there exists a real function $\mathcal{W} = \mathcal{W}(\mathbf{X}, \mathbf{F})$ defined on $\bar{\Omega}_R \times \mathbb{M}_3^+$, differentiable with respect to \mathbf{F} such that the first Piola-Kirchhoff stress tensor $\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}}$. The function \mathcal{W} is called the strain energy function and is measured by units of volume of the reference configuration.

A hyperelastic material has a reversible mechanical behavior and there is no dissipation during the cycle of modification.

Proposition 3. *The strain energy \mathcal{W} of an isotropic hyperelastic material is a function of the three invariants I_1, I_2 , and I_3 , defined in equation (1.22):*

$$\mathcal{W} = \mathcal{W}(I_1, I_2, I_3). \quad (1.30)$$

The Cauchy stress tensor $\boldsymbol{\sigma}$ can be obtained as a consequence of Rivlin-Eriksen's theorem. For an isotropic hyperelastic compressible material, $\boldsymbol{\sigma}$ reads as [Ogd03]:

$$\boldsymbol{\sigma} = 2(\det \mathbf{F})^{-1} \left[I_3 \mathcal{W}_3 \mathbf{Id} + (\mathcal{W}_1 + I_1 \mathcal{W}_2) \mathbf{B} - \mathcal{W}_2 \mathbf{B}^2 \right], \quad \text{with } \mathcal{W}_i = \partial \mathcal{W} / \partial I_i, \quad i = 1, 2, 3. \quad (1.31)$$

Let $\boldsymbol{\tau}$ be the field of unit vectors of the privileged direction of a transverse isotropic hyperelastic material in the reference configuration. Such a material may be characterized by a strain energy depending on the deformation gradient and the vector $\boldsymbol{\tau}$:

$$\mathcal{W} = \mathcal{W}(\mathbf{C}, \boldsymbol{\tau}). \quad (1.32)$$

Proposition 4. *In transverse isotropy, the strain energy \mathcal{W} depends on the three invariants I_1, I_2 , and I_3 defined in equation (1.22), along with mixed invariants of \mathbf{C} and $\boldsymbol{\tau}$, abusively called additional invariants I_4 and I_5 depending on $\boldsymbol{\tau}$ and defined by :*

$$I_4 = \boldsymbol{\tau} \cdot (\mathbf{C}\boldsymbol{\tau}) \quad \text{and} \quad I_5 = \boldsymbol{\tau} \cdot (\mathbf{C}^2 \boldsymbol{\tau}), \quad (1.33)$$

where \mathbf{C} is the right Cauchy strain tensor. We have :

$$\mathcal{W} = \mathcal{W}(I_1, I_2, I_3, I_4, I_5). \quad (1.34)$$

Note that the joint invariant I_4 is equal to $\|\mathbf{F}\boldsymbol{\tau}\|^2$ representing the elongation along the direction $\boldsymbol{\tau}$.

When the material is hyperelastic transverse isotropic and compressible, the Cauchy stress tensor $\boldsymbol{\sigma}$ is expressed as [Ogd03]:

$$\boldsymbol{\sigma} = 2(\det \mathbf{F})^{-1} \left[I_3 \mathcal{W}_3 \mathbf{Id} + (\mathcal{W}_1 + I_1 \mathcal{W}_2) \mathbf{B} - \mathcal{W}_2 \mathbf{B}^2 + \mathcal{W}_4 (\mathbf{F}\boldsymbol{\tau})^T \otimes (\mathbf{F}\boldsymbol{\tau})^T + \mathcal{W}_5 ((\mathbf{B}\mathbf{F}\boldsymbol{\tau})^T \otimes (\mathbf{F}\boldsymbol{\tau})^T + (\mathbf{F}\boldsymbol{\tau})^T \otimes (\mathbf{B}\mathbf{F}\boldsymbol{\tau})^T) \right], \quad (1.35)$$

with $\mathcal{W}_i = \partial \mathcal{W} / \partial I_i$, $i = 1, \dots, 5$. For an isotropic material the terms with \mathcal{W}_4 and \mathcal{W}_5 are suppressed.

Definition 1.4.12. (Incompressibility): *A material is incompressible if its volume does not change during deformation. This is translated by the condition:*

$$\det(\mathbf{F}) = \lambda_1 \lambda_2 \lambda_3 = 1, \quad \text{i.e. } I_3 = 1. \quad (1.36)$$

In the case of a hyperelastic incompressible material, the Cauchy stress tensor is given by [Ogd03]:

$$\boldsymbol{\sigma} = -p \mathbf{I} + 2\mathbf{F} \frac{\partial \mathcal{W}}{\partial \mathbf{C}} \mathbf{F}^T, \quad \det(\mathbf{F}) = 1, \quad (1.37)$$

where p is the Lagrange multiplier associated to the incompressibility constraint, it is called the "hydrostatic pressure", see [Ogd03]. Accordingly, the first Piola-Kirchhoff stress tensor \mathbf{P} , is given by:

$$\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} - p \text{Cof}(\mathbf{F}), \quad \det(\mathbf{F}) = 1.$$

1.4.3 Constitutive laws of the myocardium

The earliest models of the cardiac muscle were simple, describing its behavior as linear, elastic, isotropic and homogeneous [GGBM72, SD63, WR68]. More recent anisotropic models accounted for the direction of the fibers and the heterogeneity of the muscle. First, such models were in the framework of linear elasticity with the infinitesimal strain approach [Cha82, OC88]. Nonlinear models taking into consideration the cardiac fibrous structure and anisotropy were developed in the context of the large (finite) strain theory (see for instance [SH91, McC86, Ogd03]) and new constitutive laws were proposed: some are transverse isotropic (e.g. [HSY90, LY98, Cai98]) and others are orthotropic (e.g. [NH00, UMM00]). The advantage of transverse isotropic models is that the functional form of the strain energy is directly deduced from experimental data. However, the anatomy of the heart shows that it is composed of several layers of fibers [LSC⁺95]. Such a structure corresponds to an orthotropic structure. We consider in the following part two examples of constitutive laws of the myocardium illustrating the transverse isotropy and the orthotropy assumptions.

A transverse isotropic model: Lin and Yin's model

Lin and Yin [LY98] proposed a multiaxial law for the active and passive myocardium. Some assumptions were made such as hyperelasticity, incompressibility and transverse isotropy of the material where the privileged direction is the predominant fiber direction. Moreover, the strain energy is supposed to depend on the invariants I_1 and I_4 of the deformation. The strains in the active and passive states are measured with respect to the cardiac muscle at rest. They noted that there are significant stresses in the transverse direction to the fibers showing the important effect due to the collagen fibers that protect the muscle of excessive stretch.

For the passive myocardium, they have chosen an exponential function to express the strain energy in terms of the invariants I_1 and I_4 :

$$\mathcal{W}_{pas} = C_1(e^Q - 1), \quad \text{with} \quad Q = C_2(I_1 - 3)^2 + C_3(I_1 - 3)(I_4 - 1) + C_4(I_4 - 1)^2. \quad (1.38)$$

At the active state, they showed that the response to stress is more linear than that at the passive state. This suggested that active and passive myocardia are different types of material having different strain energies describing their rheology. Hence, they suggested a polynomial function for the strain energy of the passive myocardium as given in the following expression:

$$\mathcal{W}_{act} = C_0 + C_1(I_1 - 3)(I_4 - 1) + C_2(I_1 - 3)^2 + C_3(I_4 - 1)^2 + C_4(I_1 - 3) + C_5(I_4 - 1). \quad (1.39)$$

In both expressions of the strain energy, the rheology parameters C_i must satisfy some conditions. See [LY98] for further details.

An orthotropic model: Usyk-Mazhari-McCulloch model

Usyk et al. [UMM00] have studied the effects of orthotropy in the left ventricle of dogs. They have used for the left ventricle in the passive state a constitutive relation defined by an exponential strain energy function \mathcal{W} , corresponding to a nonlinear, orthotropic and nearly incompressible law:

$$\begin{aligned} \mathcal{W} &= C(e^Q - 1) + C_{compr}(J \ln J - J + 1), \\ Q &= b_{ll}E_{ll}^2 + b_{tt}E_{tt}^2 + b_{nn}E_{nn}^2 + \\ &\quad b_{lt}(E_{lt}^2 + E_{tl}^2) + b_{ln}(E_{ln}^2 + E_{nl}^2) + b_{nt}(E_{nt}^2 + E_{tn}^2), \end{aligned} \quad (1.40)$$

where E_{ij} are the components of Green's strain tensor \mathbf{E} in the material coordinate system (l, t, n) . The term J is the determinant of the deformation gradient \mathbf{F} and the material constants are given by: $C = 0.88$ kPa; $b_{ll} = 6.0$; $b_{tt} = 7.0$; $b_{nn} = 3.0$; $b_{lt} = 12.0$; $b_{ln} = 3.0$; $b_{nt} = 3.0$; and $C_{compr} = 100.0$ kPa.

The quasi-incompressibility is obtained by penalization. Indeed, the term $C_{compr}(J \ln J - J + 1)$ is introduced by a big enough coefficient C_{compr} imposing on the quantity $J \ln J - J + 1$ to be infinitesimal, or almost equal to 0, so that the product $C_{compr}(J \ln J - J + 1)$ has the same magnitude as the term $C(e^Q - 1)$. Consequently, the value of J is forced to be very close to 1.

The ventricular contraction is modeled by defining the Cauchy stress tensor $\boldsymbol{\sigma}$ as the sum of a passive stress tensor $\boldsymbol{\sigma}^{(p)}$ derived from the strain energy function and of an active stress tensor $\boldsymbol{\sigma}^{(a)}$:

$$\boldsymbol{\sigma} = \boldsymbol{\sigma}^{(p)} + \boldsymbol{\sigma}^{(a)}. \quad (1.41)$$

The components $\sigma_{ij}^{(a)}$ of the active stress tensor are derived from the diagonal stress tensor $\boldsymbol{\sigma}_{active}$ in the material coordinate system (X_l, X_t, X_n) using a rotation matrix \mathbf{q} that defines the relation between the global coordinate system in use and the local material coordinate system:

$$\boldsymbol{\sigma}^{(a)} = \mathbf{q}^T \boldsymbol{\sigma}_{active} \mathbf{q}. \quad (1.42)$$

The components of the tensor $\boldsymbol{\sigma}_{active}$ are functions of the intracellular calcium concentration $[\text{Ca}^{2+}]_i(t)$ and of the length of the sarcomeres.

$$[\text{Ca}^{2+}]_i(t) = [\text{Ca}^{2+}]_0 + ([\text{Ca}^{2+}]_{\max} - [\text{Ca}^{2+}]_0) \frac{t}{\tau_{\text{Ca}}} e^{1-t/\tau_{\text{Ca}}}, \quad (1.43)$$

where $[\text{Ca}^{2+}]_0$ designates the intracellular calcium concentration at rest and $[\text{Ca}^{2+}]_{\max}$ is the maximum value that $[\text{Ca}^{2+}]_i(t)$ can attain at time instant $t = \tau_{\text{Ca}}$. They have chosen as parameters in the expression of $[\text{Ca}^{2+}]_i(t)$ the following values: $[\text{Ca}^{2+}]_0 = 0.01 \mu\text{M}$, $[\text{Ca}^{2+}]_{\max} = 1 \mu\text{M}$ and $\tau_{\text{Ca}} = 60$ ms.

1.5 Electromechanical coupling models

Cardiac deformation can be modeled by the equations of motion of a hyperelastic material, written in the reference configuration. However, like any living tissue, its contraction is influenced by intrinsic mechanisms taking place at the microscopic level. This ability to actively deform has been 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 ([GK10, LAVH12, NH00, NP04, Tra11]). Another approach is the active strain formulation, [NT07, CFNT08], where the deformation gradient is factorized into active and passive factors, and fiber contraction rewrites in the mechanical balance of forces as a prescribed *active* deformation. In the following sections, we illustrate how the electromechanical coupling is achieved in each of the two approaches and we establish the strong mechanical-to-electrical coupling framework.

1.5.1 The active strain model

The electrical to mechanical coupling in the “active strain model” [CFNT08] factorizes the deformation gradient \mathbf{F} 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, [AANQ11]:

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

where γ_s , $s \in \{l, t, n\}$ are quantities that depend on the electrophysiology equations.

Such a factorization of the deformation tensor \mathbf{F} assumes the existence of a virtual intermediate configuration between the reference and the current frames. In that configuration, the strain energy function depends solely on the deformation at the macroscale \mathbf{F}_p , [NQRB12]:

$$\mathcal{W} = \mathcal{W}(\mathbf{F}_p) = \mathcal{W}(\mathbf{F}\mathbf{F}_a^{-1}),$$

and by a pull back to the reference configuration, one has $\hat{\mathcal{W}} = \det(\mathbf{F}_a) \mathcal{W}(\mathbf{F}\mathbf{F}_a^{-1})$. The corresponding Piola-Kirchhoff stress tensor is given by :

$$\mathbf{P} = \frac{\partial \hat{\mathcal{W}}}{\partial \mathbf{F}}.$$

For instance, in the case of a Neo-Hookean constitutive law, one has

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

where μ is the shear modulus. Then it can be shown that the first Piola-Kirchhoff stress tensor reads as

$$\mathbf{P} = \mu \mathbf{F} \mathbf{C}_a^{-1},$$

where $\mathbf{C}_a^{-1} := \det(\mathbf{F}_a) \mathbf{F}_a^{-1} \mathbf{F}_a^{-T}$ (see also Refs. [AANQ11, NQRB12]). If in addition, the considered material is incompressible, then the condition $\det(\mathbf{F}) = 1$ must be imposed and the hydrostatic pressure p is introduced as a Lagrange multiplier. Accordingly, one gets

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

Further examining the expression of \mathbf{F}_a , one can notice that mechanical activation is mainly influenced by intracellular calcium release [NNN⁺11, POK13, SLC⁺07], 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. [Ber02]. Using a physiological ionic model, the aforementioned fact suggests that, ideally the recovery variables \mathbf{w} and the concentration variable z approximate the spatio-temporal structure of calcium. More physiologically-involved activation models require a dependence of γ_s not only on calcium, but also on local stretch, local stretch rate, sliding velocity of crossbridges, and on other force-length experimental relations [POK13, RLRB⁺14, RBGR⁺14], 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 γ_l , γ_t and γ_n can be written as functions of a parameter γ :

$$\gamma_{l,t,n} = \gamma_{l,t,n}(\gamma), \tag{1.44}$$

where $\gamma_{l,t,n} : \mathbb{R} \mapsto [-\Gamma_{l,t,n}, 0]$ are Lipschitz continuous monotone functions. The values $\Gamma_{l,t,n}$ should be small enough, in order to ensure that $\det(\mathbf{F}_a)$ stays uniformly far from zero, for $\gamma \in \mathbb{R}$. The scalar field γ is the solution of the following ODE associated to the solution (v_i, v_e, w) of the bidomain system (1.8)-(1.9):

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

where $S(\gamma, \mathbf{w}) = \beta(\sum_{j=1}^k \eta_j w_j - \eta_0 \gamma)$, for positive physiological parameters $\beta, \eta_j, j = 0, 1, \dots, k$ (see Ref. [RBAP⁺13]). Moreover, the functions $\gamma_{l,t,n}$ are assumed to be of the form:

$$\gamma_{l,t,n} = -\Gamma_{l,t,n} \frac{2}{\pi} \arctan(\gamma^+ / \gamma_R), \quad \text{where } \gamma^+ := \max(0, \gamma) \text{ and } \gamma_R \text{ is a reference value.}$$

Further details can be found in [LRBQ13, RBGR⁺14] for example.

1.5.2 The active stress model

In the active stress model [NH00, Mou03], the Cauchy stress tensor is considered as the sum of a passive stress modeling the material elastic properties and an active stress modeling the material internal forces generated from the electrical activity.

The basic formulation which corresponds to the active stress model is the following

$$\boldsymbol{\sigma} = \frac{\partial \mathcal{W}^{pas}}{\partial \mathbf{F}} \mathbf{F}^T + T(t, \lambda_f, [Ca^{++}]_i) \mathbf{F} \boldsymbol{\tau} \otimes \mathbf{F} \boldsymbol{\tau},$$

where \mathcal{W}^{pas} is the passive strain energy and T represents the tension along the fiber direction $\boldsymbol{\tau}$. The variable t denotes the time, λ_f is the elongation of the fibers and $[Ca^{++}]_i$ is the intracellular Calcium concentration. Also it is possible to replace $T(t, \lambda_f, [Ca^{++}]_i)$ by $T(t, \lambda_f, v_i, v, w)$ where v_i is the intracellular voltage, v is the transmembrane potential and w represents the recovery and the gating variables and the ionic concentrations.

The active stress can be rewritten in another way [Mou03]. Let W_λ be a primitive with respect to λ of the function $\lambda T(\lambda)$, i.e. $W'_\lambda = \lambda T(\lambda)$. We have :

$$\frac{\partial W_\lambda}{\partial \mathbf{F}} \mathbf{F}^T = T \mathbf{F} \boldsymbol{\tau} \otimes \mathbf{F} \boldsymbol{\tau}. \quad (1.45)$$

Indeed, first we have, $\frac{\partial W_\lambda}{\partial \mathbf{F}} = W'_\lambda \frac{\partial \lambda}{\partial \mathbf{F}} = \lambda T(\lambda) \frac{\partial \lambda}{\partial \mathbf{F}}$.

The variable λ denotes the fiber elongation, i.e. $\lambda^2 = I_4 = \|\mathbf{F} \boldsymbol{\tau}\|^2$. Differentiating with respect to \mathbf{F} , we obtain: $2\lambda \frac{\partial \lambda}{\partial \mathbf{F}} = 2\mathbf{F} \boldsymbol{\tau} \otimes \boldsymbol{\tau}$. Therefore, the derivative of λ with respect to \mathbf{F} is equal to

$\frac{\partial \lambda}{\partial \mathbf{F}} = \frac{1}{\lambda} \mathbf{F} \boldsymbol{\tau} \otimes \boldsymbol{\tau}$. This leads to Equation (1.45).

Consequently, we let $\mathcal{W} = \mathcal{W}^{pas} + W_\lambda$ be the total strain energy function. The expression of the Cauchy stress tensor can be rewritten as:

$$\boldsymbol{\sigma} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} \mathbf{F}^T. \quad (1.46)$$

Finally, the first Piola-Kirchhoff stress tensor is given by :

$$\mathbf{P} = \det(\mathbf{F}) \boldsymbol{\sigma} \mathbf{F}^{-T} = \det(\mathbf{F}) \frac{\partial \mathcal{W}}{\partial \mathbf{F}}. \quad (1.47)$$

This shows that the constitutive law is given by (1.47) where \mathcal{W} depends on the electrophysiology parameters modeling the electrical activity of the heart.

1.5.3 Mechanical to electrical coupling

The *mechanical-to-electrical* coupling is achieved by a change of variables in the bidomain equations from the current configuration (Eulerian coordinates) to the reference configuration (Lagrangian coordinates), which leads to a conduction term depending on the deformation gradient \mathbf{F} :

$$\mathbf{M}_k(\mathbf{x}, \mathbf{F}) := (\mathbf{F})^{-1} \mathbf{K}_k(\mathbf{x}) (\mathbf{F})^{-T}, \quad k \in \{i, e\}. \quad (1.48)$$

We will only show how the change of variables is performed in one of the two bidomain equations, the other one follows similarly. Starting from:

$$\chi C_m \partial_t v - \nabla \cdot (\mathbf{K}_i \nabla v_i) + \chi I_{\text{ion}}(v, w) = I_{\text{app}}^i, \quad (\mathbf{x}, t) \in \Omega \times (0, T),$$

multiplying by $\varphi \in \mathcal{D}(\Omega)$ and integrating over Ω , we get the equation:

$$\int_{\Omega} \chi C_m \partial_t v \varphi - \nabla \cdot (\mathbf{K}_i \nabla v_i) \varphi + \chi I_{\text{ion}} \varphi(\mathbf{x}) \, d\mathbf{x} = \int_{\Omega} I_{\text{app}}^i \varphi \, d\mathbf{x}.$$

Now by Green's formula and using the fact that $\varphi = 0$ on $\partial\Omega$, we get:

$$\int_{\Omega} \chi C_m \partial_t v \varphi + (\mathbf{K}_i \nabla v_i) : \nabla \varphi + \chi I_{\text{ion}} \varphi \, d\mathbf{x} = \int_{\Omega} I_{\text{app}}^i \varphi \, d\mathbf{x}.$$

Substituting $\mathbf{x} = \boldsymbol{\phi}(\mathbf{X})$ and accordingly $d\mathbf{x} = |\nabla \boldsymbol{\phi}(\mathbf{X})| d\mathbf{X} = J d\mathbf{X}$, we have:

$$\int_{\Omega_R} \chi C_m \partial_t v(\boldsymbol{\phi}(\mathbf{X})) + (\mathbf{K}_i \nabla v_i) : \nabla \varphi(\boldsymbol{\phi}(\mathbf{X})) + \chi I_{\text{ion}} \varphi(\boldsymbol{\phi}(\mathbf{X})) \, J d\mathbf{X} = \int_{\Omega_R} I_{\text{app}}^i \varphi(\boldsymbol{\phi}(\mathbf{X})) \, J d\mathbf{X}.$$

Consider in particular the term:

$$\int_{\Omega_R} (\mathbf{K}_i \nabla v_i) : \nabla \varphi(\boldsymbol{\phi}(\mathbf{X})) \, J d\mathbf{X},$$

we will first use the chain rule, then the properties of inner product of matrices to get

$$\begin{aligned} & \int_{\Omega_R} (\mathbf{K}_i(\boldsymbol{\phi}(\mathbf{X})) \nabla v_i(\boldsymbol{\phi}(\mathbf{X})) : \nabla \varphi(\boldsymbol{\phi}(\mathbf{X})) \, J d\mathbf{X} \\ &= \int_{\Omega_R} \left(\mathbf{K}_i(\boldsymbol{\phi}(\mathbf{X})) \nabla \boldsymbol{\phi}^{-T} \nabla v_i(\mathbf{X}) \right) : \nabla \boldsymbol{\phi}^{-T} \nabla \varphi(\mathbf{X}) \, J d\mathbf{X} \\ &= \int_{\Omega_R} \nabla \boldsymbol{\phi}^{-1}(\mathbf{X}) \left(\mathbf{K}_i(\boldsymbol{\phi}(\mathbf{X})) \nabla \boldsymbol{\phi}^{-T} \nabla v_i(\mathbf{X}) \right) : \nabla \varphi(\mathbf{X}) \, J d\mathbf{X} \\ &= \int_{\Omega_R} -\nabla \cdot \left(\mathbf{F}^{-1}(\mathbf{X}) (\mathbf{K}_i(\boldsymbol{\phi}(\mathbf{X})) \mathbf{F}^{-T} \nabla v_i(\mathbf{X})) \right) \varphi(\mathbf{X}) \, J d\mathbf{X}, \end{aligned}$$

where the last equality results from Green's formula and from replacing $\nabla\phi$ by \mathbf{F} . This means that

$$-\nabla_{\mathbf{x}} \cdot \left(\mathbf{K}_i(\mathbf{x}) \nabla_{\mathbf{x}} v_i(\mathbf{x}) \right) = \mathbf{f}(\mathbf{x}), \quad \forall \mathbf{x} \in \Omega$$

is equivalent to

$$-\nabla_{\mathbf{X}} \cdot \left(\mathbf{F}^{-1} \mathbf{K}_i(\phi(\mathbf{X})) \mathbf{F}^{-T} \nabla_{\mathbf{X}} v_i(\mathbf{X}) \right) = \mathbf{f}(\phi(\mathbf{X})), \quad \forall \mathbf{X} \in \Omega_R.$$

Unfolding Homogenization of the Bidomain Model

2.1 Introduction

This chapter is devoted to study, in the context of the unfolding homogenization technique, the asymptotic behaviour of a microscopic-level modeling problem for cardiac electrical activity. Indeed, there are two scales in cardiac electrophysiology: the microscopic scale describing the source of the electric wave in the cells, and the macroscopic scale describing the propagation of the electrical wave at the level of the organ. Since the microscopic model is unsuitable for numerical computations due to the complexity of the underlying geometry, a rigorous derivation of the macroscopic model is needed while taking into account the properties of the physiological and microscopic structure.

2.1.1 Homogenization Techniques

Classically, homogenization has been done by means of the multiple-scale method which permits to formally obtain the homogenized problem based on a formal asymptotic expansion [CD99, BLP11]. There are now various mathematical methods related to this theory: the oscillating test functions method due to L. Tartar in [Tar76], the two-scale convergence method introduced by G. Nguetseng in [Ngu89], and further developed by G. Allaire in [All92], and the most recent is the periodic unfolding method introduced by D. Cioranescu, A. Damlamian and G. Griso for the study of classical periodic homogenization in the case of fixed domains and adapted to homogenization in domains with holes in [CDZ06]. The idea of the unfolding operator was used in [BLM96, ADH90, Vog82] under the name of periodic modulation or dilation operator. The name “unfolding operator” was then introduced in [CDZ06] and deeply studied in [CDG08, CDD⁺12]. The interest of the unfolding method comes, on one hand, from the fact that it only deals with functions and classical notions of convergence in L^p spaces and it does

not necessitate the use of a special class of test functions. On the other hand, the unfolding operator maps functions defined on oscillating domains into functions defined on fixed domains. Hence, the proof of homogenization results becomes quite simple.

Regarding the asymptotic behavior of a microscopic-level modeling problem for the bioelectric activity of the heart, we mention the work by M. Pennachio, G. Savaré, and P. Franzone that rigorously studies the derivation of the bidomain model in the framework of Γ -convergence theory presented in [PSF05] for a specific ionic model. This theory is actually suitable when the model is described as the minimization of a convex functional but this is not the case for all ionic models. Recently, the two-scale method has been used in [CI18, GK18] to obtain the homogenized macroscopic model using different ionic models and assumptions on the conductivity matrices. In [CI18], the authors derive a macroscopic bidomain model using simplified ionic models whereas in [GK18], the authors use the FitzHugh-Nagumo ionic model. In the present work, we treat a generalized class of ionic models including the FitzHugh-Nagumo model along with physiological models involving ionic concentrations that appear as arguments of a logarithmic function and that must be shown to be bounded away from 0. We further note that in [CI18, GK18], the cardiac domain was assumed to be a cube in \mathbb{R}^3 . Regarding the mathematical analysis of the microscopic model, we point out that in [Ven06], the author used Schauder's fixed point theorem and in [FS02b], the authors used a variational approach to establish the well-posedness of the microscopic problem under different initial and boundary conditions. In this chapter, we prove first the existence of solution for the microscopic problem by a constructive method based on the Faedo-Galerkin approach without the restrictive assumption, usually found in the literature, on the conductivity matrices to have the same basis of eigenvectors or to be diagonal matrices (see for instance [BCP09] where the authors prove the existence of a local in time strong solution of the bidomain equations after introducing the so-called bidomain operator). Secondly, the convergence of solutions of a sequence of microscopic problems to the solution of the macroscopic problem is established in properly chosen function spaces. We use the unfolding method in perforated domains [CDG08, CDZ06], for sequences of functions bounded in L^2 , H^1 or in $H^{1/2}$ on a micro-periodic domain. The degenerate structure of the equations of the bidomain model, in combination with the highly oscillating underlying geometry make the homogenization proof nontrivial and standard parabolic a priori estimates are not immediately available [FS02b]. On the other hand, the (nonlinear) dynamics of the cellular model take place on the cell membrane which is a wildly oscillating surface. Hence, an ambiguity arises in defining a proper notion of "strong convergence" of functions in this context. However, some kind of strong convergence is required to pass to the limit in the nonlinear equations. For this reason, we also use the boundary unfolding operator along with a Kolmogorov-Riesz compactness argument [Ama00, GNR16]. We point out that we will not restrict our study to the homogenization method of the bidomain model with nonlinear ionic function of FitzHugh-Nagumo type but also with physiological ionic function of Luo-Rudy type. Moreover, the approach presented herein can be extended to electropermeabilization models. We cite for instance [AWZ16] where a dynamical homogenization scheme is obtained from a physiological cell model and [AGG⁺16] where a conductivity dependent macroscopic tissue model is for the first time derived from first principles.

Note that thanks to homogenization, the resulting macroscopic bidomain model describes averaged intra and extracellular potential by a nonlinear anisotropic reaction-diffusion system. The cardiac tissue is then considered (at the macroscopic level) as the superposition of two anisotropic continuous media: the intra- and extracellular spaces, coexisting along with the cell

membrane, at each point of the tissue. The most substantial mathematical description of the bidomain model is found in the review paper by Henriquez [Hen93], which presents a formal definition of the model from its origins in the core conductor model, and outlines many of the approximations that can be made.

This chapter is outlined as follows. In Section 2.2, a formal derivation of the macroscopic bidomain model from the microscopic model is obtained using asymptotic expansions. The main assumptions used for homogenization are presented in Section 2.3 and the main results are stated. In Section 2.4, existence of weak solutions to the microscopic problem is proved based on a Faedo-Galerkin approach, a priori estimates and a compactness argument. In Section 2.5, some estimates on the solutions of the microscopic problem are obtained and the microscopic problem is formulated using the unfolding operator. The passage to the limit using compactness and the unfolding method are established in Section 2.6. Then in Section 2.7, the macroscopic bidomain equations are recuperated from the limit equations obtained in Section 2.6 and the cell problem is decoupled. Finally, in Section 2.8, a microscopic bidomain model with physiological ionic model is homogenized to obtain the corresponding macroscopic model.

2.2 Formal derivation of cardiac electrophysiology model

In this section we derive formally a mathematical model (macroscopic bidomain model) from the propagation of cardiac action potentials at the cellular level (microscopic bidomain model). Note that a similar derivation may be found in [HY09] and the appendix of [FS02b] under simplifying assumptions.

The cardiac cellular media can be viewed as composed of two volumes: the intracellular space Ω_i (inside the cells) and the extracellular space Ω_e (outside the cells) separated by the active membrane Γ . For the derivation of the macroscopic bidomain model, the cells' microstructure medium is idealized (see Figure 4). We assume that all cells have the same shape and are arranged in space in a regular fashion, and have the same pattern of connections with neighbors. This means that in this case the structure of the tissue is approximated by a spatially periodic model.

2.2.1 The Microscopic Bidomain Model

Using Ohm's law in the intra- and extracellular media Ω_i and Ω_e , the current is given by

$$I_j = \mathbf{M}_j \nabla u_j, \text{ for } j = i, e.$$

Due to the current conservation law, the normal current flux through the membrane is continuous

$$\mathbf{M}_i \nabla u_i \cdot \boldsymbol{\mu}_i + \mathbf{M}_e \nabla u_e \cdot \boldsymbol{\mu}_e = 0 \text{ on } \Gamma_T := (0, T) \times \Gamma.$$

On the other hand, since the only active source elements lie on the membrane, each flux equals the transmembrane current per unit area \mathcal{I}_m :

$$\mathcal{I}_m = -\mathbf{M}_i \nabla u_i \cdot \boldsymbol{\mu}_i = \mathbf{M}_e \nabla u_e \cdot \boldsymbol{\mu}_e \text{ on } \Gamma_T.$$

Moreover, assuming the electroneutrality of the solutions away from the cell membrane [JNT83, Mor06], u_j is governed by

$$-\nabla \cdot (\mathbf{M}_j \nabla u_j) = 0 \text{ in } \Omega_{j,T} := (0, T) \times \Omega_j. \quad (2.1)$$

Herein, the potentials u_i and u_e are intra- and extracellular electric potentials respectively, \mathbf{M}_i and \mathbf{M}_e are the corresponding conductivity tensors, μ_i is the exterior unit normal to the boundary Γ from intra- to extracellular space and $\mu_e = -\mu_i$. Note that the conductivities \mathbf{M}_j , $j = i, e$, are assumed to be tensorial and depend on x . Such an assumption would further allow the analysis of more complex models such as models incorporating the influence of heart's mechanical deformations [CGM15, GK10] or of gap junctions [HP10].

Since the electric current that hits the membrane can be blocked by the membrane or can pass through the membrane with ionic current $I_{\text{ion}} - I_{\text{app}}$, the charge conservation gives

$$\begin{aligned} \frac{\partial q_i}{\partial t} + I_{\text{ion}} - I_{\text{app}} &= \mathcal{I}_m & \text{on } \Gamma_T, \\ \frac{\partial q_e}{\partial t} - I_{\text{ion}} + I_{\text{app}} &= -\mathcal{I}_m & \text{on } \Gamma_T, \end{aligned}$$

where q_j , $j = i, e$ is the surface charge on each side of the membrane, I_{app} is an applied current and I_{ion} is the ionic function that depends on the considered ionic model (the current is directed from the intra- to the extracellular medium). Moreover, under the assumption that any charge accumulation on one side of the membrane is balanced by a charge on the other side, there holds

$$q_i = -q_e.$$

Also, considering the membrane as a capacitor, the surface charge is proportional to the transmembrane potential

$$q_i = C_m v,$$

with the proportion being the capacitance per unit area C_m . Consequently, regarding the dynamical structure of the membrane, its electrical potential $v = u_i - u_e$ on Γ satisfies the following dynamic boundary equation

$$\begin{aligned} C_m \partial_t v + I_{\text{ion}}(v, w) - I_{\text{app}} &= \mathcal{I}_m & \text{on } \Gamma_T := (0, T) \times \Gamma, \\ \partial_t w - H(v, w) &= 0 & \text{on } \Gamma_T. \end{aligned} \tag{2.2}$$

Note that \mathcal{I}_m is the sum of a capacitive current, of an applied current I_{app} and of the nonlinear ionic functions $I_{\text{ion}}(v, w)$. The functions $I_{\text{ion}}(v, w)$ and $H(v, w)$ correspond to the chosen ionic model of the membrane dynamics (here w corresponds to the various ionic gating variables). Hence, equations (2.1) and (2.2) give a description of the microscopic representation of the electric potentials in the cardiac tissue.

2.2.2 Nondimensional Analysis

In order to understand the relative influences and amplitudes of the terms involved in the system and the interaction of the microscopic and macroscopic scales, a nondimensionalisation of the system turns out to be an essential ingredient of the asymptotic analysis. Few works are available in the literature in this direction, we cite for instance [NK93] where the authors derived a macroscopic model of tissue from an idealized version of the microscopic model and [RB13] for the nondimensional analysis of the ionic current I_{ion} (see also [HY09, PSF05]).

We define the dimensionless scale parameter:

$$\varepsilon := \sqrt{\frac{d_c}{R_m \lambda}},$$

where d_c is the typical measure of a single cell (unit L where L is the macroscopic unit of length), R_m is the surface specific resistivity of the membrane (unit RL^2 , where R is the resistance unit) and λ is a normalization of the conductivity tensor \mathbf{M}_j for $j = i, e$ (unit $R^{-1}L^{-1}$). Now, we nondimensionalize (2.1) and (2.2) by scaling space and time using the following change of variables:

$$\tilde{x} := \frac{x}{L} \text{ and } \tilde{t} := \frac{t}{\tau},$$

where $\tau = R_m C_m$. We also scale the electric potentials:

$$v = \delta v \tilde{v}, \quad u_j = \delta v \tilde{u}_j \text{ and } w = \delta w \tilde{w},$$

where δv and δw are convenient units to measure electric potentials v , u_j and the gating variable w , respectively, for $j = i, e$. By the chain rule, we obtain:

$$\frac{LC_m}{\tau} \partial_{\tilde{t}} \tilde{v} + \frac{L}{\delta v} (I_{\text{ion}} - I_{\text{app}}) = -\mathbf{M}_i \nabla_{\tilde{x}} \tilde{u}_i \cdot \mu_i = \mathbf{M}_e \nabla_{\tilde{x}} \tilde{u}_e \cdot \mu_e.$$

Recalling that $\tau = R_m C_m$ and normalizing the conductivities using

$$\tilde{\mathbf{M}}_j = \frac{1}{\lambda} \mathbf{M}_j, \text{ for } j = i, e,$$

we get

$$\frac{L}{R_m \lambda} \partial_{\tilde{t}} \tilde{v} + \frac{L}{\delta v \lambda} (I_{\text{ion}} - I_{\text{app}}) = -\tilde{\mathbf{M}}_i \nabla_{\tilde{x}} \tilde{u}_i \cdot \mu_i = \tilde{\mathbf{M}}_e \nabla_{\tilde{x}} \tilde{u}_e \cdot \mu_e.$$

Regarding the ionic functions I_{ion} , the applied current I_{app} and H , we nondimensionalize them by using the following scales

$$\tilde{I}_{\text{ion}}(\tilde{v}, \tilde{w}) = \frac{R_m}{\delta v} I_{\text{ion}}(v, w), \quad \tilde{I}_{\text{app}} = \frac{R_m}{\delta v} I_{\text{app}} \text{ and } \tilde{H}(\tilde{v}, \tilde{w}) = \frac{\tau}{\delta w} H(v, w).$$

Consequently, we have

$$\frac{L}{R_m \lambda} \left(\partial_{\tilde{t}} \tilde{v} + \tilde{I}_{\text{ion}} - \tilde{I}_{\text{app}} \right) = -\tilde{\mathbf{M}}_i \nabla_{\tilde{x}} \tilde{u}_i \cdot \mu_i = \tilde{\mathbf{M}}_e \nabla_{\tilde{x}} \tilde{u}_e \cdot \mu_e.$$

Finally, recalling that the dimensionless parameter ε , given by $\varepsilon := \sqrt{\frac{d_c}{R_m \lambda}}$, is the ratio between the microscopic cell length d_c and the macroscopic length L , i.e.

$$\varepsilon = \frac{d_c}{L},$$

and solving for ε , we obtain

$$\varepsilon = \frac{L}{R_m \lambda}.$$

Collecting and substituting all previous definitions in equations (2.1) and (2.2), we obtain the following dimensionless system:

$$\begin{aligned} -\nabla_{\tilde{x}} \cdot (\tilde{\mathbf{M}}_j \nabla_{\tilde{x}} \tilde{u}_j) &= 0 \text{ in } \Omega_{j,T}, \\ \varepsilon (\partial_{\tilde{t}} \tilde{v} + \tilde{I}_{\text{ion}}(\tilde{v}, \tilde{w}) - \tilde{I}_{\text{app}}) &= \tilde{\mathcal{I}}_m \text{ on } \Gamma_T, \\ \tilde{\mathcal{I}}_m &= -\tilde{\mathbf{M}}_i \nabla_{\tilde{x}} \tilde{u}_i \cdot \mu_i = \tilde{\mathbf{M}}_e \nabla_{\tilde{x}} \tilde{u}_e \cdot \mu_e \text{ on } \Gamma_T, \\ \partial_{\tilde{t}} \tilde{w} - \tilde{H}(\tilde{v}, \tilde{w}) &= 0 \text{ on } \Gamma_T. \end{aligned} \tag{2.3}$$

2.2.3 The Two-Scale Asymptotic Expansion

For completeness in this section, we use a formal homogenization (asymptotic expansion) to obtain from the microscopic model (2.3), the macroscopic bidomain model. We aim at obtaining the limit of v and u_j as $\varepsilon \rightarrow 0$ for $j = i, e$. We define now Y_i and Y_e as portions of intra- and extra-cellular spaces Ω_i and Ω_e (see Figure 4). The solutions u_i , u_e and w have the following asymptotic ε -power expansion of the dimensionless parameter ε ($u := u_i, u_e, w$):

$$u(t, x, \xi) = u_0(t, x, \xi) + \varepsilon u_1(t, x, \xi) + \varepsilon^2 u_2(t, x, \xi) + \dots,$$

where $\xi = x/\varepsilon$ is the fast microscopic variable, x is the slow macroscopic variable and u_0, u_1, u_2 are $[0, 1]^3$ -periodic in the variable ξ . We assume that the functions, involved in the asymptotic expansion, are smooth. Next, we use the following full derivative operators:

$$\begin{aligned}\nabla &= \varepsilon^{-1} \nabla_\xi + \nabla_x, \\ \Delta &= \varepsilon^{-2} \Delta_{\xi\xi} + \varepsilon^{-1} (\nabla_\xi \cdot \nabla_x + \nabla_x \cdot \nabla_\xi) + \Delta_{xx}.\end{aligned}$$

Now we substitute the asymptotic expansions of $u := u_i$ into the microscopic system (2.3) (for simplicity, we replace $\tilde{t}, \tilde{x}, \tilde{\mathbf{M}}_j, \tilde{I}_{\text{ion}}, \tilde{H}$ and $\tilde{I}_{\text{app},j}$ by $t, x, \mathbf{M}_j, I_{\text{ion}}, H$ and I_{app} , respectively). Collecting the terms of the power coefficients $\varepsilon := -2, -1, 0$, we obtain the following equations:

$$\left\{ \begin{array}{l} (BV1) \left\{ \begin{array}{ll} -\nabla_\xi \cdot (\mathbf{M}_i \nabla_\xi u_{i,0}) = 0 & \text{in } Y_i, \\ \mathbf{M}_i \nabla_\xi u_{i,0} \cdot \mu_i = 0 & \text{on } \Gamma, \end{array} \right. \\ \\ (BV2) \left\{ \begin{array}{ll} -\nabla_\xi \cdot (\mathbf{M}_i \nabla_\xi u_{i,1}) - (\nabla_\xi \cdot \mathbf{M}_i \nabla_x + \nabla_x \cdot \mathbf{M}_i \nabla_\xi) u_{i,0} = 0 & \text{in } Y_i, \\ (\mathbf{M}_i \nabla_\xi u_{i,1} + \mathbf{M}_i \nabla_x u_{i,0}) \cdot \mu_i = 0 & \text{on } \Gamma, \end{array} \right. \\ \\ (BV3) \left\{ \begin{array}{ll} -\nabla_\xi \cdot (\mathbf{M}_i \nabla_\xi u_{i,2}) - (\nabla_\xi \cdot \mathbf{M}_i \nabla_x + \nabla_x \cdot \mathbf{M}_i \nabla_\xi) u_{i,1} & \text{in } Y_i, \\ \quad \quad \quad -\nabla_x \cdot (\mathbf{M}_i \nabla_x u_{i,0}) = 0 & \text{in } Y_i, \\ -(\mathbf{M}_i \nabla_\xi u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) \cdot \mu_i = \partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}} & \text{on } \Gamma. \end{array} \right. \end{array} \right.$$

Note that in the previous problems, x is a parameter and we look for periodic solutions in ξ in the reference cell Y_i .

Observe that by a classical result, the first boundary value problem (BV1) has a unique periodic solution up to a constant (see for e.g. [GT15] for more details). Moreover, this problem has a constant solution with respect to ξ , thus the periodic solution $u_{i,0}$ depends only on the macroscopic variable x , i.e.

$$u_{i,0}(t, x, \xi) = u_{i,0}(t, x).$$

Regarding the second boundary value problem, since $u_{i,0}$ is independent of ξ , (BV2) becomes:

$$\left\{ \begin{array}{ll} -\nabla_\xi \cdot (\mathbf{M}_i \nabla_\xi u_{i,1}) - \nabla_\xi \cdot (\mathbf{M}_i \nabla_x u_{i,0}) = 0 & \text{in } Y_i, \\ (\mathbf{M}_i \nabla_\xi u_{i,1} + \mathbf{M}_i \nabla_x u_{i,0}) \cdot \mu_i = 0 & \text{on } \Gamma. \end{array} \right.$$

For this problem, it is not difficult to establish the existence of a periodic solution $u_{i,1}$ (see for instance the remark on p. 13-14 of [BLP11] or [OSY09]) provided that

$$\int_{\partial Y_i} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu(\xi) ds(\xi) = \int_\Gamma \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu_i(\xi) ds(\xi).$$

Indeed, one can exploit the definition of $\partial Y_i := (\partial Y \cap \partial Y_i) \cup \Gamma$ (see Figure 4) and the equality of trace of $H_{per}^1(Y)$ functions on both sides of the cube (i.e. $\int_{\partial Y \cap \partial Y_i} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu(\xi) ds(\xi) = 0$), to verify that

$$\begin{aligned} \int_{\partial Y_i} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu(\xi) ds(\xi) &= \int_{\partial Y \cap \partial Y_i} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu(\xi) ds(\xi) + \int_{\Gamma} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu_i(\xi) ds(\xi) \\ &= \int_{\Gamma} \mathbf{M}_i \nabla_x u_{i,0} \cdot \mu_i(\xi) ds(\xi) \end{aligned}$$

The solution of (BV2), being unique up to an additive constant, can be represented by the following ansatz [BLP11]:

$$u_{i,1}(t, x, \xi) = f_i(\xi) \cdot \nabla_x u_{i,0} + \tilde{u}_{1,i}(t, x),$$

where each component of the vector $f_i(\xi) = (f_{1,i}(\xi), f_{2,i}(\xi), f_{3,i}(\xi))^T$ satisfies the following elliptic equation

$$\begin{cases} -\nabla_{\xi} \cdot (\mathbf{M}_i \nabla_{\xi} f_{k,i}) = \nabla_{\xi} \cdot (\mathbf{M}_i e_k) & \text{in } Y_i \\ \mathbf{M}_i \nabla_{\xi} f_{k,i} \cdot \mu_i = -\mu_i \cdot \mathbf{M}_i e_k & \text{on } \Gamma, \end{cases}$$

where e_k , $k = 1, 2, 3$, are the standard basis vectors in \mathbb{R}^3 . Similarly as before, we have the existence of periodic solution ($f_{k,i}$ for $k = 1, 2, 3$) that is unique up to a constant for this problem. For the last boundary value problem (BV3), it can be rewritten as:

$$\begin{cases} \nabla_{\xi} \cdot (\mathbf{M}_i \nabla_{\xi} u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) = -\nabla_x \cdot (\mathbf{M}_i \nabla_x u_{i,0}) - \nabla_x \cdot (\mathbf{M}_i \nabla_{\xi} u_{i,1}) & \text{in } (0, T) \times Y_i \\ -(\mathbf{M}_i \nabla_{\xi} u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) \cdot \mu_i = \partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}} & \text{on } (0, T) \times \Gamma. \end{cases}$$

Integrating the first equation over the unit cell portion Y_i , and using Gauss' divergence theorem we get

$$\int_{\partial Y_i} (\mathbf{M}_i \nabla_{\xi} u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) \cdot \mu_i ds(\xi) = - \int_{Y_i} \nabla_x \cdot (\mathbf{M}_i \nabla_x u_{i,0} + \mathbf{M}_i \nabla_{\xi} u_{i,1}) d\xi.$$

Recalling that $\partial Y_i = (\partial Y \cap \partial Y_i) \cup \Gamma$ and $\int_{\partial Y \cap \partial Y_i} (\mathbf{M}_i \nabla_{\xi} u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) \cdot \mu_i ds(\xi) = 0$ (by periodicity of \mathbf{M}_i , $u_{i,2}$ and $u_{i,1}$), we have

$$\int_{\partial Y_i} (\mathbf{M}_i \nabla_{\xi} u_{i,2} + \mathbf{M}_i \nabla_x u_{i,1}) \cdot \mu_i ds(\xi) = - \int_{\Gamma} (\partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}}) ds(\xi).$$

So that

$$- \int_{Y_i} \nabla_x \cdot (\mathbf{M}_i \nabla_x u_{i,0} + \mathbf{M}_i \nabla_{\xi} u_{i,1}) d\xi = - \int_{\Gamma} (\partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}}) ds(\xi).$$

Using $u_{i,1} = f_i(\xi) \cdot \nabla_x u_{i,0} + \tilde{u}_{1,i}(t, x)$ and $|\Gamma|$ the surface measure of Γ , we reach (recall that $v_0, w_0, u_{0,i}$ and I_{app} do not depend on ξ)

$$-\nabla_x \cdot \left(\left[\int_{Y_i} \mathbf{M}_i + \mathbf{M}_i \nabla_{\xi} f_i d\xi \right] \nabla_x u_{i,0} \right) = - |\Gamma| (\partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}}).$$

Hence, we get

$$-\nabla_x \cdot (\mathcal{M}_i \nabla_x u_{i,0}) = -|\Gamma| (\partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}}),$$

where the tensor \mathcal{M}_i is defined by

$$\mathcal{M}_i := \int_{Y_i} (\mathbf{M}_i + \mathbf{M}_i \nabla_\xi f(\xi)) d\xi. \quad (2.4)$$

Similarly, we can obtain the dimensionless averaged equations for the extracellular potential and gating variable

$$\nabla_x \cdot (\mathcal{M}_e \nabla_x u_{e,0}) = -|\Gamma| (\partial_t v_0 + I_{\text{ion}}(v_0, w_0) - I_{\text{app}}),$$

where the tensor \mathcal{M}_e is defined by

$$\mathcal{M}_e := \int_{Y_e} (\mathbf{M}_e + \mathbf{M}_e \nabla_\xi f(\xi)) d\xi. \quad (2.5)$$

2.3 Mathematical Assumptions on the Microscopic Bidomain Model

2.3.1 Assumptions on the Domain

For our model we assume that Ω (the cardiac tissue) is a bounded open subset of \mathbb{R}^3 with smooth boundary $\partial\Omega$. The cardiac tissue is composed of two connected regions, the intracellular $\Omega_{i,\varepsilon}$ and the extracellular $\Omega_{e,\varepsilon}$. These two regions are separated by an active membrane surface $\Gamma_\varepsilon = \partial\Omega_{i,\varepsilon} \cap \partial\Omega_{e,\varepsilon}$. Here $\varepsilon > 0$ is the small dimensionless parameter which is proportional to the ratio between the micro scale of the length of the cells and the macro scale of the length of the cardiac fibers. Following the standard approach of homogenization theory, we are assuming that the cells are distributed according to an ideal periodic organization similar to a regular lattice of interconnected cylinders.

Let $Y := [0, 1]^3$ be the representation of the unit cell in \mathbb{R}^3 . We denote by $Y_{i,e} \subset Y$ its intra- and extracellular parts and by Γ the common boundary of the intra- and extracellular domains Y_i and Y_e ($\Gamma = \partial Y_i \cap \partial Y_e$). So $Y_i \cup Y_e \cup \Gamma = Y$. The elementary unit cell Y represents a reference unit volume box containing a single cell Y_i .

The main geometrical assumption is that the physical intra- or extracellular regions are the ε -dilation of the reference lattices $Y_{i,e}$ extended periodically, defined as: for $k \in \mathbb{Z}^3$ each cell

$$Y_{j,k,\varepsilon} := \varepsilon k + \varepsilon Y_j = \{\varepsilon \xi : \xi \in k + Y_j\},$$

and the corresponding common periodic boundary

$$\Gamma_{k,\varepsilon} := \varepsilon k + \varepsilon \Gamma = \{\varepsilon \xi : \xi \in k + \Gamma\}.$$

Therefore, the physical region Ω occupied by the heart is decomposed into the intra- and extracellular domains $\Omega_{j,\varepsilon}$ for $j = i, e$ that can be simply obtained by intersecting Ω with $Y_{j,k,\varepsilon}$ for $j = i, e$, i.e.:

$$\Omega_{j,\varepsilon} = \Omega \cap \bigcup_{k \in \mathbb{Z}^3} Y_{j,k,\varepsilon}.$$

Similarly,

$$\Gamma_\varepsilon = \Omega \cap \bigcup_{k \in \mathbb{Z}^3} \Gamma_{k,\varepsilon}.$$

One can observe that the domain $\Omega_{i,\varepsilon}$ may be considered as a perforated domain obtained from Ω by removing the perforations which correspond to the extracellular domain $\Omega_{e,\varepsilon}$. The same observation holds for the extracellular domain. The boundary Γ is a smooth manifold such that Γ_ε is smooth and connected. Furthermore, $\Omega_{j,\varepsilon}$ are both assumed to be connected bounded domains in \mathbb{R}^3 so that a Poincaré-Wirtinger inequality is satisfied in both domains. (We refer the reader to the geometrical hypothesis \mathbf{H}_p in [CDD⁺12] for such domains.)

2.3.2 Assumptions on the Data

The electric properties of the tissue are described by the *intracellular* $u_{i,\varepsilon}$ and *extracellular* $u_{e,\varepsilon}$ electric potentials. Herein, $u_{j,\varepsilon} : \Omega_{j,\varepsilon} \rightarrow \mathbb{R}$ for $j = i, e$, and $v_\varepsilon := (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} : \Gamma_\varepsilon \rightarrow \mathbb{R}$ is known as the *transmembrane* potential and satisfies a dynamic condition on Γ_ε involving the auxiliary function $w_\varepsilon : \Gamma_\varepsilon \rightarrow \mathbb{R}$ (the so called gating variable).

The following coupled reaction-diffusion system forms the microscopic bidomain model: for $j = i, e$ (see e.g. [SLC⁺07, Yin05]):

$$-\nabla \cdot (\mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon}) = 0 \text{ in } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \quad (2.6a)$$

$$\varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, w_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m \text{ on } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \quad (2.6b)$$

$$\mathcal{I}_m = -\mathbf{M}_{i,\varepsilon} \nabla u_{i,\varepsilon} \cdot \mu_i = \mathbf{M}_{e,\varepsilon} \nabla u_{e,\varepsilon} \cdot \mu_e \text{ on } \Gamma_{\varepsilon,T}, \quad (2.6c)$$

$$\partial_t w_\varepsilon - H(v_\varepsilon, w_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}. \quad (2.6d)$$

We augment (2.6) with no-flux boundary conditions

$$(\mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon}) \cdot \mu_j = 0 \text{ on } (0, T) \times (\partial \Omega_{j,\varepsilon} \setminus \Gamma_\varepsilon), \quad j \in \{e, i\}, \quad (2.7)$$

where μ_j are the exterior unit normals to the boundaries of $\Omega_{j,\varepsilon}$, for $j = i, e$ respectively, and $\mu_i = -\mu_e$ on Γ_ε .

The system is also supplemented with appropriate initial conditions for the transmembrane potential and gating variable

$$v_\varepsilon(0, \cdot) = v_{0,\varepsilon}(\cdot), \quad w_\varepsilon(0, \cdot) = w_{0,\varepsilon}(\cdot) \text{ on } \Gamma_\varepsilon. \quad (2.8)$$

Assumptions on the tensors. The conductivity of the tissue is represented by scaled symmetric Lipschitz continuous tensors $\mathbf{M}_{i,\varepsilon}(x) = \mathbf{M}_i(x, x/\varepsilon)$ and $\mathbf{M}_{e,\varepsilon}(x) = \mathbf{M}_e(x, x/\varepsilon)$ satisfying (the ellipticity and periodicity conditions): there exist constants $m_1, m_2 > 0$ such that for $j = i, e$

$$m_1 |\zeta|^2 \leq \mathbf{M}_j(x, \xi) \zeta \cdot \zeta \leq m_2 |\zeta|^2, \quad (2.9a)$$

$$\mathbf{M}_j(x, \xi + e_k) = \mathbf{M}_j(x, \xi), \quad (2.9b)$$

for all $(x, \xi) \in \Omega \times Y_j$ and for all $\zeta \in \mathbb{R}^3$.

Assumptions on the ionic model. The ionic current $I_{\text{ion}}(v, w)$ is assumed to be decomposed into $I_{1,\text{ion}}(v)$ and $I_{2,\text{ion}}(w)$, where $I_{\text{ion}}(v, w) = I_{1,\text{ion}}(v) + I_{2,\text{ion}}(w)$. Furthermore, the function $I_{1,\text{ion}} : \mathbb{R} \rightarrow \mathbb{R}$ is considered as a C^1 function, and the functions $I_{2,\text{ion}} : \mathbb{R} \rightarrow \mathbb{R}$ and $H : \mathbb{R}^2 \rightarrow \mathbb{R}$ are considered as linear functions. Also, we assume that there exist $r \in (2, +\infty)$ and constants $\alpha_1, \alpha_2, \alpha_3, L > 0, l \geq 0$ such that

$$\begin{aligned} \frac{1}{\alpha_1} |v|^{r-1} &\leq |I_{1,\text{ion}}(v)| \leq \alpha_1 (|v|^{r-1} + 1), \\ \text{and } I_{2,\text{ion}}(w)v - \alpha_2 H(v, w)w &\geq \alpha_3 |w|^2, \end{aligned} \quad (2.10)$$

$$\tilde{I}_{1,\text{ion}} : z \mapsto I_{1,\text{ion}}(z) + Lz + l \quad \text{is strictly increasing on } \mathbb{R} \text{ with } \lim_{z \rightarrow 0} \tilde{I}_{1,\text{ion}}(z)/z = 0 \quad (2.11a)$$

$$\text{and } \forall z, s \in \mathbb{R} \quad (\tilde{I}_{1,\text{ion}}(z) - \tilde{I}_{1,\text{ion}}(s))(z - s) \geq \frac{1}{C}(1 + |z| + |s|)^{r-2} |z - s|^2. \quad (2.11b)$$

Remark 2. One can easily show that: $I_{1,\text{ion}}(0) = -l$, $I'_{1,\text{ion}}(0) = -L$ and $I'_{1,\text{ion}}(z) \geq -L$ for all $z \in \mathbb{R}$.

Remark 3. The function H in the ODE of (2.6)-(2.7) and the function I_{ion} , may correspond to one of the simplified models for the membrane and ionic currents. We mention, for instance, the Mitchell-Schaeffer membrane model [MS03]

$$H(v, w) = \frac{w_\infty(v/v_p) - w}{R_m c_m \eta_\infty(v/v_p)}, \quad (2.12a)$$

$$I_{\text{ion}}(v, w) = \frac{v_p}{R_m} \left(\frac{v}{v_p \eta_2} - \frac{v^2(1 - v/v_p)w}{v_p^2 \eta_1} \right), \quad (2.12b)$$

where the dimensionless time constant and state variable constant are respectively given by

$$\eta_\infty(s) = \begin{cases} \eta_3 & \text{for } s < \eta_5, \\ \eta_4 & \text{otherwise,} \end{cases} \quad w_\infty(s) = \begin{cases} 1 & \text{for } s < \eta_5, \\ 0 & \text{otherwise.} \end{cases}$$

The quantity R_m is the surface resistivity of the membrane, and $v_p, \eta_1, \eta_2, \eta_3, \eta_4, \eta_5$ are given parameters. A simpler choice for the membrane kinetics is given by the widely known FitzHugh-Nagumo model [Fit61], often used by researchers to avoid computational difficulties. In this case,

$$H(v, w) = av - bw, \quad (2.13a)$$

$$I_{\text{ion}}(v, w) = (\lambda v(1 - v)(v - \theta)) + (-\lambda w) := I_{1,\text{ion}}(v) + I_{2,\text{ion}}(w), \quad (2.13b)$$

where a, b, λ, θ are given parameters with $a, b \geq 0$, $\lambda < 0$ and $0 < \theta < 1$. According to FitzHugh-Nagumo's model, the most appropriate value is $r = 4$, which means that the non-linearity I_{ion} is of cubic growth at infinity (recall that in the Mitchell-Schaeffer membrane model, the gating variable w is bounded in L^∞). Assumptions (2.10), (2.11) are automatically satisfied by any cubic polynomial I_{ion} with positive leading coefficient. This is indeed the case for the FitzHugh-Nagumo model but not for the Mitchell-Schaeffer model.

2.3. MATHEMATICAL ASSUMPTIONS ON THE MICROSCOPIC BIDOMAIN MODEL 65

Assumptions on the source term. There exists a constant C independent of ε such that the source term $I_{\text{app},\varepsilon}$ satisfies the following bound:

$$\|\varepsilon^{1/2} I_{\text{app},\varepsilon}\|_{L^2(\Gamma_{\varepsilon,T})} \leq C. \quad (2.14)$$

Furthermore, I_{app} is the weak limit of the corresponding unfolding sequence.

Assumptions on the initial data. The initial data $v_{0,\varepsilon}$ and $w_{0,\varepsilon}$ satisfy

$$\|\varepsilon^{1/r} v_{0,\varepsilon}\|_{L^r(\Gamma_\varepsilon)} + \|\varepsilon^{1/2} v_{0,\varepsilon}\|_{L^2(\Gamma_\varepsilon)} + \|\varepsilon^{1/2} w_{0,\varepsilon}\|_{L^2(\Gamma_\varepsilon)} \leq C, \quad (2.15)$$

for some constant C independent of ε . Moreover, $v_{0,\varepsilon}$ and $w_{0,\varepsilon}$ are assumed to be traces of uniformly bounded sequences in $C^1(\bar{\Omega})$.

Observe that the equations in (2.6) are invariant under the change of $u_{i,\varepsilon}$ and $u_{e,\varepsilon}$ into $u_{i,\varepsilon} + k$; $u_{e,\varepsilon} + k$, for any $k \in \mathbb{R}$. Hence, we may impose the following normalization condition:

$$\int_{\Omega_{e,\varepsilon}} u_{e,\varepsilon}(t, x) \, d\mathbf{x} = 0 \text{ for a.e. } t \in (0, T). \quad (2.16)$$

2.3.3 Main Results

We state herein the main results of the chapter as given in the following theorems.

Theorem 2.3.1 (Microscopic Bidomain Model). *Assume that conditions (2.9), (2.10), (2.11), (2.14), and (2.15) hold. Then the microscopic bidomain problem (2.6), (2.7), (2.8) possesses a unique weak solution in the sense of Definition 2.4.1.*

Theorem 2.3.2 (Macroscopic Bidomain Model). *A sequence of solutions $(u_{i,\varepsilon}, u_{e,\varepsilon}, w_\varepsilon)_\varepsilon$ of the microscopic system (2.6)-(2.8) (obtained in Theorem 2.3.1) converges to a weak solution (u_i, u_e, w) with $v = u_i - u_e$, $u_i, u_e \in L^2(0, T; H^1(\Omega))$, $v \in L^2(0, T; H^1(\Omega)) \cap L^r(\Omega_T)$, $\partial_t v \in L^2(0, T; (H^1(\Omega))') + L^{r/(r-1)}(\Omega_T)$ and $w \in C(0, T; L^2(\Omega))$, of the macroscopic problem*

$$|\Gamma| \partial_t v - \nabla \cdot (\mathcal{M}_i(x) \nabla u_i) + |\Gamma| I_{\text{ion}}(v, w) = |\Gamma| I_{\text{app}} \text{ in } \Omega_T, \quad (2.17a)$$

$$|\Gamma| \partial_t v + \nabla \cdot (\mathcal{M}_e(x) \nabla u_e) + |\Gamma| I_{\text{ion}}(v, w) = |\Gamma| I_{\text{app}} \text{ in } \Omega_T, \quad (2.17b)$$

$$\partial_t w - H(v, w) = 0 \text{ in } \Omega_T. \quad (2.17c)$$

supplemented with no-flux boundary conditions, representing an insulated cardiac tissue

$$(\mathcal{M}_j(x) \nabla u_j) \cdot \mathbf{n} = 0 \text{ on } \Sigma_T := \partial\Omega \times (0, T), \quad j \in \{e, i\}, \quad (2.18)$$

and appropriate initial conditions in Ω , namely v_0 and $w_0 \in L^2(\Omega)$, for the transmembrane potential and gating variable

$$v(0, x) = v_0(x), \quad w(0, x) = w_0(x). \quad (2.19)$$

Herein, the tensors \mathcal{M}_i and \mathcal{M}_e are defined respectively in (2.4) and (2.5), and \mathbf{n} is the outward unit normal to the boundary of Ω .

2.4 Existence of solutions for the microscopic model

This section is devoted to proving existence of solutions to the microscopic bidomain model for fixed $\varepsilon > 0$. The existence proof is based on the Faedo-Galerkin method, a priori estimates, and the compactness method.

We start with a weak formulation of the microscopic model.

Definition 2.4.1 (Weak Formulation). A solution of problem (2.6), (2.7), (2.8) is a four tuple $(u_{i,\varepsilon}, u_{e,\varepsilon}, v_\varepsilon, w_\varepsilon)$ such that $u_{i,\varepsilon} \in L^2(0, T; H^1(\Omega_{i,\varepsilon}))$, $u_{e,\varepsilon} \in L^2(0, T; H^1(\Omega_{e,\varepsilon}))$, $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon)) \cap L^r(\Gamma_\varepsilon, T)$, $w_\varepsilon \in L^2(\Gamma_\varepsilon, T)$, $\partial_t v_\varepsilon, \partial_t w_\varepsilon \in L^2(\Gamma_\varepsilon, T)$, and satisfying the following weak formulation for a.e. $t \in (0, T)$

$$\begin{aligned} \int_{\Gamma_\varepsilon} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, dx \\ + \int_{\Gamma_\varepsilon} \varepsilon I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \varphi \, ds(x) = \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x), \end{aligned} \quad (2.20)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_\varepsilon \zeta \, ds(x) - \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon) \zeta \, ds(x) = 0, \quad (2.21)$$

for all $\varphi_j \in H^1(\Omega_{j,\varepsilon})$ with $\varphi := (\varphi_i - \varphi_e)|_{\Gamma_\varepsilon} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$ for $j = i, e$ and $\zeta \in L^2(\Gamma_\varepsilon)$.

We prove now Theorem 2.3.1.

Proof. In this proof, we will remove the ε -dependence in the solution $(v_\varepsilon, u_{i,\varepsilon}, u_{e,\varepsilon}, w_\varepsilon)$ for simplification of notation. To prove existence of weak solutions, we use a Faedo-Galerkin approach and a priori estimates. For this sake, we first carefully construct an appropriate basis for our systems.

Step 1: Construction of the basis

We first consider functions $\phi \in C^0(\bar{\Omega}_{j,\varepsilon})$ and we define the inner product denoted $\langle \cdot, \cdot \rangle_{V_{0,j}}$ by

$$\langle \Theta, \tilde{\Theta} \rangle_{V_{0,j}} := \int_{\Omega_{j,\varepsilon}} \phi \tilde{\phi} \, dx + \int_{\Gamma_\varepsilon} \phi|_{\Gamma_\varepsilon} \tilde{\phi}|_{\Gamma_\varepsilon} \, ds, \text{ for } j = i, e$$

where $\Theta = \begin{pmatrix} \phi \\ \phi|_{\Gamma_\varepsilon} \end{pmatrix}$ and $\tilde{\Theta} = \begin{pmatrix} \tilde{\phi} \\ \tilde{\phi}|_{\Gamma_\varepsilon} \end{pmatrix}$. Then we let $V_{0,j}$ denote the completion of $C^0(\bar{\Omega}_{j,\varepsilon})$ under the norm induced by the inner product $\langle \cdot, \cdot \rangle_{V_{0,j}}$. Similarly, for functions $\phi, \tilde{\phi} \in C^1(\bar{\Omega}_{j,\varepsilon})$, we define the inner product denoted $\langle \cdot, \cdot \rangle_{V_{1,j}}$ by:

$$\langle \Theta, \tilde{\Theta} \rangle_{V_{1,j}} := \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon} \nabla \phi \cdot \nabla \tilde{\phi} \, dx + \int_{\Gamma_\varepsilon} \phi|_{\Gamma_\varepsilon} \tilde{\phi}|_{\Gamma_\varepsilon} \, ds + \int_{\Gamma_\varepsilon} \nabla_{\Gamma_\varepsilon} \phi \cdot \nabla_{\Gamma_\varepsilon} \tilde{\phi} \, ds,$$

where $\nabla_{\Gamma_\varepsilon}$ denotes the tangential gradient operator on Γ_ε and we let $V_{1,j}$ denote the completion of $C^1(\bar{\Omega}_{j,\varepsilon})$ under the norm induced by the inner product $\langle \cdot, \cdot \rangle_{V_{1,j}}$. We note that the following injections hold:

$$V_{0,j} \subset L^2(\Omega_{j,\varepsilon}), \text{ and } V_{1,j} \subset H^1(\Omega_{j,\varepsilon}).$$

Moreover, the injection from $V_{1,j}$ into $V_{0,j}$ is continuous and compact. We refer the reader to [Gal08, RZ03] for similar approaches.

It follows from a well-known result (see e.g. [Tem12] p. 54) that the closed bilinear form $a(\Theta, \tilde{\Theta}) := \langle \Theta, \tilde{\Theta} \rangle_{V_{1,j}}$ defines a strictly positive self-adjoint unbounded operator

$$\mathcal{B}_j : D(\mathcal{B}_j) = \{\Theta \in V_{1,j} : \mathcal{B}_j \Theta \in V_{0,j}\} \rightarrow V_{0,j}$$

such that, for any $\tilde{\Theta} \in V_{1,j}$, we have $\langle \mathcal{B}_j \Theta, \tilde{\Theta} \rangle_{V_{0,j}} = a(\Theta, \tilde{\Theta})$. Thus, for $k \in \mathbb{N}$, we take a complete system of eigenfunctions $\left\{ \Theta_{k,j} = \begin{pmatrix} \phi_{k,j} \\ \psi_{k,j} \end{pmatrix} \right\}_k$ of the problem $\mathcal{B}_j \Theta_{k,j} = \lambda_k \Theta_{k,j}$ in $V_{0,j}$ with $\Theta_{k,j} \in D(\mathcal{B}_j)$, and $\psi_{k,j} = \phi_{k,j}|_{\Gamma_\varepsilon}$ where $\phi_{k,j}$ and $\psi_{k,j}$ are regular enough.

Moreover, the eigenvectors $\{\Theta_{k,j}\}_k$ form an orthogonal basis in $V_{1,j}$ and $V_{0,j}$, and they may be assumed to be normalized in the norm of $V_{0,j}$. Since $C^1(\bar{\Omega}_{j,\varepsilon}) \subset V_{1,j} \subset H^1(\Omega_{j,\varepsilon})$, and $C^1(\bar{\Omega}_{j,\varepsilon})$ is dense in $H^1(\Omega_{j,\varepsilon})$, then $V_{1,j}$ is dense in $H^1(\Omega_{j,\varepsilon})$ for the H^1 norm. Therefore, $\{\Theta_{k,j}\}_k$ is a basis in $H^1(\Omega_{j,\varepsilon})$ for the H^1 norm.

On the other hand, we consider a basis $\{\zeta_k\}_k$, $k \in \mathbb{N}$ that is orthonormal in $L^2(\Gamma_\varepsilon)$ and orthogonal in $H^1(\Gamma_\varepsilon)$ and we set the spaces

$$\mathcal{T}_{j,n} = \text{span}\{\Theta_{1,j}, \dots, \Theta_{n,j}\}, \quad \mathcal{T}_{j,\infty} = \bigcup_{n=1}^{\infty} \mathcal{T}_{j,n},$$

$$\mathcal{K}_n = \text{span}\{\zeta_1, \dots, \zeta_n\}, \quad \mathcal{K}_\infty = \bigcup_{n=1}^{\infty} \mathcal{K}_n,$$

where \mathcal{T}_∞ and \mathcal{K}_∞ are dense subspaces of $V_{1,j}$ and $H^1(\Gamma_\varepsilon)$ respectively.

Step 2: Construction of approximate solutions

For any $n \in \mathbb{N}$, we are looking for functions of the form

$$\begin{pmatrix} u_{j,n} \\ \bar{u}_{j,n} \end{pmatrix} = \sum_{k=1}^n d_{j,k}(t) \begin{pmatrix} \phi_{j,k} \\ \psi_{j,k} \end{pmatrix}, \quad j = i, e, \quad \text{with } \phi_{j,k}|_{\Gamma_\varepsilon} = \psi_{j,k} \quad \text{and } w_n = \sum_{k=1}^n c_k(t) \zeta_k(x), \quad (2.22)$$

solving the approximate regularized problem:

$$\begin{aligned} (\varepsilon + \delta_n) \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{i,n} \psi_i ds(x) - \varepsilon \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{e,n} \psi_i ds(x) + \delta_n \int_{\Omega_{i,\varepsilon}} \partial_t u_{i,n} \phi_i dx \\ = \int_{\Gamma_\varepsilon} (-I_{\text{ion}}(v_n, w_n) + I_{\text{app},\varepsilon}) \psi_i ds(x) - \int_{\Omega_{i,\varepsilon}} \mathbf{M}_{i,\varepsilon}(x) \nabla u_{i,n} \cdot \nabla \phi_i dx \end{aligned} \quad (2.23)$$

$$\begin{aligned} - \varepsilon \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{i,n} \psi_e ds(x) + (\varepsilon + \delta_n) \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{e,n} \psi_e ds(x) + \delta_n \int_{\Omega_{e,\varepsilon}} \partial_t u_{e,n} \phi_e dx \\ = \int_{\Gamma_\varepsilon} (I_{\text{ion}}(v_n, w_n) - I_{\text{app},\varepsilon}) \psi_e |_{\Gamma_\varepsilon} ds(x) - \int_{\Omega_{e,\varepsilon}} \mathbf{M}_{e,\varepsilon}(x) \nabla u_{e,n} \cdot \nabla \phi_e dx \end{aligned} \quad (2.24)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_n \zeta \, ds(x) = \int_{\Gamma_\varepsilon} H(v_n, w_n) \zeta \, ds(x), \quad (2.25)$$

where $\delta_n = \frac{1}{n}$, $\Theta_j = \begin{pmatrix} \phi_j \\ \psi_j \end{pmatrix} \in \mathcal{T}_{j,n}$, for $j = i, e$ and $\zeta \in \mathcal{K}_n$. The terms $\delta_n \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{j,n} \psi_j \, ds(x)$ and $\delta_n \int_{\Omega_{j,\varepsilon}} \partial_t u_{j,n} \phi_j \, d\mathbf{x}$, $j = i, e$ were added to overcome the degeneracy in (2.20).

We aim to apply standard existence theorems for ODEs. For this purpose, if n fixed, we choose $\Theta_i = \Theta_{k,i}$, $\Theta_e = \Theta_{k,e}$ and $\zeta = \zeta_k$, $1 \leq k \leq n$ and we substitute the expressions (2.22) in the unknowns $u_{i,n}$, $\bar{u}_{i,n}$, $u_{e,n}$, $\bar{u}_{e,n}$, and w_n . The ODE system, that we obtain, has as unknowns the column vectors $\mathbf{d}_i = \{d_{i,k}\}_{k=1}^n$, $\mathbf{d}_e = \{d_{e,k}\}_{k=1}^n$ and $\mathbf{c} = \{c_k\}_{k=1}^n$. It can be written as follows:

$$\begin{cases} (\delta_n + \varepsilon) \bar{\mathbb{A}}_{ii} \mathbf{d}'_i - \varepsilon \bar{\mathbb{A}}_{ie} \mathbf{d}'_e + \delta_n \mathbb{A}_{ii} \mathbf{d}'_i = \mathbb{F}_i(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}) \\ -\varepsilon \bar{\mathbb{A}}_{ie} \mathbf{d}'_i + (\delta_n + \varepsilon) \bar{\mathbb{A}}_{ee} \mathbf{d}'_e + \delta_n \mathbb{A}_{ee} \mathbf{d}'_e = \mathbb{F}_e(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}) \\ \mathbb{G} \mathbf{c}'(t) = \mathbb{H}(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}), \end{cases} \quad (2.26)$$

where the (k, l) entry of the matrix $\bar{\mathbb{A}}_{mj}$, $m, j = i, e$ is $\langle \psi_{m,k}, \psi_{j,l} \rangle_{L^2(\Gamma_\varepsilon)}$, for $1 \leq k, l \leq n$, the (k, l) entry of the matrix \mathbb{A}_{jj} , $j = i, e$, is $\langle \phi_{j,k}, \phi_{j,l} \rangle_{L^2(\Omega_{j,\varepsilon})}$, the (k, l) entry of the matrix \mathbb{G} is $\langle \zeta_k, \zeta_l \rangle_{L^2(\Gamma_\varepsilon)}$ and where the right hand side vectors \mathbb{F}_i , \mathbb{F}_e and \mathbb{H} assemble the right hand sides of the equations given in (2.23)-(2.25).

Note that by the orthonormality of the basis, the matrix

$$\mathbb{G} = \left(\langle \zeta_k, \zeta_l \rangle_{L^2(\Gamma_\varepsilon)} \right)_{1 \leq k, l \leq n} = \mathbb{I}_{n \times n},$$

is the identity matrix. Furthermore, the first two systems of equations in system (2.26) can be written in the following form:

$$\left(\delta_n \begin{bmatrix} \bar{\mathbb{A}}_{ii} + \mathbb{A}_{ii} & 0 \\ 0 & \bar{\mathbb{A}}_{ee} + \mathbb{A}_{ee} \end{bmatrix} + \varepsilon \begin{bmatrix} \bar{\mathbb{A}}_{ii} & -\bar{\mathbb{A}}_{ie} \\ -\bar{\mathbb{A}}_{ie}^T & \bar{\mathbb{A}}_{ee} \end{bmatrix} \right) \begin{bmatrix} \mathbf{d}'_i \\ \mathbf{d}'_e \end{bmatrix} = \begin{bmatrix} \mathbb{F}_i \\ \mathbb{F}_e \end{bmatrix}. \quad (2.27)$$

Now making use of the orthonormality of the bases in the spaces $V_{0,j}$, the matrices $\bar{\mathbb{A}}_{jj} + \mathbb{A}_{jj}$, for $j = i, e$, are equal to the identity $n \times n$ matrix $\mathbb{I}_{n \times n}$. So system (2.27) may be written as

$$\mathbb{M} \begin{bmatrix} \mathbf{d}'_i \\ \mathbf{d}'_e \end{bmatrix} = \begin{bmatrix} \mathbb{F}_i \\ \mathbb{F}_e \end{bmatrix}, \text{ where } \mathbb{M} = \delta_n \begin{bmatrix} \mathbb{I}_{n \times n} & 0 \\ 0 & \mathbb{I}_{n \times n} \end{bmatrix} + \varepsilon \begin{bmatrix} \bar{\mathbb{A}}_{ii} & -\bar{\mathbb{A}}_{ie} \\ -\bar{\mathbb{A}}_{ie}^T & \bar{\mathbb{A}}_{ee} \end{bmatrix}. \quad (2.28)$$

In order to write $\begin{bmatrix} \mathbf{d}'_i \\ \mathbf{d}'_e \end{bmatrix} = \mathbb{M}^{-1} \begin{bmatrix} \mathbb{F}_i \\ \mathbb{F}_e \end{bmatrix}$, one needs to prove that the matrix \mathbb{M} is invertible. For

this sake, it is enough to prove that the matrix $\mathbb{N} := \begin{bmatrix} \bar{\mathbb{A}}_{ii} & -\bar{\mathbb{A}}_{ie} \\ -\bar{\mathbb{A}}_{ie}^T & \bar{\mathbb{A}}_{ee} \end{bmatrix}$ is positive semi-definite.

Let $\mathbf{d} = \begin{pmatrix} \mathbf{d}_i \\ \mathbf{d}_e \end{pmatrix}$, where $\mathbf{d}_i = (d_{i,1}, \dots, d_{i,n})^T \in \mathbb{R}^n$ and $\mathbf{d}_e = (d_{e,1}, \dots, d_{e,n})^T \in \mathbb{R}^n$. Then

$$\mathbf{d}^T \mathbb{N} \mathbf{d} = \mathbf{d}_i^T \bar{\mathbb{A}}_{ii} \mathbf{d}_i - 2\mathbf{d}_i^T \bar{\mathbb{A}}_{i,e} \mathbf{d}_e + \mathbf{d}_e^T \bar{\mathbb{A}}_{ee} \mathbf{d}_e$$

So we have

$$\begin{aligned}
\mathbf{d}^T \mathbf{N} \mathbf{d} &= \sum_{k,l} \left[d_{i,k} d_{i,l} \int_{\Gamma_\varepsilon} \psi_{ik} \psi_{il} - 2d_{i,k} d_{e,l} \int_{\Gamma_\varepsilon} \psi_{ik} \psi_{el} + d_{e,k} d_{e,l} \int_{\Gamma_\varepsilon} \psi_{ek} \psi_{el} \right] \\
&= \int_{\Gamma_\varepsilon} \sum_{k,l} [d_{i,k} d_{i,l} \psi_{ik} \psi_{il} - 2d_{i,k} d_{e,l} \psi_{ik} \psi_{el} + d_{e,k} d_{e,l} \psi_{ek} \psi_{el}] \\
&= \int_{\Gamma_\varepsilon} \left[\sum_l d_{i,l} \psi_{il} - \sum_l d_{e,l} \psi_{el} \right]^2 \geq 0.
\end{aligned}$$

Thus the matrix \mathbb{M} is symmetric positive definite, hence invertible. Consequently, the whole system (2.26) can be written as a system of ordinary differential equations in the form $y'(t) = f(t, y(t))$.

Moreover, the problem that we obtained is supplemented with initial conditions

$$\begin{aligned}
u_{i,n}(0, x) &= u_{0,i,n}(x) := \sum_{l=1}^n d_{i,l}(0) \phi_{i,l}(x), \\
\bar{u}_{i,n}(0, x) &= \bar{u}_{0,i,n}(x) := \sum_{l=1}^n d_{i,l}(0) \psi_{i,l}(x), \quad d_{i,l}(0) := \left\langle \begin{pmatrix} u_{i,0} \\ \bar{u}_{i,0} \end{pmatrix}, \Theta_{i,l} \right\rangle_{V_{i,0}}, \\
u_{e,n}(0, x) &= u_{0,e,n}(x) := \sum_{l=1}^n d_{e,l}(0) \phi_{e,l}(x), \\
\bar{u}_{e,n}(0, x) &= \bar{u}_{0,e,n}(x) := \sum_{l=1}^n d_{e,l}(0) \psi_{e,l}(x), \quad d_{e,l}(0) := \left\langle \begin{pmatrix} u_{e,0} \\ \bar{u}_{e,0} \end{pmatrix}, \Theta_{e,l} \right\rangle_{V_{e,0}}, \\
w_n(0, x) &= w_{0,n}(x) := \sum_{l=1}^n c_{n,l}(0) \zeta_l(x), \quad c_{n,l}(0) := (w_0, \zeta_l)_{L^2(\Gamma_\varepsilon)}.
\end{aligned} \tag{2.29}$$

Proceeding exactly as in Ref. [BK06], we prove that the entries of \mathbb{F}_i , \mathbb{F}_e and \mathbb{H} are Carathéodory functions bounded by L^1 functions and we obtain the local existence on the interval $[0, t')$ of the Faedo-Galerkin solutions $u_{i,n}$, $u_{e,n}$, v_n and w_n .

The global existence of the Faedo-Galerkin solutions is a consequence of the n -independent estimates that are derived in the next section. For more details, consult Ref. [BK06].

Step 3: Energy estimates

Note that the Galerkin solutions satisfy the following weak formulations:

$$\begin{aligned}
&\int_{\Gamma_\varepsilon} \varepsilon \partial_t v_n \varphi_n ds(x) + \sum_{i,e} \int_{\Gamma_\varepsilon} \delta_n \varepsilon \partial_t \bar{u}_{j,n} \bar{\varphi}_{j,n} ds(x) + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} \delta_n \partial_t u_{j,n} \varphi_{j,n} d\mathbf{x} \\
&\quad + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,n} \cdot \nabla \varphi_{j,n} d\mathbf{x} + \int_{\Gamma_\varepsilon} \varepsilon I_{\text{ion}}(v_n, w_n) \varphi_n ds(x) \\
&= \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} \varphi_n ds(x),
\end{aligned} \tag{2.30}$$

$$\int_{\Gamma_\varepsilon} \partial_t w_n e_n ds(x) - \int_{\Gamma_\varepsilon} H(v_n, w_n) e_n ds(x) = 0, \tag{2.31}$$

where the functions $\varphi_{j,n}(t, x) := \sum_{l=1}^n b_{j,n,l}(t)\phi_{j,l}(x)$, $e_n(t, x) := \sum_{l=1}^n z_{n,l}(t)\zeta_l(x)$ and $\varphi_n := \bar{\varphi}_{i,n} - \bar{\varphi}_{e,n}$ for some given absolutely continuous coefficients $b_{j,n,l}(t)$, $z_{n,l}(t)$ for $j = i, e$. Herein, $\bar{\varphi}_{j,n}$ is the trace of $\varphi_{j,n}$ on Γ_ε for $j = i, e$.

Now, substituting $\varphi_{j,n} = u_{j,n}$ and $e_n = \varepsilon\alpha_2 w_n$ in (2.30) and (2.31), respectively, integrating over $(0, s)$ for $s \in (0, T]$ and summing the resulting equations, one obtains upon using (2.10) and (2.11), Young's inequality, the uniform ellipticity of $\mathbf{M}_{j,\varepsilon}$ and the L^2 bound on $I_{\text{app},\varepsilon}$:

$$\begin{aligned}
& \frac{1}{2} \left(\|\varepsilon^{1/2} v_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 + \alpha_2 \|\varepsilon^{1/2} w_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\varepsilon^{1/2} \delta_n^{1/2} \bar{u}_{j,n}(s)\|_{L^2(\Gamma_\varepsilon)}^2 \right. \\
& \left. + \sum_{i,e} \|\delta_n^{1/2} u_{j,n}(s)\|_{L^2(\Omega_{j,\varepsilon})}^2 \right) + m_1 \sum_{i,e} \|\nabla u_{j,n}\|_{L^2(\Omega_{j,\varepsilon,s})}^2 + \|\varepsilon \tilde{I}_{1,\text{ion}}(v_n) v_n\|_{L^1(\Gamma_{\varepsilon,s})} \\
\leq & \frac{1}{2} \left(\|\varepsilon^{1/2} v_{0,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \|w_{0,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\varepsilon^{1/2} \delta_n^{1/2} \bar{u}_{0,j,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\delta_n^{1/2} u_{0,j,n}\|_{L^2(\Omega_{j,\varepsilon})}^2 \right) \\
& + \int_0^s \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} v_n ds(x) dt - \int_0^s \int_{\Gamma_\varepsilon} \varepsilon I_{2,\text{ion}}(w_n) v_n ds(x) dt \\
& + \alpha_2 \varepsilon \int_0^s \int_{\Gamma_\varepsilon} H(v_n, w_n) w_n ds(x) dt + \int_0^s \int_{\Gamma_\varepsilon} \varepsilon (L v_n + l) v_n ds(x) dt \\
\leq & C \left(\int_0^s (\|\varepsilon^{1/2} v_n\|_{L^2(\Gamma_\varepsilon)}^2 + \|\varepsilon^{1/2} w_n\|_{L^2(\Gamma_\varepsilon)}^2) dt + 1 \right), \tag{2.32}
\end{aligned}$$

for some constant C independent of n and ε . Note that in the sequel C is a generic constant whose value can change from one line to another.

One obtains from (2.32), the following inequality

$$\|\varepsilon^{1/2} v_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 + \|\varepsilon^{1/2} w_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 \leq C \left(\int_0^s (\|\varepsilon^{1/2} v_n\|_{L^2(\Gamma_\varepsilon)}^2 + \|\varepsilon^{1/2} w_n\|_{L^2(\Gamma_\varepsilon)}^2) dt + 1 \right).$$

Hence, by an application of Gronwall's inequality, one gets for a.e. $t \in (0, T)$,

$$\|\varepsilon^{1/2} v_n(t)\|_{L^2(\Gamma_\varepsilon)}^2 + \|\varepsilon^{1/2} w_n(t)\|_{L^2(\Gamma_\varepsilon)}^2 \leq C.$$

Therefore,

$$\|\varepsilon^{1/2} v_n\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} + \|\varepsilon^{1/2} w_n\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \leq C.$$

Exploiting this last inequality along with (2.32) and (2.11), one obtains

$$\|\sqrt{\varepsilon} v_n\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} + \sum_{j=i,e} \left\| \sqrt{\delta_n} \sqrt{\varepsilon} \bar{u}_{j,n} \right\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \tag{2.33}$$

$$+ \sum_{j=i,e} \left\| \sqrt{\delta_n} u_{j,n} \right\|_{L^\infty(0,T;L^2(\Omega_{j,\varepsilon}))} + \|\sqrt{\varepsilon} w_n\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \leq C,$$

$$\|\varepsilon \tilde{I}_{1,\text{ion}}(v_n) v_n\|_{L^1(\Gamma_{\varepsilon,T})} + \sum_{j=i,e} \|\nabla u_{j,n}\|_{L^2(\Omega_{j,\varepsilon,T})} \leq C, \tag{2.34}$$

$$\|\varepsilon^{1/r} v_n\|_{L^r(\Gamma_{\varepsilon,T})} \leq C, \tag{2.35}$$

$$\|\sqrt{\varepsilon} v_n\|_{L^2(\Gamma_{\varepsilon,T})} + \|\sqrt{\varepsilon} w_n\|_{L^2(\Gamma_{\varepsilon,T})} \leq C, \tag{2.36}$$

for some constant $C > 0$ not depending on n and ε . Moreover, one can obtain some uniform estimates on the time derivatives as follows. Substitute $\varphi_{i,n} = \partial_t u_{i,n}$ and $\varphi_{e,n} = \partial_t u_{e,n}$ in (2.30), and integrate in time to deduce

$$\begin{aligned} & \varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_{\varepsilon,T}} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 d\mathbf{x} dt \\ & + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,n} \cdot \nabla (\partial_t u_{j,n}) d\mathbf{x} dt + \varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{1,\text{ion}}(v_n) \partial_t v_n ds(x) dt \\ & + \varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{2,\text{ion}}(w_n) \partial_t v_n ds(x) dt = \varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{\text{app},\varepsilon} \partial_t v_n ds(x) dt. \end{aligned} \quad (2.37)$$

Now, set $\mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(t) = \frac{1}{2} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon} \nabla u_{j,n} \cdot \nabla u_{j,n} d\mathbf{x}$ and $\mathcal{I}_1(s) = \int_0^s I_{1,\text{ion}}(v) dv$. Observe that

$$\iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_j \nabla u_{j,n} \cdot \nabla (\partial_t u_{j,n}) d\mathbf{x} dt = \int_0^T \partial_t (\mathcal{P}_{\mathbf{M}_{j,\varepsilon}}) dt = \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(T) - \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0),$$

and

$$\begin{aligned} \iint_{\Gamma_{\varepsilon,T}} I_{1,\text{ion}}(v_n) \partial_t v_n ds(x) dt &= \int_0^T \partial_t \left(\int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n) ds(x) \right) dt \\ &= \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(T, x)) ds(x) - \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, x)) ds(x). \end{aligned}$$

Using this and Young's inequality, one gets from (2.37)

$$\begin{aligned} & \varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_{\varepsilon,T}} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 d\mathbf{x} dt \\ & + \sum_{j=i,e} \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(T) + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(T, x)) ds(x) \\ & \leq -\varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{2,\text{ion}}(w_n) \partial_t v_n ds(x) dt + \sum_{j=i,e} \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0) + \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, x)) ds(x) \\ & + \varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{\text{app},\varepsilon} \partial_t v_n ds(x) dt \\ & \leq \frac{\varepsilon}{2} \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + C\varepsilon \iint_{\Gamma_{\varepsilon,T}} |w_n|^2 ds(x) dt + \sum_{j=i,e} \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0) \\ & + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, x)) ds(x) + C\varepsilon \int_{\Gamma_{\varepsilon,T}} |I_{\text{app},\varepsilon}|^2 ds(x) dt, \end{aligned} \quad (2.38)$$

for some constant $C > 0$ not depending on ε and δ_n (recall that $0 < \varepsilon \leq 1$). Note that by Taylor's theorem and Remark 2, one has

$$\mathcal{I}_1(v) = -lv + \int_0^1 (1-t) I'_{1,\text{ion}}(tv) dt.$$

So by monotonicity of $\tilde{I}_{1,\text{ion}}$ (see (2.11)), one can obtain

$$\varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(T, x)) + \frac{L}{2} |v_n(T, x)|^2 + lv_n(T, x) ds(x) \geq 0.$$

Finally, use

$$\begin{aligned} \sum_{j=i,e} |\mathcal{P}_{M_{j,\varepsilon}}(0)| + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, x)) ds(x) \\ \leq C \left[\sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} |\nabla u_{j,n}(0, x)|^2 d\mathbf{x} + \varepsilon \int_{\Gamma_\varepsilon} |v_n(0, x)|^r ds(x) \right], \end{aligned}$$

(for some constant $C > 0$) and estimates (2.33), (2.34) and (2.35) to get from (2.38)

$$\begin{aligned} \varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_{\varepsilon,T}} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt \\ + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 d\mathbf{x} dt \leq C, \end{aligned} \quad (2.39)$$

for some constant $C > 0$. Hence, one has the estimate

$$\sqrt{\varepsilon} \|\partial_t v_n\|_{L^2(0,T;L^2(\Gamma_\varepsilon))} + \sum_{i,e} \sqrt{\delta_n} \sqrt{\varepsilon} \|\partial_t \bar{u}_{j,n}\|_{L^2(0,T;L^2(\Gamma_\varepsilon))} \leq C, \quad (2.40)$$

for some constant $C > 0$ not depending on n . Also, exploiting the structure of (2.31) along with estimate (2.36), one obtains

$$\|\sqrt{\varepsilon} \partial_t w_n\|_{L^2(\Gamma_{\varepsilon,T})} \leq C, \quad (2.41)$$

for some constant $C > 0$ independent of n .

The above estimates are not sufficient since estimates on the L^2 norms of the intracellular and extracellular potentials are needed in $\Omega_{i,\varepsilon}$ and $\Omega_{e,\varepsilon}$ respectively. Due to the compatibility condition (2.16), an application of Poincaré's inequality (see for instance [CDD⁺12]) implies that

$$\|u_{e,n}\|_{L^2(0,T;H^1(\Omega_{e,\varepsilon}))} \leq C. \quad (2.42)$$

Furthermore, making use of the trace inequality as stated in [ADH95], one has

$$\varepsilon \|\bar{u}_{e,n}\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C (\|u_{e,n}\|_{L^2(\Omega_{e,\varepsilon,T})}^2 + \varepsilon \|\nabla u_{e,n}\|_{L^2(\Omega_{e,\varepsilon,T})}^2),$$

and consequently

$$\varepsilon \|\bar{u}_{e,n}\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C. \quad (2.43)$$

Moreover, having $\varepsilon \|v_n\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C$, there holds

$$\varepsilon \|\bar{u}_{i,n}\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C. \quad (2.44)$$

Finally, making use of this last inequality, of (2.34) and of Lemma C.2 in [AGG⁺16], one gets

$$\|u_{i,n}\|_{L^2(\Omega_{i,\varepsilon})}^2 \leq C \varepsilon \|\bar{u}_{i,n}\|_{L^2(\Gamma_\varepsilon)}^2 + C \varepsilon^2 \|\nabla u_{i,n}\|_{L^2(\Omega_{i,\varepsilon})}^2 \leq C.$$

Therefore, the following estimate holds

$$\|u_{i,n}\|_{L^2(0,T;H^1(\Omega_{i,\varepsilon}))} \leq C. \quad (2.45)$$

The next step is to show that the local solution constructed above can be extended to the whole time interval $[0, T)$ (independent of n) but this can be done using the above estimates as in Ref. [BK06], so we omit the details.

Step 4: Passage to the limit and existence of solutions

From (2.45) and (2.42), it is easy to see that $v_n, \bar{u}_{j,n}$ are bounded in $L^2(0, T; H^{1/2}(\Gamma_\varepsilon))$ for $j = i, e$. This is a consequence of the fact that the trace of a function in H^1 is a function in $H^{1/2}$ and of the continuity of the trace map. Moreover, we deduce from (2.36), (2.43) and (2.44) the uniform bound on $v_n + (-1)^j \sqrt{\delta_n} \bar{u}_{j,n}$ in $L^2(\Gamma_{\varepsilon,T})$ for $j = i, e$. Recall that by the Aubin-Lions compactness criterion, the injection

$$\mathcal{W} = \{u \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon)) \text{ and } \partial_t u \in L^2(0, T; H^{-1/2}(\Gamma_\varepsilon))\} \subset L^2(\Gamma_{\varepsilon,T})$$

is compact. Therefore, we can assume that there exist limit functions $u_{i,\varepsilon}, u_{e,\varepsilon}, v_\varepsilon, w_\varepsilon$ with $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} := \bar{u}_{i,\varepsilon} - \bar{u}_{e,\varepsilon}$ on $\Gamma_{\varepsilon,T}$ such that as $n \rightarrow \infty$ (for fixed ε and up to an unlabeled subsequence)

$$\left\{ \begin{array}{l} v_n + (-1)^j \sqrt{\delta_n} \bar{u}_{j,n} \rightarrow v_\varepsilon \text{ a.e. in } \Gamma_{\varepsilon,T}, \text{ strongly in } L^2(\Gamma_{\varepsilon,T}), \\ \text{and weakly in } L^2(0, T; H^{1/2}(\Gamma_\varepsilon)) \text{ for } j = i, e, \\ u_{j,n} \rightharpoonup u_{j,\varepsilon} \text{ weakly in } L^2(0, T; H^1(\Omega_{j,\varepsilon})) \text{ for } j = i, e, \\ v_n \rightarrow v_\varepsilon \text{ a.e. in } \Gamma_{\varepsilon,T}, \text{ strongly in } L^2(\Gamma_{\varepsilon,T}), \\ w_n \rightharpoonup w_\varepsilon \text{ weakly in } L^2(\Gamma_{\varepsilon,T}), \\ I_{1,\text{ion}}(v_n) \rightarrow I_{1,\text{ion}}(v_\varepsilon) \text{ a.e. in } \Gamma_{\varepsilon,T} \text{ and weakly in } L^{r/(r-1)}(\Gamma_{\varepsilon,T}), \\ \partial_t v_n \rightharpoonup \partial_t v_\varepsilon \text{ weakly in } L^2(\Gamma_{\varepsilon,T}) \text{ and } \delta_n \partial_t \bar{u}_{j,n} \rightharpoonup 0 \text{ in } \mathcal{D}'(0, T; L^2(\Gamma_\varepsilon)) \text{ for } j = i, e, \\ \partial_t w_n \rightharpoonup \partial_t w_\varepsilon \text{ weakly in } L^2(\Gamma_{\varepsilon,T}), \\ \delta_n \partial_t u_{j,n} \rightharpoonup 0 \text{ in } \mathcal{D}'(0, T; L^2(\Omega_{j,\varepsilon})) \text{ for } j = i, e. \end{array} \right. \quad (2.46)$$

Keeping in mind (2.46), (2.33) and (2.40) we infer, by letting $n \rightarrow \infty$ in (2.23), (2.24) and (2.25),

$$\begin{aligned} \varepsilon \int_{\Gamma_\varepsilon} \partial_t v_\varepsilon \varphi \, ds(x) + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} M_j^\varepsilon(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, d\mathbf{x} \\ + \varepsilon \int_{\Gamma_\varepsilon} I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \varphi \, ds(x) = \varepsilon \int_{\Gamma_\varepsilon} I_{\text{app},\varepsilon} \varphi \, ds(x), \end{aligned} \quad (2.47)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_\varepsilon \phi \, ds(x) - \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon) \phi \, ds(x) = 0, \quad (2.48)$$

for all $\varphi_j \in H^1(\Omega_{j,\varepsilon})$, $j = i, e$, with $\varphi := (\varphi_i - \varphi_e)|_{\Gamma_\varepsilon} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$ and $\phi \in L^2(\Gamma_\varepsilon)$.

Step 5: Uniqueness.

Let $(u_{i,\varepsilon,1}, u_{e,\varepsilon,1}, w_{\varepsilon,1})$ and $(u_{i,\varepsilon,2}, u_{e,\varepsilon,2}, w_{\varepsilon,2})$ be two weak solutions satisfying (2.47)-(2.48), with $v_{\varepsilon,k} = (u_{i,\varepsilon,k} - u_{e,\varepsilon,k})|_{\Gamma_\varepsilon}$ for $k = 1, 2$ and with ‘‘data’’ $v_{\varepsilon,0} = v_{\varepsilon,1,0}$, $w_{\varepsilon,0} = w_{\varepsilon,1,0}$ and $v_{\varepsilon,0} =$

$v_{\varepsilon,2,0}, w_{\varepsilon,0} = w_{\varepsilon,2,0}$ respectively. Note that the following equations hold for all test functions $\varphi_j \in L^2(0, T; H^1(\Omega_{j,\varepsilon}))$, $j = i, e$, with $\varphi := (\varphi_i - \varphi_e) |_{\Gamma_\varepsilon} \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon)) \cap L^r(\Gamma_{\varepsilon,T})$ and $\phi \in L^2(\Gamma_{\varepsilon,T})$:

$$\begin{aligned} & \iint_{\Gamma_{\varepsilon,t}} \varepsilon \partial_t (v_{\varepsilon,1} - v_{\varepsilon,2}) \varphi \, ds(x) \, ds + \sum_{i,e} \iint_{\Omega(j,\varepsilon,t)} \mathbf{M}_{j,\varepsilon}(x) \nabla(u_{j,\varepsilon,1} - u_{j,\varepsilon,2}) \cdot \nabla \varphi_j \, d\mathbf{x} \, ds \\ & \quad + \iint_{\Gamma_{\varepsilon,t}} \varepsilon (I_{\text{ion}}(v_{\varepsilon,1}, w_{\varepsilon,1}) - I_{\text{ion}}(v_{\varepsilon,2}, w_{\varepsilon,2})) \varphi \, ds(x) \, ds = 0, \\ & \iint_{\Gamma_{\varepsilon,t}} \partial_t (w_{\varepsilon,1} - w_{\varepsilon,2}) \phi \, ds(x) \, ds - \iint_{\Gamma_{\varepsilon,t}} (H(v_{\varepsilon,1}, w_{\varepsilon,1}) - H(v_{\varepsilon,2}, w_{\varepsilon,2})) \phi \, ds(x) \, ds = 0, \end{aligned}$$

for $0 < t \leq T$. Substituting $\varphi_j = (u_{j,\varepsilon,1} - u_{j,\varepsilon,2})$ and $\phi = w_{\varepsilon,1} - w_{\varepsilon,2}$ in the two equations above, then adding the resulting ones, we arrive at

$$\begin{aligned} & \frac{1}{2} \int_{\Gamma_\varepsilon} \left(\varepsilon |(v_{\varepsilon,1} - v_{\varepsilon,2})(t)|^2 + |(w_{\varepsilon,1} - w_{\varepsilon,2})(t)|^2 \right) ds(x) \\ & \quad - \frac{1}{2} \int_{\Gamma_\varepsilon} \left(\varepsilon |v_{\varepsilon,1,0} - v_{\varepsilon,2,0}|^2 + |w_{\varepsilon,1,0} - w_{\varepsilon,2,0}|^2 \right) ds(x) \\ & \quad + \sum_{j=i,e} \int_0^t \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon} \nabla(u_{j,\varepsilon,1} - u_{j,\varepsilon,2}) \cdot \nabla(u_{j,\varepsilon,1} - u_{j,\varepsilon,2}) \, d\mathbf{x} \, ds \\ & \quad + \int_0^t \int_{\Gamma_\varepsilon} \varepsilon (I_{\text{ion}}(v_{\varepsilon,1}, w_{\varepsilon,1}) - I_{\text{ion}}(v_{\varepsilon,2}, w_{\varepsilon,2})) (v_{\varepsilon,1} - v_{\varepsilon,2}) \, ds(x) \, ds \\ & = \int_0^t \int_{\Gamma_\varepsilon} (H(v_{\varepsilon,1}, w_{\varepsilon,1}) - H(v_{\varepsilon,2}, w_{\varepsilon,2})) (w_{\varepsilon,1} - w_{\varepsilon,2}) \, ds(x) \, dt. \end{aligned}$$

Now using (2.9), one has for $j = i, e$

$$\int_0^t \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon} \nabla(u_{j,\varepsilon,1} - u_{j,\varepsilon,2}) \cdot \nabla(u_{j,\varepsilon,1} - u_{j,\varepsilon,2}) \, d\mathbf{x} \, ds \geq 0.$$

Also, by (2.11) there holds

$$\int_0^t \int_{\Gamma_\varepsilon} \varepsilon (I_{1,\text{ion}}(v_{\varepsilon,1}) - I_{1,\text{ion}}(v_{\varepsilon,2})) (v_{\varepsilon,1} - v_{\varepsilon,2}) \, ds(x) \, dt \geq -L\varepsilon \int_0^t \int_{\Gamma_\varepsilon} (v_{\varepsilon,1} - v_{\varepsilon,2})^2 \, ds(x) \, dt.$$

Moreover, exploiting the linearity of $H(v, w)$ and $I_{2,\text{ion}}(w)$, and using Young's inequality one can deduce

$$\begin{aligned} & \frac{1}{2} \int_{\Gamma_\varepsilon} \left(\varepsilon |(v_{\varepsilon,1} - v_{\varepsilon,2})(t)|^2 + |(w_{\varepsilon,1} - w_{\varepsilon,2})(t)|^2 \right) ds(x) \\ & \leq C \left(\int_0^t \int_{\Gamma_\varepsilon} \left(\varepsilon |v_{\varepsilon,1} - v_{\varepsilon,2}|^2 + |w_{\varepsilon,1} - w_{\varepsilon,2}|^2 \right) ds(x) \, ds \right. \\ & \quad \left. + \frac{1}{2} \int_{\Gamma_\varepsilon} \left(\varepsilon |v_{\varepsilon,1,0} - v_{\varepsilon,2,0}|^2 + |w_{\varepsilon,1,0} - w_{\varepsilon,2,0}|^2 \right) ds(x) \right) \end{aligned}$$

for some constant $C > 0$. Finally, an application of Gronwall's inequality yields

$$\begin{aligned} & \int_{\Gamma_\varepsilon} \left(\varepsilon |(v_{\varepsilon,1} - v_{\varepsilon,2})(t)|^2 + |(w_{\varepsilon,1} - w_{\varepsilon,2})(t)|^2 \right) ds(x) \\ & \leq C \int_{\Gamma_\varepsilon} \left(\varepsilon |v_{\varepsilon,1,0} - v_{\varepsilon,2,0}|^2 + |w_{\varepsilon,1,0} - w_{\varepsilon,2,0}|^2 \right) ds(x). \end{aligned}$$

for some constant $C > 0$. This completes the uniqueness proof. \square

2.5 Convergence of solutions to the macroscopic problem

This section consists in preparing the ground for the passage to the limit as $\varepsilon \rightarrow 0$. First, some a priori estimates are obtained on the solutions of the microscopic problem. Then, the unfolding operator for perforated domains and the boundary unfolding operator are introduced and some of their properties are recalled. Finally, the microscopic problem is written in an equivalent formulation, the so called ‘‘unfolded’’ formulation, making use of the unfolding operators.

2.5.1 Energy estimates for the microscopic solutions

Lemma 2.5.1. *Assume (2.10), (2.11), (2.6) and (2.7) hold. Then there exist constants $c_1, c_2, c_3, c_4, c_5, c_6 > 0$, not depending on ε such that*

$$\|\sqrt{\varepsilon}v_\varepsilon\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} + \|\sqrt{\varepsilon}w_\varepsilon\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \leq c_1, \quad (2.49)$$

$$\sum_{j=i,e} \|u_{j,\varepsilon}\|_{L^2(0,T;H^1(\Omega_{j,\varepsilon}))} \leq c_3 \quad (2.50)$$

$$\|\varepsilon^{1/r}v_\varepsilon\|_{L^r(\Gamma_{\varepsilon,T})} \leq c_4 \text{ and } \|\varepsilon^{(r-1)/r}I_{1,\text{ion}}(v_\varepsilon)\|_{L^{r/(r-1)}(\Gamma_{\varepsilon,T})} \leq c_5. \quad (2.51)$$

If $v_{\varepsilon,0} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$, then there exists a constant $c_4 > 0$ not depending on ε such that

$$\|\sqrt{\varepsilon}\partial_t v_\varepsilon\|_{L^2(\Gamma_{\varepsilon,T})} \leq c_6. \quad (2.52)$$

Proof. Substituting $\varphi_i = u_{i,\varepsilon}$, $\varphi_e = u_{e,\varepsilon}$ and $\varphi = \varepsilon w_\varepsilon$ in (2.47) and (2.48), respectively, and then summing the resulting equations, we get

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\Gamma_\varepsilon} |\sqrt{\varepsilon}v_\varepsilon|^2 ds(x) + \frac{1}{2} \frac{d}{dt} \int_{\Gamma_\varepsilon} |\sqrt{\varepsilon}w_\varepsilon|^2 ds(x) + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla u_{j,\varepsilon} dx \\ & + \varepsilon \int_{\Gamma_\varepsilon} I_{1,\text{ion}}(v_\varepsilon)v_\varepsilon ds(x) \\ & = -\varepsilon \int_{\Gamma_\varepsilon} I_{2,\text{ion}}(w_\varepsilon)v_\varepsilon ds(x) + \varepsilon \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon)w_\varepsilon ds(x) + \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon}v_\varepsilon ds(x). \end{aligned} \quad (2.53)$$

Using assumptions (2.10) on $I_{1,\text{ion}}, I_{2,\text{ion}}, H$ and the ellipticity condition on $\mathbf{M}_{j,\varepsilon}$ for $j = i, e$, we get from (2.53) (after an application of Young's inequality)

$$\frac{1}{2} \frac{d}{dt} \int_{\Gamma_\varepsilon} \left(|\sqrt{\varepsilon} v_\varepsilon|^2 + |\sqrt{\varepsilon} w_\varepsilon|^2 \right) ds(x) \leq C_1 \int_{\Gamma_\varepsilon} \left(|\sqrt{\varepsilon} v_\varepsilon|^2 + |\sqrt{\varepsilon} w_\varepsilon|^2 \right) ds(x), \quad (2.54)$$

for some constant $C_1 > 0$ not depending on ε .

Integrating (2.54) over $(0, t)$ and then from Gronwall's inequality, there exists a constant $c_2 > 0$ such that

$$\int_{\Gamma_\varepsilon} \left(|\sqrt{\varepsilon} v_\varepsilon(t, x)|^2 + |\sqrt{\varepsilon} w_\varepsilon(t, x)|^2 \right) ds(x) \leq C_2, \quad (2.55)$$

for all $t \in (0, T]$.

In view of (2.55), it follows from (2.53) that

$$\sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} |\nabla u_{j,\varepsilon}|^2 d\mathbf{x} dt \leq C_3, \quad (2.56)$$

and

$$\varepsilon \iint_{\Gamma_{\varepsilon,T}} |v_\varepsilon|^r ds(x) dt \leq C_4, \quad (2.57)$$

for some constants $C_3, C_4 > 0$ independent of ε . The other estimate in (2.51) is a direct consequence of (2.57) and assumption (2.10) on $I_{1,\text{ion}}$. Also, the second estimate in (2.34) can be obtained by making use of the trace inequalities, as in the previous section.

To prove (2.52), we substitute $\varphi_i = \partial_t u_{i,\varepsilon}$ and $\varphi_e = \partial_t u_{e,\varepsilon}$ in (2.47), we integrate in time and we proceed exactly as in the previous section to deduce

$$\varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_\varepsilon|^2 ds(x) dt \leq C,$$

for some constant $C > 0$. This completes the proof of Lemma 2.5.1. □

2.5.2 A new formulation of the microscopic problem

In this subsection, we view the domains $\Omega_{j,\varepsilon}$, $j = i, e$ as perforated domains and we define the unfolding operator $\mathcal{T}_\varepsilon^j$, $j = i, e$ following the same notation as in [CDD⁺12].

Definition of The Unfolding Operator

First, we define the following sets in \mathbb{R}^3 (see Figure 2.1):

- $\Xi_\varepsilon = \{\ell \in \mathbf{Z}^n, \varepsilon(\ell + Y) \subset \Omega\}$,
- $\hat{\Omega}_\varepsilon = \text{interior} \left\{ \bigcup_{\ell \in \Xi_\varepsilon} \varepsilon(\ell + \bar{Y}) \right\}$
- $\hat{\Omega}_\varepsilon^j = \text{interior} \left\{ \bigcup_{\ell \in \Xi_\varepsilon} \varepsilon(\ell + \bar{Y}_j) \right\}$, $j = i, e$

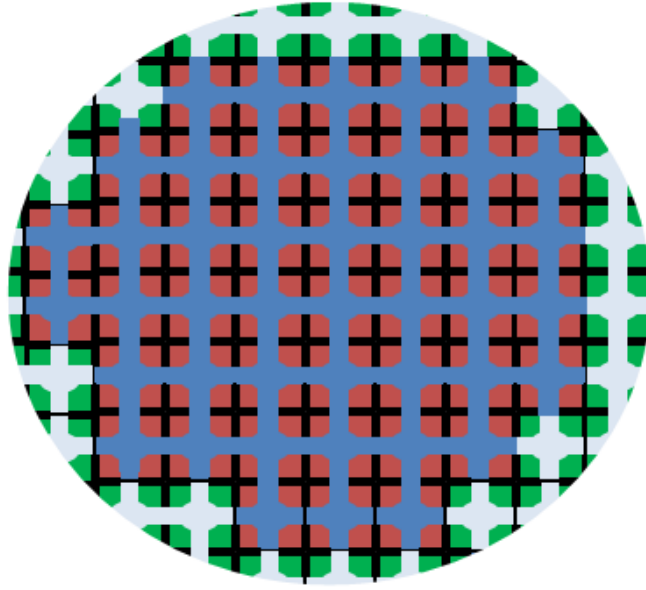


Figure 2.1 – The set $\hat{\Omega}_\varepsilon^e$ in dark red, the set $\hat{\Omega}_\varepsilon^i$ in dark blue and the region Λ_ε in dark green and light blue.

- $\hat{\Omega}_{\varepsilon,T} = (0, T) \times \hat{\Omega}_\varepsilon$,
- $\hat{\Omega}_{\varepsilon,T}^j = (0, T) \times \hat{\Omega}_\varepsilon^j$,
- $\hat{\Gamma}_\varepsilon := \{y \in \Gamma_\varepsilon : y \in \hat{\Omega}_\varepsilon\}$,
- $\Lambda_\varepsilon = \Omega \setminus \hat{\Omega}_\varepsilon$,
- $\Lambda_{\varepsilon,T} = (0, T) \times \Omega \setminus \hat{\Omega}_\varepsilon$.

Secondly, for $z \in \mathbb{R}^3$, we let $[z]_Y$ denote the unique integer combination of the periods such that $z - [z]_Y$ belongs to Y and we set

$$\{z\}_Y = z - [z]_Y \in Y, \text{ a.e. for } z \in \mathbb{R}^n.$$

We recall the definition of the time dependent unfolding operator in perforated domains.

Definition 2.5.1. For any function ϕ Lebesgue-measurable on $(0, T) \times \Omega_{j,\varepsilon}$, the unfolding operator is defined by

$$\mathcal{T}_\varepsilon^j(\phi)(t, x, y) = \begin{cases} \phi\left(t, \varepsilon \left[\frac{x}{\varepsilon}\right]_Y + \varepsilon y\right) & \text{a.e. for } (t, x, y) \in \hat{\Omega}_{\varepsilon,T} \times Y_j \\ 0 & \text{a.e. for } (t, x, y) \in (0, T) \times \Lambda_\varepsilon \times Y_j. \end{cases} \quad (2.58)$$

Observe that the function $\varepsilon \left[\frac{x}{\varepsilon}\right]$ represents the lattice translation point of the ε -cellular medium containing x . In particular, one has

$$x = \varepsilon \left(\left[\frac{x}{\varepsilon}\right]_Y + \left\{\frac{x}{\varepsilon}\right\}_Y \right) \text{ for all } x \in \mathbb{R}^n.$$

Properties of the Unfolding Operator

For the sake of completeness, we recall some properties of the unfolding operator and we refer the reader to [CDZ06, CDD⁺12] for details.

Proposition 2.5.2. *For $p \in [1, \infty)$, the operator $\mathcal{T}_\varepsilon^j$ is linear and continuous from $L^p((0, T) \times \Omega_{j,\varepsilon})$ to $L^p(\Omega_T \times Y_j)$. For every $\phi \in L^1((0, T) \times \Omega_{j,\varepsilon})$ and $v, w \in L^p((0, T) \times \Omega_{j,\varepsilon})$, there holds*

1. $\mathcal{T}_\varepsilon^j(vw) = \mathcal{T}_\varepsilon^j(v)\mathcal{T}_\varepsilon^j(w)$,
2. $\int_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(\phi)(t, x, y) \, d\mathbf{x} \, dy = \int_{\hat{\Omega}_{j,\varepsilon}} \phi(t, x) \, d\mathbf{x}$,
3. $\|\mathcal{T}_\varepsilon^j(w)\|_{L^p(\Omega \times Y_j)} = \|w1_{\hat{\Omega}_{j,\varepsilon}^j}\|_{L^p(\Omega_{j,\varepsilon})} \leq \|w\|_{L^p(\Omega_{j,\varepsilon})}$.

The Boundary Unfolding Operator

Since the dynamic equations are defined on the surface Γ_ε , we resort to the use of the boundary unfolding operator, developed in [CDZ06, CDD⁺12] and defined as follows (recall that $\Gamma_{\varepsilon,T} = (0, T) \times \Gamma_\varepsilon$).

Definition 2.5.2. For any function u Lebesgue-measurable on $(0, T) \times (\partial\hat{\Omega}_{i,\varepsilon} \cap \Gamma_\varepsilon)$, the boundary unfolding operator $\mathcal{T}_\varepsilon^b$ is defined by

$$\mathcal{T}_\varepsilon^b u(t, x, y) = \begin{cases} u(t, \varepsilon(\lfloor \frac{x}{\varepsilon} \rfloor + y)), & \text{a.e. for } (t, x, y) \in \hat{\Omega}_{\varepsilon,T} \times \Gamma, \\ 0, & \text{a.e. for } (t, x, y) \in (0, T) \times \Lambda_\varepsilon \times \Gamma. \end{cases} \quad (2.59)$$

We also list herein some properties of the boundary unfolding operator as given in [CDD⁺12].

Proposition 2.5.3. *The boundary unfolding operator has the following properties:*

1. $\mathcal{T}_\varepsilon^b$ is a linear operator from $L^p(\Gamma_{\varepsilon,T})$ to $L^p(\Omega_T \times \Gamma)$.
2. $\mathcal{T}_\varepsilon^b(\phi\psi) = \mathcal{T}_\varepsilon^b(\phi)\mathcal{T}_\varepsilon^b(\psi)$, $\forall \phi, \psi \in L^p(\Gamma_{\varepsilon,T})$, $p \in (1, +\infty)$.
3. For every $\phi \in L^1(\Gamma_{\varepsilon,T})$, we have the following integration formula

$$\int_{\hat{\Gamma}_\varepsilon} \phi(t, x) \, ds(x) = \frac{1}{\varepsilon|Y|} \int_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(\phi)(t, x, y) \, d\mathbf{x} \, ds(y).$$

4. For every $\phi \in L^p(\hat{\Gamma}_{\varepsilon,T})$ with $p \in (1, +\infty)$, one has

$$\|\mathcal{T}_\varepsilon^b(\phi)\|_{L^p(\Omega_T \times \Gamma)} = \varepsilon^{1/p} |Y|^{1/p} \|\phi\|_{L^p((0,T) \times \hat{\Gamma}_\varepsilon)}.$$

5. For every $\varphi \in \mathcal{D}(\Omega_T \times \Gamma)$ and $w \in W^{1,1}(0, T; L^1(\Gamma_\varepsilon))$, the following integration by parts formula holds

$$\int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t w) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt = - \int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(w) \mathcal{T}_\varepsilon^b(\partial_t \varphi) \, ds(y) \, d\mathbf{x} \, dt.$$

Remark 4. Note that the last property (which is not listed in [CDD⁺12]) is a direct consequence of the integration by parts formula:

$$\int_0^T \int_{\Gamma_\varepsilon} \partial_t w \varphi \, ds(x) \, dt = - \int_0^T \int_{\Gamma_\varepsilon} w \partial_t \varphi \, ds(x) \, dt,$$

and the integration formula in property (3) of Proposition 2.5.3.

“Unfolded” Formulation of the Microscopic Problem

In order to make use of the unfolding method in the homogenization of the microscopic problem, we rewrite the corresponding equations (2.47) and (2.48) in the “unfolded” form. We have the following identities:

$$\begin{aligned}
\iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, d\mathbf{x} \, dt &= \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) \, d\mathbf{x} \, dy \, dt \\
&\quad + \iint_{(0,T) \times \Lambda_\varepsilon^j} \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, d\mathbf{x} \, dy \, dt \\
&:= \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) \, d\mathbf{x} \, dy \, dt + r_1,
\end{aligned}$$

$$\begin{aligned}
\iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt &= \iint_{\hat{\Gamma}_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt + \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt \\
&= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt \\
&\quad + \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt \\
&:= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt + r_2,
\end{aligned}$$

$$\begin{aligned}
\iint_{\Gamma_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt &= \iint_{\hat{\Gamma}_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt + \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt \\
&:= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt + r_3,
\end{aligned}$$

$$\begin{aligned}
\iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{1,\text{ion}}(v_\varepsilon) \varphi \, ds(x) \, dt &= \iint_{\hat{\Gamma}_{\varepsilon,T}} \varepsilon I_{1,\text{ion}}(v_\varepsilon) \varphi \, ds(x) \, dt \\
&\quad + \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \varepsilon I_{1,\text{ion}}(v_\varepsilon) \varphi \, ds(x) \, dt \\
&:= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{1,\text{ion}}(v_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt + r_4,
\end{aligned}$$

$$\begin{aligned}
\iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{2,\text{ion}}(w_\varepsilon) \varphi \, ds(x) \, dt &= \iint_{\hat{\Gamma}_{\varepsilon,T}} \varepsilon I_{2,\text{ion}}(w_\varepsilon) \varphi \, ds(x) \, dt \\
&\quad + \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \varepsilon I_{2,\text{ion}}(w_\varepsilon) \varphi \, ds(x) \, dt \\
&:= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{2,\text{ion}}(w_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt + r_5 \\
&= \iiint_{\Omega_T \times \Gamma} I_{2,\text{ion}}(\mathcal{T}_\varepsilon^b(w_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) \, ds(y) \, d\mathbf{x} \, dt + r_5
\end{aligned}$$

Due to the above equalities, one obtains the following equivalent “unfolded” formulation of (2.47):

$$\begin{aligned}
& \iint\limits_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt + \sum_{i,\varepsilon} \iint\limits_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) d\mathbf{x} dy dt \\
& - \lambda \iint\limits_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(w_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt + \iint\limits_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{1,\text{ion}}(v_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt \\
& = \iint\limits_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt + r_2 - r_5 - r_4 - r_3 - r_1.
\end{aligned} \tag{2.60}$$

Similarly, the “unfolded” formulation of (2.48) is given by:

$$\begin{aligned}
& \iint\limits_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t w_\varepsilon) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt - \iint\limits_{\Omega_T \times \Gamma} H(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(w_\varepsilon)) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt \\
& = -\varepsilon \iint\limits_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \partial_t w_\varepsilon \phi ds(x) dt + \varepsilon \iint\limits_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} H(v_\varepsilon, w_\varepsilon) \phi ds(x) dt \\
& := r_6 + r_7.
\end{aligned} \tag{2.61}$$

2.6 “Unfolding” compactness

In this section, we establish the passage to the limit in (2.60) and (2.61). Note that by estimates (2.49)-(2.52) obtained above one has

$$r_1, \dots, r_7 \rightarrow 0 \text{ as } \varepsilon \rightarrow 0.$$

For the sake of completeness, we illustrate this result by proving that $r_1 \rightarrow 0$ as $\varepsilon \rightarrow 0$. The proof that the other terms $r_2, \dots, r_7 \rightarrow 0$ is similar. Actually, by Cauchy-Schwartz’ inequality, one has

$$\begin{aligned}
& \iint\limits_{(0,T) \times \Lambda_\varepsilon^j} \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j d\mathbf{x} dt \\
& \leq \| \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \|_{L^2(\Omega_{j,\varepsilon,T})} \left(\iint\limits_{(0,T) \times \Lambda_\varepsilon^j} |\nabla \varphi_j|^2 \right)^{1/2}.
\end{aligned}$$

In addition, since $|\Lambda_\varepsilon^j| \rightarrow 0$ and $\nabla \varphi_j \in L^2(\Omega_{j,\varepsilon})$, then by Lebesgue’s dominated convergence theorem, one can show that

$$\iint\limits_{(0,T) \times \Lambda_\varepsilon^j} |\nabla \varphi_j|^2 \rightarrow 0, \text{ as } \varepsilon \rightarrow 0.$$

Finally, the result follows by making use of estimate (2.50) and of assumption 2.9. Now, by regularity of the test functions φ and ϕ , there holds

$$\mathcal{T}_\varepsilon^b \varphi \rightarrow \varphi \text{ and } \mathcal{T}_\varepsilon^b \phi \rightarrow \phi \text{ strongly in } L^2(\Omega_T \times \Gamma),$$

and

$$\mathcal{T}_\varepsilon^j \varphi_j \rightarrow \varphi_j \text{ strongly in } L^2(\Omega_T \times Y_j).$$

Moreover, besides the unfolding operator, the second ingredient of the unfolding homogenization is the separation of the microscopic and macroscopic scales known as scale-splitting

[CDZ06, CDG08, CDD⁺12]. This is illustrated herein by the choice of the test functions. Consider Ψ_j and θ_j in $\mathcal{D}(\Omega_T)$ and $\psi_j = \psi_j(\xi)$ in $H_{per}^1(Y_j)$ such that $\int_{Y_j} \psi_j = 0$ and test equation (2.60) with functions $\varphi_j^\varepsilon = \Psi_j + \varepsilon\theta_j\psi_{j,\varepsilon}$ where $\psi_{j,\varepsilon}(x) = \psi(\frac{x}{\varepsilon})$ (see for e.g. [CDD⁺12]). Since

$$\nabla\varphi_j^\varepsilon = \nabla_x\Psi_j + \varepsilon\psi_{j,\varepsilon}\nabla_x\theta_j + \theta_j(\nabla_\xi\psi_{j,\varepsilon}),$$

and thanks to Proposition 2.8 in [CDD⁺12] (see also [GP14]), there holds

$$\begin{aligned} \mathcal{T}_\varepsilon^j(\varphi_j^\varepsilon) &\rightarrow \Psi_j \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \mathcal{T}_\varepsilon^j(\theta_j\psi_{j,\varepsilon}) &\rightarrow \theta_j(x)\psi_j(\xi) \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \mathcal{T}_\varepsilon^j(\nabla\varphi_j^\varepsilon) &\rightarrow \nabla\Psi_j + \theta_j\nabla_\xi\psi_j \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \text{and } \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) &\rightarrow \Psi \text{ strongly in } L^2(\Omega_T \times \Gamma), \end{aligned} \quad (2.62)$$

where $\varphi^\varepsilon = (\varphi_i^\varepsilon - \varphi_e^\varepsilon)|_{\Gamma_{\varepsilon,T}}$ and $\Psi = (\Psi_i - \Psi_e)|_{\Omega_T \times \Gamma}$. Hence, to establish the passage to the limit in (2.60) and (2.61), we need to verify that the remaining terms of the equations are weakly convergent.

Now, making use of estimate (2.50), there exist limit functions $u_j \in L^2(0, T; H^1(\Omega))$ and $\hat{u}_j \in L^2(0, T; L^2(\Omega, H_{per}^1(Y_j)))$ such that, up to a subsequence (see for instance theorem 3.12 in [CDD⁺12]), the following hold

$$\begin{cases} \mathcal{T}_\varepsilon^j(u_j^\varepsilon) \rightharpoonup u_j \text{ weakly in } L^2(0, T; L^2(\Omega, H^1(Y_j))), \\ \mathcal{T}_\varepsilon^j(\nabla u_j^\varepsilon) \rightharpoonup \nabla u_j + \nabla_\xi \hat{u}_j \text{ weakly in } L^2(\Omega_T \times Y_j). \end{cases}$$

Thus, since $\mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \rightarrow \mathbf{M}_j$ a.e. in $\Omega \times Y_j$, one obtains (recall the strong convergence (2.62))

$$\begin{aligned} &\sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla \varphi_j^\varepsilon) dy d\mathbf{x} dt \\ &\rightarrow \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j(\nabla u_j + \nabla_\xi \hat{u}_j)(\nabla \Psi_j + \theta_j \nabla_\xi \psi_j(\xi)) dy d\mathbf{x} dt \text{ as } \varepsilon \rightarrow 0. \end{aligned}$$

Furthermore, since

$$\|\mathcal{T}_\varepsilon^b(w_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq \varepsilon^{1/2} \|w_\varepsilon\|_{L^2(\Gamma_{\varepsilon,T})} \leq C,$$

then up to a subsequence

$$\mathcal{T}_\varepsilon^b w_\varepsilon \rightharpoonup w \text{ in } L^2(\Omega_T \times \Gamma).$$

Consequently, by linearity of $I_{2,\text{ion}}$,

$$\iiint_{\Omega_T \times \Gamma} I_{2,\text{ion}}(\mathcal{T}_\varepsilon^b(w_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) ds(y) d\mathbf{x} dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{2,\text{ion}}(w) \Psi ds(y) d\mathbf{x} dt.$$

Similarly, exploiting assumption (2.14), one obtains

$$\iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) ds(y) d\mathbf{x} dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{\text{app}} \Psi ds(y) d\mathbf{x} dt.$$

In order to establish the convergence of $\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon)$, first note that

$$\|\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq \varepsilon^{1/2} \|\partial_t v_\varepsilon\|_{L^2\Gamma_{\varepsilon,T}} \leq C.$$

So there exists $h \in L^2(\Omega_T \times \Gamma)$ such that $\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \rightharpoonup h$ weakly in $L^2(\Omega_T \times \Gamma)$. One still needs to identify h to $\partial_t v$ (where $\mathcal{T}_\varepsilon^b(v_\varepsilon) \rightarrow v$ strongly in $L^2(\Omega_T \times \Gamma)$ as detailed in the next section; consult Lemma 6.3). For this sake, consider a test function $\varphi \in \mathcal{D}(\Omega_T \times \Gamma)$, then

$$\mathcal{T}_\varepsilon^b(\varphi) \rightarrow \varphi \text{ and } \mathcal{T}_\varepsilon^b(\partial_t \varphi) \rightarrow \partial_t \varphi \text{ strongly in } L^2(\Omega_T \times \Gamma).$$

Furthermore, taking limits on both sides of

$$\int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt = - \int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(v_\varepsilon) \mathcal{T}_\varepsilon^b(\partial_t \varphi) ds(y) d\mathbf{x} dt,$$

one has

$$\int_0^T \iint_{\Omega \times \Gamma} h \varphi ds(y) d\mathbf{x} dt = - \int_0^T \iint_{\Omega \times \Gamma} v \partial_t \varphi ds(y) d\mathbf{x} dt.$$

Therefore, $h \equiv \partial_t v$ and

$$\iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt \rightarrow \iint_{\Omega_T \times \Gamma} \partial_t v \Psi ds(y) d\mathbf{x} dt.$$

It remains to obtain the passage to the limit in the term containing the ionic function $I_{1,\text{ion}}$. Indeed due to the nonlinearity, it is difficult to pass to the limit in $I_{1,\text{ion}}$ on the microscopic membrane surface and one needs to establish the passage to the limit in:

$$\lim_{\varepsilon \rightarrow 0} \int_0^T \int_\Omega \int_\Gamma I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) ds(y) dx dt.$$

By regularity of φ^ε , we have

$$\mathcal{T}_\varepsilon^b \varphi \rightarrow \Psi \text{ strongly in } L^r((0, T) \times \Omega \times \Gamma).$$

It remains to show the weak convergence of $I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b v_\varepsilon)$ to $I_{1,\text{ion}}(v)$ in $L^{r/(r-1)}(\Omega_T \times \Gamma)$. Therefore, we show the strong convergence of $\mathcal{T}_\varepsilon^b v_\varepsilon$ to v in $L^2(\Omega_T \times \Gamma)$. Then, by the properties of $I_{1,\text{ion}}$ we actually obtain the strong convergence of $I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b v_\varepsilon)$ to $I_{1,\text{ion}}(v)$ in $L^q(\Omega_T \times \Gamma)$ for all $q \in [1, r/(r-1))$. For this sake, we make use of Kolmogorov-Riesz-type compactness criterion for the space $L^p(\Omega, B)$ that can be found as Corollary 2.5 in [GNR16].

Proposition 2.6.1. *Let $\Omega \subset \mathbb{R}^n$ be an open and bounded set. Let $p \in [1, \infty)$, B be a Banach space and $F \subset L^p(\Omega, B)$. Then F is relatively compact in $L^p(\Omega, B)$ iff*

- (i) *for every measurable set $C \subset \Omega$, the set $\{\int_C f d\mathbf{x} : f \in F\}$ is relatively compact in B ,*
- (ii) *for all $\delta > 0$ and $z \in \mathbb{R}^n$ and $z_i \geq 0, i = 1, \dots, n$, there holds*

$$\sup_{f \in F} \|\tau_{z_\sigma} f - f\|_{L^p(\Omega_\delta^z, B)} \rightarrow 0, \text{ for } z \rightarrow 0,$$

where $\Omega_\delta^z := \{x \in \Omega : x + z \in \Omega\}$ and $\Omega_\delta := \{x \in \Omega : \text{dist}(x, \partial\Omega) > \delta\}$,

- (iii) *for $\delta > 0$, there holds $\sup_{f \in F} \int_{\Omega \setminus \Omega_\delta} |f(x)|^p d\mathbf{x} \rightarrow 0$ for $\delta \rightarrow 0$.*

First, we prove an estimate on the space translates of the transmembrane potential v_ε that is needed later to obtain an estimate on the space translate of $\mathcal{T}_\varepsilon^b(v_\varepsilon)$. Now, we fix open sets K and K' such that

$$K \subset\subset K' \subset\subset \Omega,$$

and we let $z \in \mathbb{R}$ with

$$|z| < \text{dist}(K', \partial\Omega).$$

We have the following lemma

Lemma 2.6.2. *Let $l \in \mathbb{Z}^3$ and $\varepsilon > 0$ such that $\varepsilon|l| \leq |z|$. Then the following estimate holds:*

$$\varepsilon \|v_\varepsilon(t, x + \varepsilon l) - v_\varepsilon(t, x)\|_{L^2(\Gamma_{\varepsilon, K})}^2 \leq C\varepsilon l, \quad (2.63)$$

where $\Gamma_{\varepsilon, K} = \Gamma_\varepsilon \cap K$ and C is a positive constant.

For simplicity of notation, we use

$$\tau_{\varepsilon l} v(t, x) := v(t, x + \varepsilon l).$$

Proof. In this proof, we consider $\varphi_j \in H^1(\Omega_{j, \varepsilon})$ with $\text{supp} \varphi_j \subset K$, for $j = i, e$. We use the translations of φ_j , $j = i, e$ i.e. $\varphi_j(x - \varepsilon l)$ as test functions in the variational formulation (2.20). In the resulting equation, we make the substitution $x \mapsto x + \varepsilon l$, and we exploit the periodicity of the domain to get

$$\begin{aligned} \varepsilon \int_{\Gamma_\varepsilon \cap K} \partial_t(\tau_{\varepsilon l} v_\varepsilon)(\varphi_i - \varphi_e) ds + \sum_{j=i, e} \int_{\Omega_{j, \varepsilon} \cap K} \tau_{\varepsilon l} \mathbf{M}_{j, \varepsilon} \nabla \tau_{\varepsilon l} u_{j, \varepsilon} \cdot \nabla \varphi_j dx \\ + \varepsilon \int_{\Gamma_\varepsilon \cap K} I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon)(\varphi_i - \varphi_e) ds = \int_{\Gamma_\varepsilon \cap K} \tau_{\varepsilon l} I_{\text{app}, \varepsilon} \varphi ds. \end{aligned} \quad (2.64)$$

Noting that the last equality is valid for test functions with support in K' , let $\eta \in \mathcal{D}(K')$ be a cutoff function for K , with $0 \leq \eta \leq 1$, $\eta = 1$ in K and zero outside K' . We test the variational equation for $(\tau_{\varepsilon l} u_{j, \varepsilon} - u_{j, \varepsilon})$, $j = i, e$ with

$$\varphi_j = \eta^2(\tau_{\varepsilon l} u_{j, \varepsilon} - u_{j, \varepsilon}), \quad j = i, e,$$

we get

$$\begin{aligned} \frac{\varepsilon}{2} \frac{d}{dt} \int_{\Gamma_\varepsilon \cap K'} \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)^2 ds \\ + \sum_{j=i, e} \int_{\Omega_{j, \varepsilon} \cap K'} \left(\tau_{\varepsilon l} \mathbf{M}_{j, \varepsilon} \nabla \tau_{\varepsilon l} u_{j, \varepsilon} - \mathbf{M}_{j, \varepsilon} \nabla u_{j, \varepsilon} \right) \cdot \nabla \left(\eta^2 (\tau_{\varepsilon l} u_{j, \varepsilon} - u_{j, \varepsilon}) \right) dx \\ + \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon) - I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\ = \int_{\Gamma_\varepsilon \cap K'} (\tau_{\varepsilon l} I_{\text{app}, \varepsilon} - I_{\text{app}, \varepsilon}) \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds. \end{aligned} \quad (2.65)$$

First, we break up the second term in (2.65) as follows:

$$\begin{aligned}
& \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\eta^2 (\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon}) \right) dx \\
&= \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) dx \\
&\quad + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} 2\eta \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) \nabla \eta dx \\
&:= T_1 + T_2,
\end{aligned} \tag{2.66}$$

and we estimate T_1 exploiting the ellipticity of $\mathbf{M}_{j,\varepsilon}$ given in (2.9):

$$\begin{aligned}
T_1 &= \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \mathbf{M}_{j,\varepsilon} \left(\nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) dx \\
&\quad + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \right) \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} \right) \cdot \left(\nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \nabla u_{j,\varepsilon} \right) dx \\
&\geq 0 - C \sum_{j=i,e} \|\eta^2 (\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon})\|_{L^\infty(\Omega_{j,\varepsilon} \cap K')} \|\nabla u_{j,\varepsilon}\|_{L^2(\Omega_{j,\varepsilon} \cap K')}^2 \\
&\geq -\varepsilon |l| C \sum_{j=i,e} \|\nabla u_{j,\varepsilon}\|_{L^2(\Omega_{j,\varepsilon} \cap K')}^2.
\end{aligned} \tag{2.67}$$

In the last inequality, we used the mean value theorem to obtain:

$$\|\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon}\|_{L^\infty(\Omega_{j,\varepsilon} \cap K')} \leq \varepsilon |l| \sum_{j=i,e} \|\nabla \mathbf{M}_j^\varepsilon\|_{L^\infty(\Omega_{j,\varepsilon} \cap K')} \leq \varepsilon |l| C,$$

for some constant $C > 0$. Moreover, by regularity of η , Cauchy-Schwarz and boundedness of $\mathbf{M}_{j,\varepsilon}$, we get the following estimate on T_2 :

$$|T_2| \leq C \varepsilon |l| \sum_{j=i,e} \|u_{j,\varepsilon}\|_{H^1(\Omega_{j,\varepsilon} \cap K')}, \tag{2.68}$$

for some constant $C > 0$. On the other hand, the third term of (2.65) may be divided into two terms by making use of (2.13b) as follows:

$$\begin{aligned}
& \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon) - I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\
&= \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{1,\text{ion}}(\tau_{\varepsilon l} v_\varepsilon) - I_{1,\text{ion}}(v_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\
&\quad + \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{2,\text{ion}}(\tau_{\varepsilon l} w_\varepsilon) - I_{2,\text{ion}}(w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\
&:= T_3 + T_4.
\end{aligned} \tag{2.69}$$

By monotonicity (2.11), we estimate T_3 :

$$T_3 \geq -\varepsilon L \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2. \tag{2.70}$$

In addition, using the definition of η and the linearity of $I_{2,\text{ion}}$ (2.10), Cauchy-Schwarz and Young's inequalities, T_4 can be estimated by:

$$|T_4| \leq \varepsilon C (\|\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2), \tag{2.71}$$

for some constant $C > 0$. Furthermore, the source term in (2.65) satisfies the following inequality:

$$\left| \int_{\Gamma_\varepsilon \cap K'} (\tau_{\varepsilon l} I_{\text{app}, \varepsilon} - I_{\text{app}, \varepsilon}) \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds(x) \right| \leq C\varepsilon \|I_{\text{app}, \varepsilon}\|_{L^2(\Gamma_\varepsilon)} \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}. \quad (2.72)$$

Gathering all these estimates, one obtains

$$\varepsilon \frac{d}{dt} \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \leq C_1 \varepsilon |l| + C_2 \varepsilon \left(\|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right). \quad (2.73)$$

By a similar argument, one can also obtain from (2.21),

$$\varepsilon \frac{d}{dt} \|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \leq C_3 \varepsilon \left(\|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right). \quad (2.74)$$

By Grönwall’s inequality applied to the sum of (2.73) and (2.74), we obtain

$$\begin{aligned} & \varepsilon \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \varepsilon \|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \\ & \leq e^{C_4 t} \left(C_1 \varepsilon |l| t + \varepsilon \|\eta(\tau_{\varepsilon l} v_{0, \varepsilon} - v_{0, \varepsilon})\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \varepsilon \|\eta(\tau_{\varepsilon l} w_{0, \varepsilon} - w_{0, \varepsilon})\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right) \\ & \leq C(T) \left(\varepsilon |l| + \varepsilon \|\tau_{\varepsilon l} v_{0, \varepsilon} - v_{0, \varepsilon}\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \varepsilon \|\tau_{\varepsilon l} w_{0, \varepsilon} - w_{0, \varepsilon}\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right). \end{aligned}$$

Now using the assumption on $v_{0, \varepsilon}$ and $w_{0, \varepsilon}$, one obtains

$$\varepsilon \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \varepsilon \|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \leq C\varepsilon |l|$$

Furthermore, noting that

$$\|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \geq \|\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon\|_{L^2(\Gamma_\varepsilon \cap K)}^2 + \|\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon\|_{L^2(\Gamma_\varepsilon \cap K)}^2,$$

one can conclude that (2.63) holds. \square

Now, we state and prove the strong convergence of $\mathcal{T}_\varepsilon^b(v_\varepsilon)$ to v .

Lemma 2.6.3. *The following convergence holds:*

$$\mathcal{T}_\varepsilon^b(v_\varepsilon) \rightarrow v \text{ strongly in } L^2(\Omega_T \times \Gamma),$$

as $\varepsilon \rightarrow 0$. Moreover,

$$I_{1, \text{ion}}(\mathcal{T}_\varepsilon^b v_\varepsilon) \rightarrow I_{1, \text{ion}}(v) \text{ strongly in } L^q(\Omega_T \times \Gamma), \text{ for } q \in [1, r/(r-1)),$$

as $\varepsilon \rightarrow 0$

Proof. The proof of the lemma is similar to the proof of Theorem 14 in [GNRK16] but herein the domain is not the union of scaled and translated reference cells.

The proof is based on Proposition 2.6.1.

Condition (iii) follows from estimate (2.51), since

$$\int_{\Omega \setminus \Omega_\delta} |\mathcal{T}_\varepsilon^b(v_\varepsilon)|^2 d\mathbf{x} \leq |\Omega \setminus \Omega_\delta|^{\frac{r-2}{r}} \left(\int_{\Omega} |\mathcal{T}_\varepsilon^b(v_\varepsilon)|^r d\mathbf{x} \right)^{\frac{2}{r}} \leq C |\Omega \setminus \Omega_\delta|^{\frac{r-2}{r}}.$$

To prove condition (i), consider a measurable set $A \subset \Omega$, and define

$$v_A^\varepsilon(t, y) = \int_A \mathcal{T}_\varepsilon^b(v_\varepsilon)(t, x, y) dx, \text{ for a.e. } t \in (0, T), y \in \Gamma.$$

The a priori estimates (2.49), (2.50) and (2.52) obtained on v_ε imply that the sequence v_A^ε is bounded in $L^2((0, T), H^{1/2}(\Gamma)) \cap H^1((0, T), L^2(\Gamma))$. Then by Aubin-Lions Lemma, the sequence is relatively compact in $L^2((0, T), L^2(\Gamma))$. For the sake of completeness, we detail in the following lines how to obtain the estimates on v_A^ε .

First, we have by Cauchy-Schwartz

$$\int_\Gamma (v_A^\varepsilon)^2 ds(y) = \int_\Gamma \left(\int_A \mathcal{T}_\varepsilon^b v_\varepsilon(t, x, y) dx \right)^2 ds(y) \leq \int_\Gamma |A| \|\mathcal{T}_\varepsilon^b v_\varepsilon\|_{L^2(\Omega)}^2 ds(y).$$

Using the properties of the unfolding operator (see Proposition 2.5.3), we get

$$\int_\Gamma (v_A^\varepsilon)^2 ds(y) \leq |A| \int_\Gamma \int_\Omega \mathcal{T}_\varepsilon^b \left((v_\varepsilon)^2 \right) dx ds(y) \leq |A| \varepsilon |Y| \int_{\Gamma_\varepsilon} (v_\varepsilon)^2 ds(x).$$

As a result, we have

$$\int_\Gamma (v_A^\varepsilon)^2 ds(y) \leq |A| |Y| \|\sqrt{\varepsilon} v_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2.$$

Finally, upon integration over $(0, T)$ and using (2.49), we can find a constant $C > 0$ such that

$$\int_0^T \|v_A^\varepsilon\|_{L^2(\Gamma)}^2 \leq C.$$

By a similar argument and making use of the estimate on $\varepsilon^{1/2} \partial_t v_\varepsilon$, one can also show that

$$\|\partial_t v_A^\varepsilon\|_{L^2(\Gamma_T)} \leq C,$$

for some positive constant C .

On the other hand, to obtain a uniform estimate on the $L^2(0, T; H^{1/2}(\Gamma))$, we first observe that

$$\|v_A^\varepsilon\|_{H^{1/2}(\Gamma)}^2 = \|v_A^\varepsilon\|_{L^2(\Gamma)}^2 + |v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2.$$

Based on the previous estimates, we only need to bound the $H_0^{1/2}$ seminorm and this is done as follows. First, we have by Cauchy-Schwarz and Fubini

$$|v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2 \leq |A| \int_{\hat{\Omega}_\varepsilon} \int_\Gamma \int_\Gamma \frac{|v_\varepsilon(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y_1) - v_\varepsilon(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y_2)|^2}{|y_1 - y_2|^3} ds(y_1) ds(y_2) dx.$$

We note that this is equivalent to writing:

$$|v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2 \leq |A| \int_{\hat{\Omega}_\varepsilon} |v_\varepsilon(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon \cdot)|_{H_0^{1/2}(\Gamma)}^2 dx.$$

Since $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_\Gamma$ and using the triangle inequality, we get

$$|v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2 \leq 2|A| \sum_{j=i,e} \int_{\hat{\Omega}_\varepsilon} |u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon \cdot)|_{H_0^{1/2}(\Gamma)}^2 dx.$$

Now, by the trace inequality which can be found in [ADH95], we find a constant $C > 0$ such that

$$|v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2 \leq C|A| \sum_{j=i,e} \int_{\hat{\Omega}_\varepsilon} \left(\|u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon \cdot)\|_{L^2(Y_j)}^2 + \|\nabla_y(u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon \cdot))\|_{L^2(Y_j)}^2 \right) dx.$$

By the chain rule, we have

$$\nabla_y \left(u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y) \right) = \varepsilon \nabla u_{j,\varepsilon} \left(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y \right).$$

So

$$\int_{\hat{\Omega}_\varepsilon} \|\nabla_y(u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y))\|_{L^2(Y_j)}^2 dx = \int_{\hat{\Omega}_\varepsilon} \|\varepsilon \nabla u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y)\|_{L^2(Y_j)}^2 dx,$$

or equivalently

$$\int_{\hat{\Omega}_\varepsilon} \|\nabla_y(u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y))\|_{L^2(Y_j)}^2 dx = \varepsilon^2 \int_{\hat{\Omega}_\varepsilon} \int_{Y_j} \left(\nabla u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y) \right)^2 dy dx.$$

Now, using Proposition 2.5.2-(2), we get

$$\int_{\hat{\Omega}_\varepsilon} \|\nabla_y(u_{j,\varepsilon}(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y))\|_{L^2(Y_j)}^2 dx = \varepsilon^2 |Y| \int_{\hat{\Omega}_{j,\varepsilon}} \left(\nabla u_{j,\varepsilon} \right)^2 dx = \varepsilon^2 |Y| \|\nabla u_{j,\varepsilon}\|_{L^2(\hat{\Omega}_{j,\varepsilon})}^2.$$

One more time, we make use of Proposition 2.5.2-(2) to obtain:

$$\int_{\hat{\Omega}_\varepsilon} \int_{Y_j} u_{j,\varepsilon} \left(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y \right) dy d\mathbf{x} = |Y| \int_{\hat{\Omega}_{j,\varepsilon}} u_{j,\varepsilon}(t, x) d\mathbf{x},$$

and

$$|v_A^\varepsilon|_{H_0^{1/2}(\Gamma)}^2 \leq C \sum_{j=i,e} \left[\|u_j\|_{L^2(\hat{\Omega}_{j,\varepsilon})} + \varepsilon^2 \|\nabla u_{j,\varepsilon}\|_{L^2(\hat{\Omega}_{j,\varepsilon})}^2 \right].$$

Finally, integrating over $(0, T)$ and using the a priori estimates (2.34) on $u_{j,\varepsilon}$, we obtain the required result.

It remains to prove condition (ii) of Proposition 2.6.1 as follows.

Fix $\varepsilon > 0$ and let $I \subset \mathbb{Z}^3$, be an index set such that

$$\hat{\Omega}_\varepsilon = \bigcup_{i \in I} \varepsilon(Y + i).$$

Obviously, we have $x \in \varepsilon(Y + i) \Leftrightarrow [\frac{x}{\varepsilon}] = i$. For every $i \in I$ we divide the cell $\varepsilon(Y + i)$ into subsets $\varepsilon(Y + i)^k$ with $k \in \{0, 1\}^3$, defined as follows

$$\varepsilon(Y + i)^k := \left\{ x \in \varepsilon(Y + i) : \varepsilon \left[\frac{x + \{\frac{\xi}{\varepsilon}\} \varepsilon}{\varepsilon} \right] = \varepsilon(i + k) \right\},$$

for a given $\xi \in \mathbb{R}^3$ such that ξ is $O(\varepsilon)$. Then we have the following identity:

$$\varepsilon(Y + i) = \bigcup_{k \in \{0, 1\}^3} \overline{\varepsilon(Y + i)^k}.$$

Now, we compute

$$\begin{aligned} \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon) - \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times \Omega_\delta^\xi \times \Gamma)}^2 &= \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon) - \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times (\Omega_\delta^\xi \cap \hat{\Omega}_\varepsilon) \times \Gamma)}^2 \\ &\quad + \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon) - \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times (\Omega_\delta^\xi \setminus \hat{\Omega}_\varepsilon) \times \Gamma)}^2 \\ &\leq E_{1,\xi,\varepsilon} + E_{2,\xi,\varepsilon}, \end{aligned}$$

where

$$E_{1,\xi,\varepsilon} := \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon) - \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times \hat{\Omega}_\varepsilon \times \Gamma)}^2,$$

and

$$E_{2,\xi,\varepsilon} := \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon) - \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times (\Omega_\delta^\xi \setminus \hat{\Omega}_\varepsilon) \times \Gamma)}^2 = \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times (\Omega_\delta^\xi \setminus \hat{\Omega}_\varepsilon) \times \Gamma)}^2.$$

We first estimate $E_{1,\xi,\varepsilon}$, making use of the fact that $\hat{\Omega}_\varepsilon = \bigcup_{i \in I} \varepsilon(Y + i)$, and proceeding in a similar way to [Dob15, NRJ07] as follows:

$$\begin{aligned} E_{1,\xi,\varepsilon} &= \sum_{i \in I} \int_0^T \int_{\varepsilon(Y+i)} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon \left[\frac{x + \xi}{\varepsilon} \right] + \varepsilon y\right) - v^\varepsilon\left(t, \varepsilon \left[\frac{x}{\varepsilon} \right] + \varepsilon y\right) \right|^2 ds(y) d\mathbf{x} dt \\ &= \sum_{i \in I} \sum_{k \in \{0,1\}^3} \int_0^T \int_{\varepsilon(Y+i)^k} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon \left(i + k + \left[\frac{\xi}{\varepsilon} \right] \right) + \varepsilon y\right) - v^\varepsilon(t, \varepsilon i + \varepsilon y) \right|^2 ds(y) d\mathbf{x} dt \\ &\leq \sum_{i \in I} \sum_{k \in \{0,1\}^3} \int_0^T \int_{\varepsilon(Y+i)} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon \left(i + k + \left[\frac{\xi}{\varepsilon} \right] \right) + \varepsilon y\right) - v^\varepsilon(t, \varepsilon i + \varepsilon y) \right|^2 ds(y) d\mathbf{x} dt \\ &\leq \sum_{k \in \{0,1\}^3} \int_0^T \int_{\hat{\Omega}_\varepsilon} \int_\Gamma \left| \mathcal{T}_\varepsilon^b v^\varepsilon\left(t, x + \varepsilon \left(k + \left[\frac{\xi}{\varepsilon} \right] \right), y\right) - \mathcal{T}_\varepsilon^b v^\varepsilon(t, x, y) \right|^2 ds(y) d\mathbf{x} dt \\ &\leq \sum_{k \in \{0,1\}^3} \varepsilon \int_0^T \int_{\Gamma_\varepsilon} \left| v^\varepsilon\left(t, x + \varepsilon \left(\left[\frac{\xi}{\varepsilon} \right] + k \right) \right) - v^\varepsilon(t, x) \right|^2 ds(x) dt, \end{aligned}$$

where in the last inequality we used the identity $i = \left[\frac{x}{\varepsilon} \right]$ and the integration formula of Proposition 2.5.3-(3). Moreover, using estimate (2.63), we obtain

$$E_{1,\xi,\varepsilon} \leq C(|\xi| + \varepsilon).$$

Therefore, one can conclude that $E_{1,\xi,\varepsilon} \rightarrow 0$ as $\xi \rightarrow 0$ uniformly in ε , as in [GNRK16]. Indeed, to prove that

$$\forall \rho > 0, \exists \mu > 0 \text{ such that } \forall \varepsilon > 0, \forall \xi, |\xi| \leq \mu \Rightarrow E_1 < \rho,$$

one identifies two cases:

1. $\varepsilon < \frac{\rho}{2C}$: take $\mu = \frac{\rho}{2C}$, then for $\xi < \mu$, $E_1 < \rho$.
2. $\frac{\rho}{2C} < \varepsilon$: since $\varepsilon^{-1} \in \mathbb{N}$ and $\frac{1}{\varepsilon} < \frac{2C}{\rho} \leq \left[\frac{2C}{\rho} \right] + 1$, there are finitely many values ε such that $\varepsilon > \frac{\rho}{2C}$, and for each such ε_i $i = 1, \dots, m$, $\exists \mu_i$ such that $\forall \xi, |\xi| < \mu_i \Rightarrow E_1 < \rho$ by continuity of translation in L^2 . Take $\mu_0 = \min\{\mu, \mu_1, \dots, \mu_m\}$. Then the estimate follows.

Consider now $E_{2,\xi,\varepsilon}$, and note that

$$E_{2,\xi,\varepsilon} \leq \|\tau_\xi \mathcal{T}_\varepsilon^b(v^\varepsilon)\|_{L^2((0,T) \times (\Omega_\delta \setminus \hat{\Omega}_\varepsilon) \times \Gamma)}^2.$$

Observe that, for ε small enough, say $\varepsilon < \varepsilon_0$, $\Omega_\delta \subset \hat{\Omega}_\varepsilon$, so $E_{2,\xi,\varepsilon} = 0$. On the other hand, for $\varepsilon_0 < \varepsilon < 1$, since $\varepsilon^{-1} \in \mathbb{N}$, there exist finitely many $\varepsilon \in (\varepsilon_0, 1)$, say $\{\varepsilon_j\}_{j=1}^m$, $m \in \mathbb{N}$, $m < \infty$. Moreover, by continuity of the translation of L^2 functions, for each $\rho > 0$ there exists for every j , a $\beta(\varepsilon_j)$ such that

$$E_{2,\xi,\varepsilon} < \rho, \quad \forall |\xi| < \beta(\varepsilon_j).$$

Let $\beta = \min\{\beta(\varepsilon_1), \dots, \beta(\varepsilon_m)\}$, then for all $\rho > 0$, $|\xi| < \beta \Rightarrow E_{2,\xi,\varepsilon} < \rho$. Hence, $E_{2,\xi,\varepsilon} \rightarrow 0$ as $\xi \rightarrow 0$, uniformly in ε . This ends the proof of (ii) in Proposition 2.6.1.

The following result is therefore obtained:

$$\mathcal{T}_\varepsilon^b(v_\varepsilon) \rightarrow v \text{ strongly in } L^2(\Omega_T \times \Gamma),$$

as $\varepsilon \rightarrow 0$.

Finally, to prove the convergence of the nonlinear term in the ionic function, first note that from the structure of $I_{1,\text{ion}}$ and using the properties of the boundary unfolding operator, there holds

$$\mathcal{T}_\varepsilon^b(I_{1,\text{ion}}(v_\varepsilon)) = I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon)),$$

then using the estimate

$$\|\varepsilon^{(r-1)/r} I_{1,\text{ion}}(v_\varepsilon)\|_{L^{r/(r-1)}(\Gamma_{\varepsilon,T})} \leq C,$$

one obtains

$$\|\mathcal{T}_\varepsilon^b(I_{1,\text{ion}}(v_\varepsilon))\|_{L^{r/(r-1)}(\Omega_T \times \Gamma)} \leq |Y|^{(r-1)/r} \|\varepsilon^{(r-1)/r} I_{1,\text{ion}}(v_\varepsilon)\|_{L^{r/(r-1)}(\Gamma_{\varepsilon,T})} \leq C.$$

Hence, since up to a subsequence

$$\mathcal{T}_\varepsilon^b(v_\varepsilon) \rightarrow v \text{ a.e. in } \Omega_T \times \Gamma,$$

one gets, using the continuity of $I_{1,\text{ion}}$ and a classical result (see Lemma 1.3 in [Lio69]),

$$I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon)) \rightharpoonup I_{1,\text{ion}}(v) \text{ weakly in } L^{r/(r-1)}(\Omega_T \times \Gamma).$$

Moreover, using Vitali's theorem, one has the strong convergence of $I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon))$ to $I_{1,\text{ion}}(v)$ in $L^q(\Omega_T \times \Gamma)$ for $q \in [1, r/(r-1))$. □

Collecting all the convergence results stated above, one obtains the following limiting problem:

$$\begin{aligned} & |\Gamma| \iint_{\Omega_T} \partial_t v \Psi \, d\mathbf{x} \, dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j[\nabla u_j + \nabla_\xi \hat{u}_j][\nabla \Psi_j + \theta_j \nabla_\xi \psi_j] \\ & + |\Gamma| \iint_{\Omega_T} I_{2,\text{ion}}(w) \Psi \, d\mathbf{x} \, dt + |\Gamma| \iint_{\Omega_T} I_{1,\text{ion}}(v) \Psi \, d\mathbf{x} \, dt \\ & = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi \, d\mathbf{x} \, dt. \end{aligned} \tag{2.75}$$

Similarly, one can easily show that the limit of (2.61) as ε tends to 0, is given by

$$|\Gamma| \iint_{\Omega_T} \partial_t w \phi \, d\mathbf{x} \, dt - |\Gamma| \iint_{\Omega_T} H(v, w) \phi \, d\mathbf{x} \, dt = 0. \tag{2.76}$$

2.7 Macroscopic bidomain model

The next step is to obtain the weak formulation of the bidomain equations and the cell problem. So one needs to formulate the limit problem in terms of u_i and u_e alone and hence find an expression of \hat{u}_i and \hat{u}_e in terms of u_i , u_e respectively. First, to determine the cell problem, set in (2.75) Ψ_i, Ψ_e and θ_e to 0, to get

$$\iiint_{\Omega_T \times Y_i} \mathbf{M}_i[\nabla u_i + \nabla_y \hat{u}_i][\theta_i \nabla_y \psi_i] dy d\mathbf{x} dt = 0,$$

which corresponds to the classical cell problem obtained in section 2 and it can be shown that the function \hat{u}_i can be written in terms of u_i as follows (\hat{u}_i is defined up to an additive function in x , see for instance [CDD⁺12]):

$$\hat{u}_i(t, x, y) = f_i(t, x, y) \cdot \nabla_x u_i + f_{0,i}(t, x) = \sum_{k=1}^3 \frac{\partial u_i}{\partial x_k} f_{k,i}(t, x, y) + f_{0,i}(t, x), \quad (2.77)$$

where the corrector functions (i.e. the components of the function f_i) $f_{k,i} \in L^\infty(\Omega_T; H_{per}^1(Y_i))$, $k = 1, 2, 3$, are for a.e. $(t, x) \in \Omega_T$ the solutions of the cell problems

$$\begin{cases} -\nabla_y \cdot (\mathbf{M}_i \nabla_y f_{k,i}) = -\nabla_y \cdot (\mathbf{M}_i e_k) & \text{in } Y_i, \\ \mathbf{M}_i \nabla_y f_{k,i} \cdot \mu_i = \mathbf{M}_i e_k \cdot \mu_i & \text{on } \Gamma, \\ \int_{Y_i} f_{k,i} = 0, & f_{k,i} \text{ } Y \text{-periodic.} \end{cases} \quad (2.78)$$

The existence and uniqueness of the correctors follow by classical arguments from Lax-Milgram theorem (see for instance the remark on p. 13-14 of [BLP11] or [OSY09]). Finally, inserting formula (2.77) into (2.75) and setting θ_i, Ψ_e and θ_e to 0, one obtains the weak formulation of the macroscopic bidomain model

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi_i d\mathbf{x} dt + \iint_{\Omega_T} \mathcal{M}_i \nabla u_i \cdot \nabla \Psi_i + |\Gamma| \iint_{\Omega_T} I_{2,\text{ion}}(w) \Psi_i d\mathbf{x} dt \\ + |\Gamma| \iint_{\Omega_T} I_{1,\text{ion}}(v) \Psi_i d\mathbf{x} dt = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi_i d\mathbf{x} dt, \end{aligned} \quad (2.79)$$

where \mathcal{M}_i is elliptic and defined by

$$\mathcal{M}_i := \int_{Y_i} \left(\mathbf{M}_i + \mathbf{M}_i \nabla_y f_i \right).$$

Similarly, one can decouple the cell problem in the extracellular domain and define the homogenized conductivity matrix \mathcal{M}_e .

Remark 5. *Since the convergence obtained herein is shown up to a subsequence, it is required to prove uniqueness of the macroscopic problem to guarantee the convergence of the whole sequence. Indeed, uniqueness of the macroscopic bidomain model has been obtained for several ionic models, we refer for instance to [BK06, BCP09] for the case of phenomenological models of FitzHugh-Nagumo type and to [Ven09] for physiological models of Luo-Rudy type.*

2.8 Unfolding homogenization to physiological models

In this section, we extend the homogenization results obtained in the previous sections to physiological ionic models. So the ordinary differential equation (2.6d) is replaced by a system of ODEs for the gating variables w_l , $l = 1, \dots, k$ and the concentration variable z .

The kinetics of a general physiological ionic model may be represented by the functions \mathbf{R} , G and I_{ion} that satisfy assumptions (A.1)-(A.3), stated below. It can be verified that those assumptions are satisfied by the gating and ionic concentration variables in Beeler-Reuter or Luo-Rudy ionic models [Ven09, BR77, LR94].

(A.1) Define the function \mathbf{R} as $\mathbf{R}(v, \mathbf{w}) := (R_1(v, w_1), \dots, R_k(v, w_k))$ where $R_l : \mathbb{R}^2 \rightarrow \mathbb{R}$ are globally Lipschitz continuous functions given by

$$R_l(v, \mathbf{w}) = \alpha_l(v)(1 - w_l) - \beta_l(v)w_l \quad (2.80)$$

where α_l and β_l , $l = 1, \dots, k$ are positive rational functions of exponentials in v such that:

$$0 < \alpha_l(v), \beta_l(v) \leq C_{\alpha, \beta}(1 + |v|). \quad (2.81)$$

(A.2) The function $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty) \rightarrow \mathbb{R}$ has the general form:

$$I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{l=1}^k I_{\text{ion}}^l(v, w_l) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \quad (2.82)$$

where $I_{\text{ion}}^l \in C^0(\mathbb{R} \times \mathbb{R}) \cap \text{Lip}(\mathbb{R} \times [0, 1])$ and satisfies the condition:

$$|I_{\text{ion}}^l(v, w_l)| \leq C_{1,I}(1 + |w_l| + |v|), \quad (2.83)$$

and I_{ion}^z is such that:

$$I_{\text{ion}}^z \in C^1(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}^+ \times \mathbb{R}) \cap \text{Lip}(\mathbb{R} \times [0, 1]^k \times \mathbb{R}^+ \times \mathbb{R}),$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \leq C_{2,I}(1 + |v| + |w| + |z| + |\ln z|), \quad (2.84)$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3,I} \sum_{l=1}^k (|v| + w_l + w_l \ln z), \quad (2.85)$$

$$0 < \underline{\Theta}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(\mathbf{w}), \quad (2.86)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \right| \leq L(\mathbf{w}), \quad (2.87)$$

$$\frac{\partial}{\partial w_l} I_{\text{ion}}^z \leq C_{4,I}(1 + |v| + |\ln z|), \quad \forall l = 1, \dots, k, \quad (2.88)$$

$$0 \leq \frac{\partial}{\partial z} I_{\text{ion}}^z \leq C_{5,I}, \quad (2.89)$$

where $\underline{\Theta}$, $\bar{\Theta}$, L belong to $C^0(\mathbb{R}, \mathbb{R}^+)$ and $C_{1,I}, \dots, C_{5,I}$ are positive constants.

(A.3) The function $G \in \text{Lip}(\mathbb{R} \times [0, 1]^k \times \mathbb{R}^+)$ is given by:

$$G(v, \mathbf{w}, z) = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z), \quad (2.90)$$

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.

Under those assumptions, the microscopic system that we consider is given by:

$$-\nabla \cdot (\mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon}) = 0 \text{ in } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \quad j \in \{i, e\}, \quad (2.91a)$$

$$\varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m \text{ on } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \quad (2.91b)$$

$$\mathcal{I}_m = -\mathbf{M}_{i,\varepsilon} \nabla u_{i,\varepsilon} \cdot \mu_i = \mathbf{M}_{e,\varepsilon} \nabla u_{e,\varepsilon} \cdot \mu_e \text{ on } \Gamma_{\varepsilon,T}, \quad (2.91c)$$

$$\partial_t \mathbf{w}_\varepsilon - \mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}, \quad (2.91d)$$

$$\partial_t z_\varepsilon - G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}. \quad (2.91e)$$

We augment (2.91) with no-flux boundary conditions

$$(\mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon}) \cdot \mu_j = 0 \text{ on } (0, T) \times (\partial \Omega_{j,\varepsilon} \setminus \Gamma_\varepsilon), \quad j \in \{e, i\}, \quad (2.92)$$

and appropriate initial conditions for the transmembrane potential, the gating variables and the concentration variable

$$v_\varepsilon(0, \cdot) = v_{0,\varepsilon}(\cdot), \quad \mathbf{w}_\varepsilon(0, \cdot) = \mathbf{w}_{0,\varepsilon}(\cdot), \quad z_\varepsilon(0, \cdot) = z_{0,\varepsilon}(\cdot) \text{ on } \Gamma_\varepsilon, \quad (2.93)$$

where $v_{0,\varepsilon} \in H^{1/2}(\Gamma_\varepsilon)$, $z_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)$ and $\mathbf{w}_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)^k$ with $z_{0,\varepsilon} > c_0 > 0$ for some $c_0 > 0$ and $0 \leq w_{l,0,\varepsilon} \leq 1$ for $l = 1, \dots, k$.

Analogously to the microscopic model with more general FitzHugh-Nagumo dynamics, one has the following existence result.

Theorem 2.8.1. *Suppose that assumptions (A.1)-(A.3) hold. If $v_{0,\varepsilon} \in H^{1/2}(\Gamma_\varepsilon)$, $z_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)$ and $\mathbf{w}_{0,\varepsilon} \in L^2(\Gamma_\varepsilon)^k$ with $z_{0,\varepsilon} > c_0 > 0$ for some $c_0 > 0$ and $0 \leq w_{l,0,\varepsilon} \leq 1$ for $l = 1, \dots, k$, then the microscopic problem (2.91),(2.92),(2.93) possesses a weak solution defined as follows: $u_{i,\varepsilon} \in L^2(0, T; H^1(\Omega_{i,\varepsilon}))$, $u_{e,\varepsilon} \in L^2(0, T; H^1(\Omega_{e,\varepsilon}))$, with $\int_{\Omega_{e,\varepsilon} \cap \Omega} u_{e,\varepsilon} = 0$, $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})|_{\Gamma_\varepsilon} \in L^2(\Gamma_{\varepsilon,T})$, $\mathbf{w}_\varepsilon \in (L^2(\Gamma_{\varepsilon,T}))^k$, $z_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, $\partial_t v_\varepsilon, \partial_t z_\varepsilon \in L^2(\Gamma_{\varepsilon,T})$, and $\partial_t \mathbf{w}_\varepsilon \in (L^2(\Gamma_{\varepsilon,T}))^k$ such that*

$$\begin{aligned} \iint_{\Gamma_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, d\mathbf{x} \, dt \\ + \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \varphi \, ds(x) \, dt = \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt, \end{aligned} \quad (2.94)$$

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t w_{l,\varepsilon} \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} R_l(v_\varepsilon, \mathbf{w}_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (2.95)$$

for $l = 1, \dots, k$ and

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t z_\varepsilon \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (2.96)$$

for all $\varphi_j \in L^2(0, T; H^1(\Omega_{j,\varepsilon}))$ with $\varphi := (\varphi_i - \varphi_e)|_{\Gamma_\varepsilon} \in L^2(0, T; H^{1/2}(\Gamma_\varepsilon))$ for $j = i, e$ and $\phi \in L^2(\Gamma_{\varepsilon,T})$.

The proof of the theorem follows closely the steps done in the case above of more general FitzHugh-Nagumo ionic function type. Using approximation systems and applying a Faedo-Galerkin method in space, one can obtain the existence of a weak solution for the approximation systems (as in Section 2.4) then by a passage to the limit, the existence for the microscopic problem is obtained based on some technical results and a series of a priori estimates that are listed in the sequel but their detailed proofs are similar to those obtained in Chapter 4 for the electromechanical problem. We also refer to [Ven06] where a fixed point approach was used. First, the recovery variables are shown to satisfy the physiological bounds.

Lemma 2.8.2. *Let $w_{l,\varepsilon} \in C([0, T], L^2(\Gamma_\varepsilon))$ and $v_\varepsilon \in H^1(0, T, L^2(\Gamma_\varepsilon))$ such that for all $\omega \in L^2(\Gamma_\varepsilon)$:*

$$\int_{\Gamma_\varepsilon} \partial_t w_{l,\varepsilon} \omega = \int_{\Gamma_\varepsilon} R_l(v_\varepsilon, w_{l,\varepsilon}) \omega, \quad (2.97)$$

where $\mathbf{R}(v, \mathbf{w})$ is defined by (2.80). Assume that $0 \leq w_{l,0,\varepsilon} \leq 1$ a.e. in Γ_ε , then

$$0 \leq w_{l,\varepsilon} \leq 1, \quad \text{a.e. in } \Gamma_{\varepsilon,T}. \quad (2.98)$$

Secondly, one has to make sure that the concentration variable stays positive.

Lemma 2.8.3. *Let $z_\varepsilon \in C([0, T], L^2(\Gamma_\varepsilon))$, $v_\varepsilon \in H^1(0, T, L^2(\Gamma_\varepsilon))$ and $\mathbf{w}_\varepsilon \in C([0, T], L^2(\Gamma_\varepsilon)^k)$ such that for all $\omega \in L^2(\Gamma_\varepsilon)$:*

$$\int_{\Gamma_\varepsilon} \partial_t z_\varepsilon \omega = \int_{\Gamma_\varepsilon} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \omega, \quad (2.99)$$

where $G(v, \mathbf{w}, z)$ satisfies assumption (A.6) above. Let $z_{0,\varepsilon} : \Omega \rightarrow (0, +\infty)$ be such that:

$$z_{0,\varepsilon} \in L^2(\Gamma_\varepsilon), \quad z_{0,\varepsilon} > 0, \quad \text{a.e. in } \Gamma_\varepsilon.$$

Then for a.e. $(t, \mathbf{x}) \in [0, T] \times \Gamma_\varepsilon$, $z_\varepsilon > 0$.

Thirdly, the concentration variable and its logarithm $\ln z_\varepsilon$ are proved to be controlled by the norm of v_ε in the following sense.

Lemma 2.8.4. *Under the same assumptions as Lemma 2.8.3, the concentration variable z_ε satisfies the following estimates for a.e. $\mathbf{x} \in \Gamma_\varepsilon$, $t \in (0, T)$:*

$$|z_\varepsilon(t, \mathbf{x})| \leq C(1 + |z_{0,\varepsilon}(\mathbf{x})| + \|v_\varepsilon(\mathbf{x})\|_{L^2(0,t)}), \quad \forall t \in [0, T], \quad (2.100)$$

$$|\ln z_\varepsilon(t, \mathbf{x})| \leq C(1 + |z_{0,\varepsilon}(\mathbf{x})| + |v_\varepsilon(t, \mathbf{x})| + \|v_\varepsilon(\mathbf{x})\|_{L^2(0,t)}) \quad (2.101)$$

$$\int_0^t |\partial_s z_\varepsilon|^2 \leq C \left(1 + |z_{0,\varepsilon} \ln z_{0,\varepsilon}| + |z_{0,\varepsilon}|^2 + \|v_\varepsilon\|_{L^2(0,t)}^2 \right), \quad (2.102)$$

$$\int_0^t |\ln z_\varepsilon|^2 \leq C \left(1 + |z_{0,\varepsilon} \ln z_{0,\varepsilon}| + |z_{0,\varepsilon}|^2 + \|v_\varepsilon\|_{L^2(0,t)}^2 \right), \quad (2.103)$$

Using the above estimates on z_ε and \mathbf{w}_ε , one can control the L^2 norm of I_{ion} by the L^2 norm of v_ε and this result will be later used to reach a uniform in ε estimate on v_ε .

Lemma 2.8.5. *Under the same conditions of Lemma 2.8.4, there exists a constant $C > 0$ (dependent on T) such that*

$$\|I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C(1 + \|v_\varepsilon\|_{L^2(\Gamma_{\varepsilon,T})}^2). \quad (2.104)$$

Based on the previous Lemmata, and proceeding in a similar way as in Section 2.5, one can easily obtain the following estimates on the solutions to the microscopic problem that are required for the passage to the limit as $\varepsilon \rightarrow 0$ (the detailed derivation can be found in [BMST19]).

Lemma 2.8.6. *There exist constants \mathcal{C}_1 , \mathcal{C}_2 and \mathcal{C}_3 independent of ε such that*

$$\max_{t \in [0, T]} \left(\|\sqrt{\varepsilon} v_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 + \|\sqrt{\varepsilon} w_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 + \|\sqrt{\varepsilon} z_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 \right) \leq \mathcal{C}_1, \quad (2.105)$$

$$\sum_{j=i,e} \|u_{j,\varepsilon}\|_{L^2(0, T; H^1(\Omega_{j,\varepsilon}))} \leq \mathcal{C}_2, \quad (2.106)$$

$$\|\sqrt{\varepsilon} \partial_t v_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})} + \|\sqrt{\varepsilon} \partial_t w_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})^k} + \|\sqrt{\varepsilon} \partial_t z_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})} \leq \mathcal{C}_3, \quad (2.107)$$

In order to exploit the unfolding method, the weak formulation is written in its “unfolded” form as in Section 2.5.2 above. Equation (2.94) becomes:

$$\begin{aligned} & \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt + \sum_{i,e} \iint \iint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) dy d\mathbf{x} dt \\ & + \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt \\ & = \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app}, \varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt + r_{10}, \end{aligned} \quad (2.108)$$

where r_{10} is considered as a remainder term which involves integrals over the region Λ_ε whose measure tends to zero as $\varepsilon \rightarrow 0$. Similarly, the “unfolded” formulations of (2.95) and (2.96) are given by:

$$\begin{aligned} & \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t w_{l,\varepsilon}) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt - \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(R_l(v_\varepsilon, \mathbf{w}_\varepsilon)) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt \\ & = r_{11}, \end{aligned} \quad (2.109)$$

for $l = 1, \dots, k$ and

$$\begin{aligned} & \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t z_\varepsilon) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt - \iint \iint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)) \mathcal{T}_\varepsilon^b(\phi) ds(y) d\mathbf{x} dt \\ & = r_{12}, \end{aligned} \quad (2.110)$$

where r_{11} and r_{12} are remainder terms that tend to zero as $\varepsilon \rightarrow 0$.

Now, making use of Lemma 2.8.6, one can repeat the arguments from Section 2.6 to show that there exist $u_j \in L^2(0, T; H^1(\Omega))$ and $\hat{u}_j \in L^2(0, T; L^2(\Omega, H_{per}^1(Y_j)))$ such that, up to a subsequence, the following hold

$$\begin{cases} \mathcal{T}_\varepsilon^j(u_j^\varepsilon) \rightharpoonup u_j \text{ weakly in } L^2(0, T; L^2(\Omega, H^1(Y_j))), \\ \mathcal{T}_\varepsilon^j(\nabla u_j^\varepsilon) \rightharpoonup \nabla u_j + \nabla_y \hat{u}_j \text{ weakly in } L^2(\Omega_T \times Y_j). \end{cases}$$

Thus, one obtains

$$\begin{aligned} & \sum_{i,e} \iint \iint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla u_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) \\ & \rightarrow \sum_{i,e} \iint \iint_{\Omega_T \times Y_j} \mathbf{M}_j(\nabla u_j + \nabla_y \hat{u}_j) (\nabla \Psi_j + \theta_j \nabla_y \psi_j(y)) \text{ as } \varepsilon \rightarrow 0. \end{aligned}$$

Furthermore, one can also show that

$$\|\mathcal{T}_\varepsilon^b(v_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} + \|\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)^k} + \|\mathcal{T}_\varepsilon^b(z_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq C,$$

then up to a subsequence

$$\begin{aligned} \mathcal{T}_\varepsilon^b v_\varepsilon &\rightharpoonup v \text{ in } L^2(\Omega_T \times \Gamma), \\ \mathcal{T}_\varepsilon^b \mathbf{w}_\varepsilon &\rightharpoonup \mathbf{w} \text{ in } L^2(\Omega_T \times \Gamma)^k, \\ \mathcal{T}_\varepsilon^b z_\varepsilon &\rightharpoonup z \text{ in } L^2(\Omega_T \times \Gamma). \end{aligned}$$

Also, note that due to the a priori estimates on the time derivatives (Lemma 2.8.6), there exists a constant $C > 0$ such that

$$\|\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} + \|\mathcal{T}_\varepsilon^b(\partial_t \mathbf{w}_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)^k} + \|\mathcal{T}_\varepsilon^b(\partial_t z_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq C,$$

consequently one can show as in section 2.6, that

$$\begin{aligned} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) &\rightharpoonup \partial_t v, \text{ in } L^2(\Omega_T \times \Gamma), \\ \mathcal{T}_\varepsilon^b(\partial_t \mathbf{w}_\varepsilon) &\rightharpoonup \partial_t \mathbf{w} \text{ in } L^2(\Omega_T \times \Gamma)^k, \\ \mathcal{T}_\varepsilon^b(\partial_t z_\varepsilon) &\rightharpoonup \partial_t z \text{ in } L^2(\Omega_T \times \Gamma). \end{aligned}$$

Similarly, exploiting assumption (2.14) on the source term $I_{\text{app},\varepsilon}$, one obtains

$$\iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) d\mathbf{x} dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{\text{app}} \Psi ds(y) d\mathbf{x} dt.$$

It remains to establish the passage to the limit in the nonlinear terms involving the ionic function I_{ion} and the functions \mathbf{R} and G appearing in the ODE system. Indeed, making use of assumptions (A.1)-(A.3), of Lemma 2.8.5 and of Lemma 2.8.6, there exists a constant $C > 0$ such that

$$\left\| \varepsilon^{1/2} I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right\|_{L^2(\Gamma_{\varepsilon,T})} + \left\| \varepsilon^{1/2} \mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) \right\|_{L^2(\Gamma_{\varepsilon,T})^k} + \left\| \varepsilon^{1/2} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right\|_{L^2(\Gamma_{\varepsilon,T})} \leq C.$$

Consequently,

$$\left\| \mathcal{T}_\varepsilon^b \left(I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right) \right\|_{L^2(\Omega_T \times \Gamma)} + \left\| \mathcal{T}_\varepsilon^b \left(\mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) \right) \right\|_{L^2(\Omega_T \times \Gamma)^k} + \left\| \mathcal{T}_\varepsilon^b \left(G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right) \right\|_{L^2(\Omega_T \times \Gamma)} \leq C.$$

Moreover, based on Definition 2.59 of the boundary unfolding operator, one can do the following identifications for a.e. $(t, x, y) \in \hat{\Omega}_{\varepsilon,T} \times \Gamma$:

$$\begin{aligned} \mathcal{T}_\varepsilon^b \left(I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right) &= I_{\text{ion}} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right), \\ \mathcal{T}_\varepsilon^b \left(\mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) \right) &= \mathbf{R} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \right), \\ \text{and } \mathcal{T}_\varepsilon^b \left(G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \right) &= G \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right). \end{aligned}$$

Hence, there exist functions \tilde{I}_{ion} , $\tilde{\mathbf{R}}$ and \tilde{G} such that up to a subsequence, the following convergences hold

$$\begin{aligned} I_{\text{ion}} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right) &\rightharpoonup \tilde{I}_{\text{ion}}, \text{ weakly in } L^2(\Omega_T \times \Gamma), \\ \mathbf{R} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \right) &\rightharpoonup \tilde{\mathbf{R}}, \text{ weakly in } L^2(\Omega_T \times \Gamma)^k, \\ \text{and } G \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right) &\rightharpoonup \tilde{G}, \text{ weakly in } L^2(\Omega_T \times \Gamma). \end{aligned}$$

Therefore, to end the passage to the limit, it remains to relate the functions \tilde{I}_{ion} , $\tilde{\mathbf{R}}$, and \tilde{G} to $I_{\text{ion}}(v, \mathbf{w}, z)$, $\mathbf{R}(v, \mathbf{w})$ and $G(v, \mathbf{w}, z)$ where v , \mathbf{w} and z are the respective limits of $\mathcal{T}_\varepsilon^b(v_\varepsilon)$, $\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)$ and $\mathcal{T}_\varepsilon^b(z_\varepsilon)$. This is done in the following proposition.

Remark 6. *One possibility is to proceed analogously to Section 2.6 and prove the strong convergence of $\mathcal{T}_\varepsilon^b(v_\varepsilon)$, $\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)$ and $\mathcal{T}_\varepsilon^b(z_\varepsilon)$. This can be done exactly as in Section 2.6 for $\mathcal{T}_\varepsilon^b(v_\varepsilon)$. However, it seems out of reach to prove the strong convergence of $\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)$ and $\mathcal{T}_\varepsilon^b(z_\varepsilon)$ by a similar argument.*

Proposition 2.8.7. *Suppose that assumptions (A.1)-(A.3) are satisfied and let v_ε , $u_{j,\varepsilon}$, $j = i, e$, \mathbf{w}_ε and z_ε be weak solutions of the microscopic system (2.94)-(2.96) as given in Theorem 2.8.1. Then there holds*

$$\begin{cases} \tilde{I}_{\text{ion}} &= I_{\text{ion}}(v, \mathbf{w}, z), \\ \tilde{\mathbf{R}} &= \mathbf{R}(v, \mathbf{w}) \\ \tilde{G} &= G(v, \mathbf{w}, z), \end{cases}$$

where v , \mathbf{w} , z , \tilde{I}_{ion} , $\tilde{\mathbf{R}}$ and \tilde{G} are the limits of $\mathcal{T}_\varepsilon^b(v_\varepsilon)$, $\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)$, $\mathcal{T}_\varepsilon^b(z_\varepsilon)$, $\mathcal{T}_\varepsilon^b(I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon))$, $\mathcal{T}_\varepsilon^b(\mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon))$ and $\mathcal{T}_\varepsilon^b(G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon))$ respectively.

Proof. Due to assumptions (A.1)- (A.3), in particular the Lipschitz conditions, one can prove that there exists $K_I > 0$ such that

$$\begin{aligned} &(I_{\text{ion}}(v_1, \mathbf{w}_1, z_1) - I_{\text{ion}}(v_2, \mathbf{w}_2, z_2))(v_1 - v_2) - (\mathbf{R}(v_1, \mathbf{w}_1) - \mathbf{R}(v_2, \mathbf{w}_2)) \cdot (\mathbf{w}_1 - \mathbf{w}_2) \\ &- ((G(v_1, \mathbf{w}_1, z_1) - G(v_2, \mathbf{w}_2, z_2))(z_1 - z_2) \geq -K_I(|v_1 - v_2|^2 + |\mathbf{w}_1 - \mathbf{w}_2|^2 + |z_1 - z_2|^2). \end{aligned} \quad (2.111)$$

To obtain the result, we proceed as in [All92, CI18] for 2-scale convergence in nonlinear terms. Using the formulation of the unfolded equations (2.108)-(2.110) with test functions $e^{-\lambda s} u_{j,\varepsilon}$, $e^{-\lambda s} \mathbf{w}_\varepsilon$ and $e^{-\lambda s} z_\varepsilon$ respectively, then integrating by parts in time and adding the resulting equations one has

$$\begin{aligned} &\frac{1}{2} e^{-\lambda t} \|\mathcal{T}_\varepsilon^b(v_\varepsilon)\|_{L^2}^2 + \frac{1}{2} e^{-\lambda t} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon})\|_{L^2}^2 + \frac{1}{2} e^{-\lambda t} \|\mathcal{T}_\varepsilon^b(z_\varepsilon)\|_{L^2}^2 - \frac{1}{2} e^{-\lambda t} \|\mathcal{T}_\varepsilon^b(v_{\varepsilon,0})\|_{L^2}^2 \\ &- \frac{1}{2} e^{-\lambda t} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon,0})\|_{L^2}^2 - \frac{1}{2} e^{-\lambda t} \|\mathcal{T}_\varepsilon^b(z_{\varepsilon,0})\|_{L^2}^2 \\ &+ \sum_{i,e} \int_0^t e^{-\lambda s} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \cdot \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \, dy \, d\mathbf{x} \, ds \\ &+ \int_0^t e^{-\lambda s} \left[\iint_{\Omega \times \Gamma} I_{\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(v_\varepsilon) \, ds(y) \, d\mathbf{x} + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(v_\varepsilon)\|_{L^2}^2 \right] ds \\ &+ \int_0^t e^{-\lambda s} \left[\iint_{\Omega \times \Gamma} -\mathbf{R}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)) \cdot \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \, ds(y) \, d\mathbf{x} + \frac{\lambda}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon})\|_{L^2}^2 \right] ds \\ &+ \int_0^t e^{-\lambda s} \left[\iint_{\Omega \times \Gamma} -G(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(z_\varepsilon) \, ds(y) \, d\mathbf{x} + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(z_\varepsilon)\|_{L^2}^2 \right] ds \\ &= \int_0^t e^{-\lambda s} \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(v_\varepsilon) \, ds(y) \, d\mathbf{x} \, ds + \int_0^t e^{-\lambda s} (r_{10} + r_{11} + r_{12}) \, ds. \end{aligned} \quad (2.112)$$

By (2.111), observe that one can take λ large enough so that the following inequality holds

$$\begin{aligned}
& \frac{1}{2}e^{-\lambda T} \|\mathcal{T}_\varepsilon^b(v_\varepsilon) - \mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 + \frac{1}{2}e^{-\lambda T} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon}) - \mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 \\
& + \frac{1}{2}e^{-\lambda T} \|\mathcal{T}_\varepsilon^b(z_\varepsilon) - \mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \\
& + \sum_{i,\varepsilon} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon} - \nabla \varphi_{j,\varepsilon}) \cdot \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon} - \nabla \varphi_{j,\varepsilon}) dy d\mathbf{x} dt \\
& + \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} (I_{\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) - I_{\text{ion}}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon))) \right. \\
& \quad \left. (\mathcal{T}_\varepsilon^b(v_\varepsilon) - \mathcal{T}_\varepsilon^b(\varphi_\varepsilon)) ds(y) d\mathbf{x} + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(v_\varepsilon) - \mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 \right] dt \\
& + \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} -(\mathbf{R}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)) - \mathbf{R}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon))) \right. \\
& \quad \left. \cdot (\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) - \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) ds(y) d\mathbf{x} + \frac{\lambda}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon}) - \mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 \right] dt \\
& + \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} -(G(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) - G(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon))) \right. \\
& \quad \left. (\mathcal{T}_\varepsilon^b(z_\varepsilon) - \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) ds(y) d\mathbf{x} + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(z_\varepsilon) - \mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \right] dt \geq 0
\end{aligned} \tag{2.113}$$

We want to use (2.112) to simplify the previous inequality. We introduce the following notation:

$$\begin{aligned}
A^\varepsilon & := \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(v_\varepsilon) ds(y) d\mathbf{x} dt + \frac{1}{2} \|\mathcal{T}_\varepsilon^b(v_{\varepsilon,0})\|_{L^2}^2 + \frac{1}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon,0})\|_{L^2}^2 \\
& \quad + \frac{1}{2} \|\mathcal{T}_\varepsilon^b(z_{\varepsilon,0})\|_{L^2}^2 + \int_0^T e^{-\lambda t} (r_{10} + r_{11} + r_{12}) dt, \\
D^\varepsilon & := \frac{1}{2} e^{-\lambda T} \iint_{\Omega \times \Gamma} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) + \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) + \mathcal{T}_\varepsilon^b(z_\varepsilon) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) \right) ds(y) d\mathbf{x} \\
& \quad + \sum_{i,\varepsilon} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla(u_{j,\varepsilon})) \cdot \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) dy d\mathbf{x} dt, \\
E^\varepsilon & := \frac{1}{2} e^{-\lambda T} \left(\|\mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 + \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 + \|\mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \right) \\
& \quad + \sum_{i,\varepsilon} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) \cdot \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) dy d\mathbf{x} dt \\
I^\varepsilon & := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} \left(-I_{\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) \right. \right. \\
& \quad \left. \left. - I_{\text{ion}}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) (\mathcal{T}_\varepsilon^b(v_\varepsilon) - \mathcal{T}_\varepsilon^b(\varphi_\varepsilon)) - \lambda \mathcal{T}_\varepsilon^b(v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) \right) ds(y) d\mathbf{x} \right. \\
& \quad \left. + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 \right] dt,
\end{aligned}$$

$$R^\varepsilon := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} \left(\mathbf{R}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) + \mathbf{R}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) \right. \right. \\ \left. \left. \cdot (\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) - \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) - \lambda \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) \right) ds(y) d\mathbf{x} + \frac{\lambda}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 \right] dt,$$

and

$$G^\varepsilon := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} G(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) + G(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) \right. \\ \left. (\mathcal{T}_\varepsilon^b(z_\varepsilon) - \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) - \mathcal{T}_\varepsilon^b(z_\varepsilon) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) ds(y) d\mathbf{x} + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \right] dt.$$

Substituting (2.112) into (2.113), we obtain

$$A^\varepsilon - 2D^\varepsilon + E^\varepsilon + I^\varepsilon + R^\varepsilon + G^\varepsilon \geq 0. \quad (2.114)$$

Now, we set for any positive scalar τ , the following test functions

$$\psi_{l,\varepsilon}(t, x) = \psi_{l,0}(t, x, \frac{x}{\varepsilon}) + \tau \psi_l(t, x, \frac{x}{\varepsilon}), \quad \theta_\varepsilon(t, x) = \theta_0(t, x, \frac{x}{\varepsilon}) + \tau \theta(t, x, \frac{x}{\varepsilon}), \\ \varphi_j^\varepsilon(t, x) = \varphi_j^0(t, x) + \varepsilon \varphi_j^1(t, x, \frac{x}{\varepsilon}) + \tau \varphi_j(t, x), \quad \varphi^\varepsilon = (\varphi_i^\varepsilon - \varphi_e^\varepsilon)|_{\Gamma_\varepsilon}.$$

Note that the following convergence results hold strongly in $L^2(\Omega_T \times \Gamma)$:

$$\mathcal{T}_\varepsilon^b(\psi_{l,0}) \rightarrow \psi_{l,0}, \quad \mathcal{T}_\varepsilon^b(\psi_l) \rightarrow \psi_l, \quad \mathcal{T}_\varepsilon^b(\theta_0) \rightarrow \theta_0, \quad \mathcal{T}_\varepsilon^b(\theta) \rightarrow \theta, \quad \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) \rightarrow \varphi^0 + \tau \varphi.$$

Moreover

$$\mathcal{T}_\varepsilon^j \varphi_j^\varepsilon \rightarrow \varphi_j^0 + \tau \varphi_j, \quad \mathcal{T}_\varepsilon^j(\varphi_j^1) \rightarrow \varphi_j^1(t, x, y), \quad \mathcal{T}_\varepsilon^j(\nabla \varphi_j^\varepsilon) \rightarrow \nabla(\varphi_j^0 + \tau \varphi_j) + \nabla_y \varphi_j^1,$$

strongly in $L^2(\Omega_T \times Y_j)$, $j = i, e$. We pass to the limit in (2.114), showing the limit of each term separately.

$$A^0 := \lim_{\varepsilon \rightarrow 0} A^\varepsilon \\ = |\Gamma| \int_0^T e^{-\lambda t} \int_\Omega I_{\text{app}} v dx dt + \frac{|\Gamma|}{2} \left(\|v_0\|_{L^2(\Omega)}^2 + \sum_{l=1}^k \|w_{l,0}\|_{L^2(\Omega)}^2 + \|z_0\|_{L^2(\Omega)}^2 \right).$$

$$D^0 := \lim_{\varepsilon \rightarrow 0} D^\varepsilon \\ = \frac{|\Gamma|}{2} e^{-\lambda t} \int_\Omega \left(v(\varphi^0 + \tau \varphi) + \mathbf{w} \cdot (\boldsymbol{\psi}_0 + \tau \boldsymbol{\psi}) + z(\theta_0 + \tau \theta) \right) d\mathbf{x} \\ + \sum_{i,e} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} M_j(\nabla u_j + \nabla_y \hat{u}_j)(\nabla(\varphi_j^0 + \tau \nabla \varphi) + \nabla_y \varphi_j^1) dy d\mathbf{x},$$

$$E^0 := \lim_{\varepsilon \rightarrow 0} E^\varepsilon \\ = \frac{|\Gamma|}{2} e^{-\lambda T} \left(\|(\varphi^0 + \tau \varphi)(T)\|_{L^2(\Omega)}^2 + \sum_{l=1}^k \|(\psi_{l,0} + \tau \psi_l)(T)\|_{L^2(\Omega)}^2 + \|(\theta^0 + \tau \theta)(T)\|_{L^2(\Omega)}^2 \right) \\ + \sum_{i,e} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} M_j(\nabla(\varphi_j^0 + \tau \varphi_j) + \nabla_y \varphi_j^1) \cdot (\nabla(\varphi_j^0 + \tau \varphi_j) + \nabla_y \varphi_j^1) dy d\mathbf{x},$$

$$I^0 := \lim_{\varepsilon \rightarrow 0} I^\varepsilon \\ = \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} -\tilde{I}(\varphi^0 + \tau \varphi) - \left(I_{\text{ion}}(\varphi^0 + \tau \varphi, \boldsymbol{\psi}_0 + \tau \boldsymbol{\psi}, \theta_0 + \tau \theta) \right. \right. \\ \left. \left. (v - \varphi^0 - \tau \varphi) ds(y) d\mathbf{x} - \lambda |\Gamma| \int_\Omega v(\varphi^0 + \tau \varphi) d\mathbf{x} + \frac{\lambda |\Gamma|}{2} \|\varphi^0 + \tau \varphi\|_{L^2(\Omega)}^2 \right) \right] dt,$$

Similarly, the limits of R^ε and G^ε can be obtained to get from inequality (2.114)

$$A^0 - 2D^0 + E^0 + I^0 + R^0 + G^0 \geq 0. \quad (2.115)$$

This last inequality, being true for any test functions $\varphi_j^0, \varphi_j^1, \psi^0, \theta^0$, can be shown to be true by a density argument for $u_j, \hat{u}_j, j = i, e, v, \mathbf{w}$ and z . Consequently, one can simplify (2.115) using (2.112), to obtain

$$\begin{aligned} \tau \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v + \tau\varphi, \mathbf{w} + \tau\psi, z + \tau\theta) - \tilde{I} \right) \varphi + (\mathbf{R}(v + \tau\varphi, \mathbf{w} + \tau\psi) - \tilde{R}) \cdot \boldsymbol{\psi} \\ + (G(v + \tau\varphi, \mathbf{w} + \tau\psi, z + \tau\theta) - \tilde{G}) \theta \Big) dx dy dt + \mathcal{O}(\tau^2) \geq 0 \end{aligned}$$

Dividing by τ and then letting τ tends to 0, we find that for all test functions $\varphi, \boldsymbol{\psi}$ and θ , there holds

$$\begin{aligned} \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v, \mathbf{w}, z) - \tilde{I} \right) \varphi + (\mathbf{R}(v, \mathbf{w}) - \tilde{R}) \cdot \boldsymbol{\psi} \\ + (G(v, \mathbf{w}, z) - \tilde{G}) \theta \Big) dx dy dt \geq 0, \end{aligned}$$

Using $-\varphi, -\boldsymbol{\psi}$ and $-\theta$ for $\varphi, \boldsymbol{\psi}$ and θ one also gets

$$\begin{aligned} \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v, \mathbf{w}, z) - \tilde{I} \right) \varphi + (\mathbf{R}(v, \mathbf{w}) - \tilde{R}) \cdot \boldsymbol{\psi} \\ + (G(v, \mathbf{w}, z) - \tilde{G}) \theta \Big) dx dy dt \leq 0, \end{aligned}$$

which gives the result of the proposition. \square

Collecting all the convergence results stated above, one obtains the following limiting problem:

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi \, d\mathbf{x} \, dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j [\nabla u_j + \nabla_y \hat{u}_j] [\nabla \Psi_j + \theta_j \nabla_y \psi_j] \\ + |\Gamma| \iint_{\Omega_T} I_{\text{ion}}(v, \mathbf{w}, z) \Psi \, d\mathbf{x} \, dt = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi \, d\mathbf{x} \, dt, \end{aligned} \quad (2.116)$$

$$|\Gamma| \iint_{\Omega_T} \partial_t \mathbf{w} \phi \, d\mathbf{x} \, dt - |\Gamma| \iint_{\Omega_T} \mathbf{R}(v, \mathbf{w}) \phi \, d\mathbf{x} \, dt = 0, \quad (2.117)$$

and

$$|\Gamma| \iint_{\Omega_T} \partial_t z \phi \, d\mathbf{x} \, dt - |\Gamma| \iint_{\Omega_T} G(v, \mathbf{w}, z) \phi \, d\mathbf{x} \, dt = 0. \quad (2.118)$$

Finally, repeating the argument of Section 2.7 one can easily decouple the limit equations to get the equations of the macroscopic bidomain model (as (2.79)):

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi_i \, d\mathbf{x} \, dt + \iint_{\Omega_T} \mathcal{M}_i \nabla u_i \cdot \nabla \Psi_i + |\Gamma| \iint_{\Omega_T} I_{\text{ion}}(v, \mathbf{w}, z) \Psi_i \, d\mathbf{x} \, dt \\ = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi_i \, d\mathbf{x} \, dt, \end{aligned} \quad (2.119)$$

where \mathcal{M}_i is elliptic and defined by

$$\mathcal{M}_i := \int_{Y_i} \left(\mathbf{M}_i + \mathbf{M}_i \nabla_y f_i \right),$$

in addition to the corresponding cell problem given by (2.78).

2.9 Conclusion

We have presented in this chapter a complete mathematical analysis of the homogenization procedure leading to the macroscopic bidomain model based on the unfolding approach. The analysis was exhaustive meaning that we provided nondimensionalization of the microscopic equations, formal homogenization, existence and uniqueness results and unfolding homogenization. We hope that this work will allow the analysis of more complex models that may include, for instance, heterogeneous concentrations of ions inside the cells, influences of heart's mechanical deformation, gap junctions,...

Numerical Schemes For an Electrophysiology Model

3.1 Introduction

Computational models are considered as valuable tools to study many aspects of cardiac function and dysfunction, including for instance mechanisms of defibrillation and understanding cardiac mechanics [CP08]. The bidomain model represents the electrophysiology of the anisotropic cardiac tissue at the macroscale. Assuming an additional condition on the anisotropy, the monodomain model can be obtained. Although it is less detailed than the bidomain model, the monodomain model can be ten or more times faster for simulation of the same problem compared to the bidomain model. Moreover, for simulation of wave propagation in the heart, the monodomain model reproduces many of the phenomena that are observed experimentally, and is thus a reliable tool [CP08], [PDR⁺06]. In a comparative study [BP10], Bourgault and Pierre numerically estimated the discrepancy between the two models and they concluded that it is of order less than 1% in terms of activation time relative error noting that “this error is smaller than the discretisation error resulting from commonly used mesh size in biomedical engineering.”

Mathematical models for the propagation of electrical waves in the cardiac tissue have been studied in the framework of numerical methods and simulations. Regarding finite volume schemes (FV) for cardiac problems, Harrild and Henriquez gave a first approach in [HH97]. In [TLGSP05], Trew et al. introduced a FV scheme for the bidomain equations, representing physical discontinuities without the implicit removal of intracellular volume, which gives rise to linear instead of nonlinear systems. Concerning the convergence of FV schemes, a few works are available. Coudière and Pierre [CP06] proved convergence of an implicit FV approximation to the monodomain equations with FitzHugh-Nagumo ionic model. We mention also the work of Bendahmane and Karlsen [BK09] who analysed a FV method for the bidomain model with Dirichlet boundary conditions, supplying various existence, uniqueness and convergence results. We point out that in these works, the admissible mesh is adapted to the conductivity

tensor and it is practically impossible to be constructed except under isotropy condition. Moreover, Bendahmane, Bürger and Ruiz [BBRB10] analysed the bidomain equations formulated in a parabolic-elliptic form with Neumann boundary conditions, adapting the approach in [BK09], and providing some numerical experiments. We mention also the work of Andreianov et al. [ABKP11] who analyzed discrete duality finite volume (DDFV) approximations to the bidomain model (under a simplifying assumption on the ionic function) that allowed to drop the restrictions on the mesh and on the isotropy of the conductivities. Practically, DDFV schemes fail to satisfy a discrete maximum principle [HH08] which is a crucial property when dealing with physical quantities such as the transmembrane potential, the gating and the concentration variables. These variables must verify some physiological bounds and this property is not guaranteed with DDFV discretization.

In this chapter, we consider the monodomain model coupled to Beeler-Reuter cell model where physiological as well as mathematical considerations impose certain constraints on calcium concentration which appears as an argument of a logarithmic function and we need to guarantee its positivity. Moreover, the gating variables have to satisfy some physical bounds (between 0 and 1). We analyze, in the first part, a FV scheme based on two point flux approximation (TPFA) under the isotropy assumption on the conductivity of the medium. Then we establish a maximum principle, that may not be achieved for most finite element formulations but is the key ingredient of our proof of convergence. Furthermore, we use a compactness argument to prove the convergence of the scheme, as a result we do not give error estimates.

In the second part of the chapter, we consider an anisotropic conductivity tensor and we propose and analyze a positive nonlinear CVFE scheme. To get the desired discretization, a semi-implicit Euler scheme in time and a nonlinear CVFE discretization in space are considered. The diffusive term is discretized using a Godunov-like scheme. This approach permits to obtain the discrete maximum principle without the assumption on the transmissibility coefficients to be positive. Indeed, this condition is very restrictive. It is verified for isotropic conductivities and for particular meshes. For instance, in case of a triangulation, the angles of the triangles must be acute. For more details about the analysis of the CVFE method for several partial differential equations, we refer the reader to this non-exhaustive list [BP80, CMM91, EG93, FFLM97, FSS99].

We state in the following section, the mathematical assumptions used in the first part.

3.2 Mathematical Assumptions

We consider a bounded, open, polygonal, connected domain $\Omega \subset \mathbb{R}^d$, $d = 2, 3$, with boundary $\partial\Omega$, a fixed final time $T > 0$, and we set $\Omega_T = (0, T) \times \Omega$.

The equations of the monodomain model coupled with Beeler-Reuter ionic model are given by:

$$\begin{aligned} \frac{\partial v}{\partial t} &= \nabla \cdot (\Lambda \nabla v) - I_{\text{ion}}(v, \mathbf{w}, c), & \text{for a.e. } (t, x) \in \Omega_T, \\ \frac{\partial w_j}{\partial t} &= \alpha_j(v)(1 - w_j) - \beta_j(v)w_j, & \text{for a.e. } (t, x) \in \Omega_T \text{ and for } j = 1, \dots, 6, \\ \frac{\partial c}{\partial t} &= 0.07(10^{-4} - c) - 10^{-4}I_s(v, f, r, c), & \text{for a.e. } (t, x) \in \Omega_T, \end{aligned} \quad (3.1)$$

complemented with initial conditions

$$\begin{aligned} v(0, x) &= v_0(x), & \text{for a.e. } x \in \Omega, \\ \mathbf{w}(0, x) &= \mathbf{w}_0(x), & \text{for a.e. } x \in \Omega, \\ c(0, x) &= c_0(x), & \text{for a.e. } x \in \Omega, \end{aligned} \quad (3.2)$$

and a Neumann boundary condition on v

$$\Lambda \nabla v \cdot \mathbf{n} = 0 \text{ a.e. on } \partial\Omega \times (0, T). \quad (3.3)$$

For simplicity, we assumed that the surface to volume ratio χ and the capacitance C_m are equal to 1. The term $v : \Omega_T \rightarrow \mathbb{R}$ is the transmembrane potential and the term $c : \Omega_T \rightarrow \mathbb{R}^+$ is the scaled intracellular calcium concentration ($c = 10^3[Ca^{2+}]_i$). The components of the vector of gating variables $\mathbf{w} : \Omega_T \rightarrow \mathbb{R}^6$ are the variables m, o, l, f, r, z . Each of w_j , $j = 1, \dots, 6$ stands for m, o, l, f, r, z respectively and \mathbf{n} is the outward unit normal to $\partial\Omega$. We list now the mathematical assumptions on the conductivity tensor, the ionic functions and the initial data.

(H.1) Assuming an isotropic medium, the conductivity Λ is represented by the tensor $\lambda(x)\mathbf{I}$ where \mathbf{I} is the $d \times d$ identity matrix and $\lambda(x) \in L^\infty(\Omega)$ is such that

$$\lambda : \Omega \rightarrow \mathbb{R}^+, \text{ and } \exists m_0, \text{ such that } \lambda(x) \geq m_0 > 0, \text{ for a.e. } x \in \Omega. \quad (3.4)$$

(H.2) The functions α_j and β_j are Lipschitz continuous functions representing respectively the opening and closing rates and are given by

$$\alpha_j(v) = \frac{c_{1,j}e^{c_{2,j}(v+c_{3,j})} + c_{4,j}(v + c_{5,j})}{e^{c_{6,j}(v+c_{3,j})} + c_{7,j}},$$

and

$$\beta_j(v) = \frac{d_{1,j}e^{d_{2,j}(v+d_{3,j})} + d_{4,j}(v + d_{5,j})}{e^{d_{6,j}(v+d_{3,j})} + d_{7,j}},$$

for given constants $c_{i,j}$ and $d_{i,j}$, $i = 1, \dots, 7$, $j = 1, \dots, 6$ such that

$$\alpha_j(v), \beta_j(v) > 0. \quad (3.5)$$

(H.3) The function $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^6 \times \mathbb{R}^+ \rightarrow \mathbb{R}$ is the collection of membrane currents given by:

$$I_{\text{ion}}(v, \mathbf{w}, [Ca^{++}]) = I_{Pot}(v) + I_z(v, z) + I_{Na}(v, m, o, l) + I_s(v, f, r, c),$$

as detailed in Chapter 1 and the function I_s is given after the rescaling of $[Ca^{2+}]_i$ by

$$I_s(v, f, r, c) = g_s fr(v - 7.7 + 13.0287 \ln(c)).$$

We assume in this section that there exists a constant $K_I > 0$ such that:

$$\begin{aligned} & \left(I_{\text{ion}}(v_1, \mathbf{w}_1, c_1) - I_{\text{ion}}(v_2, \mathbf{w}_2, c_2) \right) (v_1 - v_2) \\ & \geq -K_I \left(|v_1 - v_2|^2 + \sum_{j=1}^6 |w_{1,j} - w_{2,j}|^2 + |c_1 - c_2|^2 \right). \end{aligned} \quad (3.6)$$

(H.4) The initial data $(v_0, \mathbf{w}_0, c_0) \in \left(L^\infty(\Omega), \left(H^1(\Omega) \right)^6, H^1(\Omega) \right)$, are assumed to satisfy

$$\begin{aligned} v_m &\leq v_0 \leq v_M && \text{a.e. in } \Omega, \\ c_m &\leq c_0 \leq c_M && \text{a.e. in } \Omega, \\ 0 &\leq w_{0,j} \leq 1 && \text{a.e. in } \Omega, \text{ for } j = 1, \dots, 6 \end{aligned} \quad (3.7)$$

where $v_m = -85$, $v_M = 127.69$, $c_m = 10^{-4}$ and $c_M = 0.0187$ are given constants such that $I_s(v_M, f, r, c_m) = 0$ for all $f, r \in [0, 1]$. We refer to [HKT06] for a heuristic motivation of these values.

3.3 Numerical Analysis of a Finite Volume Scheme

In this section, we propose a finite volume scheme for the monodomain model coupled to Beeler-Reuter ionic model given by System (3.1)-(3.3). We first define a weak solution of System (3.1)-(3.3). Then we give a definition of its finite volume discretization and we define its equivalent discrete variational formulation. Furthermore, after showing the existence and uniqueness of solution to the discrete scheme, we prove that it satisfies a maximum principle. Then we prove its convergence to the defined weak solution using a compactness argument. We point out that the limit functions satisfy the same lower and upper bounds as the initial conditions given in (3.7).

3.3.1 Weak Formulation

Before we define our finite volume scheme, we need to provide a relevant definition of a weak solution for the monodomain model.

Definition 3.3.1. A weak solution of (3.1) is a vector $\mathbf{U} = (v, \mathbf{w}, c)$, of functions such that

$$v \in L^\infty(\Omega_T) \cap L^2(0, T; H^1(\Omega)), \mathbf{w} \in L^\infty(\Omega_T)^6, c \in L^\infty(\Omega_T),$$

$$v_m \leq v \leq v_M, c_m \leq c \leq c_M, 0 \leq w_j \leq 1 \text{ for a.e. } (t, x) \in \Omega_T, \text{ for } j = 1, \dots, 6$$

and for all φ and $\xi \in \mathcal{D}([0, T] \times \bar{\Omega})$, there holds:

$$-\int_{\Omega} v_0(x) \varphi(0, x) dx + \iint_{\Omega_T} \left(-v \partial_t \varphi + \lambda \nabla v \cdot \nabla \varphi \right) dx dt = \iint_{\Omega_T} -I_{\text{ion}}(v, \mathbf{w}, c) \varphi dx dt, \quad (3.8)$$

$$-\int_{\Omega} w_{0,k}(x) \xi(0, x) dx + \iint_{\Omega_T} -w_k \partial_t \xi dx dt = \iint_{\Omega_T} (\alpha_k(v)(1 - w_k) - \beta_k(v)w_k) \xi dx dt, \quad (3.9)$$

for $k = 1, \dots, 6$, and

$$-\int_{\Omega} c_0(x) \xi(0, x) dx + \iint_{\Omega_T} -c \partial_t \xi dx dt = \iint_{\Omega_T} (0.07(10^{-4} - c) - 10^{-4} I_s(v, f, d, c)) \xi dx dt. \quad (3.10)$$

Remark 7. Observe that in Definition 3.3.1, we do not need the time continuity of v . In general, in the case of numerical schemes, there are no compactness results that allow to prove the time continuity of the solutions. However, one can make use of the weak formulation to prove that the limit solution v is continuous in time (see for instance [BF12]).

3.3.2 Discrete Problem

Space Discretization

Following [EGH00], we give a precise definition of the finite volume scheme for the monodomain equations.

We recall that Ω is an open, bounded, connected polygonal domain in \mathbb{R}^d , $d = 2, 3$, with boundary $\partial\Omega$. An admissible finite volume mesh of Ω , denoted by \mathcal{T}_h , is given by a family of “control volumes”, which are open and convex subsets K of Ω , a family of subsets of $\bar{\Omega}$ contained in hyperplanes of \mathbb{R}^d , denoted by \mathcal{E} (these are the edges (2D) or sides (3D) of the control volumes), with strictly positive $(d - 1)$ -dimensional measure, and a family of points of Ω denoted by \mathcal{P} satisfying the following properties:

- The closure of the union of the K 's is $\bar{\Omega}$, i.e. $\bar{\Omega} = \bigcup_{K \in \mathcal{T}_h} \bar{K}$.
- For any $K \in \mathcal{T}_h$, there exists a subset \mathcal{E}_K of \mathcal{E} such that $\partial K = \bar{K} \setminus K = \bigcup_{\sigma \in \mathcal{E}_K} \bar{\sigma}$. Furthermore, $\mathcal{E} = \bigcup_{K \in \mathcal{T}_h} \mathcal{E}_K$.
- The intersection between two neighboring control volumes K and L is either an interface or a vertex. In other words, for any $(K, L) \in \mathcal{T}_h^2$ with $K \neq L$, either the $(d - 1)$ -dimensional Lebesgue measure of $\bar{K} \cap \bar{L}$ is 0 or $\bar{K} \cap \bar{L} = \bar{\sigma}$ for some $\sigma \in \mathcal{E}$.
- The family $\mathcal{P} = (x_K)_{K \in \mathcal{T}}$ is such that $x_K \in \bar{K}$ (for all $K \in \mathcal{T}$) and if $\sigma = K|L$, it is assumed that $x_K \neq x_L$, and that the straight line $(x_K x_L)$ is orthogonal to $K|L$.
- For any $\sigma \in \mathcal{E}$ such that $\sigma \subset \partial\Omega$, let K be the control volume such that $\sigma \in \mathcal{E}_K$. If $x_K \notin \sigma$, let $\mathcal{D}_{K,\sigma}$ be the straight line orthogonal to σ through x_K , then we assume that $\mathcal{D}_{K,\sigma} \cap \sigma \neq \emptyset$ and we let $y_\sigma = \mathcal{D}_{K,\sigma} \cap \sigma$.

We consider an admissible mesh \mathcal{T}_h and we use the following notations:

- The mesh size: $h = \sup\{\text{diam}(K), K \in \mathcal{T}_h\}$.
- $|K| = \text{meas}(K)$ is the d -dimensional Lebesgue measure of K and $|\sigma|$ is the $(d - 1)$ -dimensional measure of an interface σ .
- The set of interior (resp. boundary) interfaces is denoted by \mathcal{E}_{int} (resp. \mathcal{E}_{ext}), that is $\mathcal{E}_{int} = \{\sigma \in \mathcal{E}; \sigma \not\subset \partial\Omega\}$ (resp. $\mathcal{E}_{ext} = \{\sigma \in \mathcal{E}; \sigma \subset \partial\Omega\}$).
- $N(K) = \{L \in \mathcal{T}_h; \exists \sigma \in \mathcal{E}_K, \bar{\sigma} = \bar{K} \cap \bar{L}\}$ is the set of neighbors of K .
- $d_{K,L}$ is the Euclidean distance between x_K and x_L and $d_{K,\sigma}$ is the distance from x_K to y_σ .
- $\sigma_{K,L}$ is the common edge to the neighboring control volumes K and L .
- $\mathbf{n}_{K,L}$ is the unit normal vector to $\sigma_{K,L}$ outward to K .
- The transmissibility coefficient through $\sigma_{K,L}$ is given by

$$\tau_{\sigma_{K,L}} = \frac{|\sigma_{K,L}|}{d_{K,L}}.$$

- $T_{K,L}$ is the convex diamond obtained from joining the centers x_K and x_L of two neighboring control volumes (K and L) to the vertices of the common interface $\sigma_{K,L}$, see Figure 5. The d -dimensional measure of $T_{K,L}$ is given by:

$$|T_{K,L}| = \frac{1}{d} |\sigma_{K,L}| d_{K,L}.$$

In the case where the interface σ is on the boundary of Ω , i.e. $\sigma \subset \partial\Omega$, we associate half a diamond $T_{K,\sigma}$. We have:

$$\bar{\Omega} = \bigcup_{K \in \mathcal{T}_h} \left(\left(\bigcup_{L \in N(K)} \bar{T}_{K,L} \right) \bigcup \left(\bigcup_{\sigma \subset \partial\Omega} T_{K,\sigma} \right) \right).$$

We also need some regularity on the mesh in the following sense. We assume that there exists $\xi > 0$ such that:

$$\forall K \in \mathcal{T}_h, \quad \sum_{L \in N(K)} |\sigma_{K,L}| d_{K,L} \leq \xi |K|. \quad (3.11)$$

Time Discretization

The discretization of the time interval $[0, T]$ is given by a time step Δt , and a positive integer N such that $N\Delta t = T$. We set $t_n = n\Delta t$ for $n \in \{0, \dots, N\}$.

Discretization of Ω_T

An admissible discretization \mathcal{D} of Ω_T is defined by

$$\mathcal{D} = \left(\mathcal{T}_h, \mathcal{E}, (x_K)_{K \in \mathcal{T}}, N, (t_n)_{n \in \{0, \dots, N\}} \right)$$

where $(\mathcal{T}_h, \mathcal{E}, (x_K)_{K \in \mathcal{T}})$ is an admissible mesh of Ω and $N, (t_n)_{n \in \{0, \dots, N\}}$ is the time discretization of $(0, T)$. One sets

$$\text{size}(\mathcal{D}) = \max(\text{size}(\mathcal{T}), \Delta t) = \max(h, \Delta t).$$

Discrete Functions

Definition 3.3.2. Define $X(\mathcal{T})$ as the set of functions from Ω to \mathbb{R} which are constant over each control volume of the mesh.

On an admissible mesh \mathcal{T}_h , a discrete function u is defined by a set $\{u_k\}_{K \in \mathcal{T}_h}$ and is identified to a function $u_h \in X(\mathcal{T})$ such that: $u_h|_K = u_k, \forall K \in \mathcal{T}_h$. Given two discrete functions w_h and u_h in $X(\mathcal{T})$, we define the inner product and the $L^2(\Omega)$ norm by:

$$(u_h, w_h)_{L^2(\Omega)} = \sum_{K \in \mathcal{T}_h} |K| w_K u_K, \quad \|w_h\|_{L^2(\Omega)}^2 = \sum_{K \in \mathcal{T}_h} |K| |w_K|^2.$$

The discrete gradient $\nabla_h u_h$ of a function $u_h \in X(\mathcal{T})$ is defined on the dual mesh as constant per diamond $T_{K,L}$:

$$\nabla_h u_h(x) = \begin{cases} d \frac{u_L - u_K}{d_{K,L}} \mathbf{n}_{K,L} & \text{if } x \in T_{K,L}, \\ 0 & \text{if } x \in T_{K,\sigma}. \end{cases}$$

When there is no confusion, we write $\sum_{\sigma_{K,L} \in \mathcal{E}}$ to be the sum over all diamonds.

Definition 3.3.3. For $u_h \in X(\mathcal{T})$, the discrete H^1 semi-norm of u_h is defined by:

$$|u_h|_{1,\mathcal{T}_h} = \left(d \sum_{\sigma_{K,L} \in \mathcal{E}} \tau_{\sigma_{K,L}} (u_L - u_K)^2 \right)^{1/2}.$$

Indeed, the discrete $H^1(\Omega)$ semi-norm of u_h coincides with the $L^2(\Omega)$ norm of $\nabla_h u_h$ as shown in the following

$$\begin{aligned} \|\nabla_h u_h\|_{L^2(\Omega)}^2 &= \sum_{\sigma_{K,L} \in \mathcal{E}} \int_{T_{K,L}} |\nabla_h u_h|^2 dx \\ &= d^2 \sum_{\sigma_{K,L} \in \mathcal{E}} |T_{K,L}| \frac{|u_L - u_K|^2}{d_{K,L}^2} \\ &= d \sum_{\sigma_{K,L} \in \mathcal{E}} \tau_{\sigma_{K,L}} (u_L - u_K)^2 \\ &= |u_h|_{1,\mathcal{T}_h}^2. \end{aligned}$$

The considered problem being time-dependent, we also need to define functions over the discretization \mathcal{D} of the space-time cylinder $(0, T) \times \Omega$. We use the subscript \mathcal{D} to denote functions that are constant per subinterval of time and control volume and we use the subscript K and the superscript n to denote its value at (t_n, x_K) , in short:

$$u_{\mathcal{D}}(t, x) = u_K^{n+1}, \text{ for a.e. } (t, x) \in (t_n, t_{n+1}) \times K, \forall K \in \mathcal{T}_h, \forall n \in \{0, \dots, N-1\}.$$

For any continuous function $f : \mathbb{R} \rightarrow \mathbb{R}$, $f(u_{\mathcal{D}})$ denotes the discrete function $(n, K) \rightarrow f(u_K^{n+1})$.

The Finite Volume Scheme

In order to discretize the equations of (3.1), we formally integrate the equations over $(t_n, t_{n+1}) \times K$ and we use Green's theorem on the diffusive term; we obtain:

$$\begin{aligned} \int_K [v(t_{n+1}, x) - v(t_n, x)] dx &= \int_{t_n}^{t_{n+1}} \int_{\partial K} (\lambda \nabla v) \cdot \mathbf{n} d\gamma dt - \int_{t_n}^{t_{n+1}} \int_K I_{\text{ion}}(v, \mathbf{w}, c) dx dt, \\ \int_K [w_j(t_{n+1}, x) - w_j(t_n, x)] dx &= \int_{t_n}^{t_{n+1}} \int_K [\alpha_j(v)(1 - w_j) - \beta_j(v)w_j] dx dt, \text{ for } j = 1, \dots, 6, \\ \int_K [c(t_{n+1}, x) - c(t_n, x)] dx &= \int_{t_n}^{t_{n+1}} \int_K [0.07(10^{-4} - c) - 10^{-4} I_s(v, f, d, c)] dx dt, \end{aligned}$$

Using an Euler semi-implicit time discretization where we set $t = t_{n+1}$ in the linear terms and $t = t_n$ in the system of ODEs for the recovery variable, we can write the following finite volume scheme with unknowns $(v_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$, $(\mathbf{w}_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$, and $(c_K^{n+1})_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$: $\forall K \in \mathcal{T}_h$,

$$v_K^0 = \frac{1}{|K|} \int_K v_0(x) dx, \mathbf{w}_K^0 = \frac{1}{|K|} \int_K \mathbf{w}_0(x) dx, \text{ and } c_K^0 = \frac{1}{|K|} \int_K c_0(x) dx \quad (3.12)$$

and $\forall n \in \{0, \dots, N-1\}, \forall K \in \mathcal{T}_h$,

$$\frac{|K|}{\Delta t}(v_K^{n+1} - v_K^n) + \sum_{\sigma \in \mathcal{E}_K \cap \mathcal{E}_{int}} F_{K,\sigma}^{n+1} = -|K| \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) \right) \quad (3.13)$$

$$+ I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n),$$

$$w_{j,K}^{n+1} - w_{j,K}^n = \Delta t \left(\alpha_j(v_K^n)(1 - w_{j,K}^{n+1}) - \beta_j(v_K^n)w_{j,K}^{n+1} \right), \text{ for } j = 1, \dots, 6, \quad (3.14)$$

$$c_K^{n+1} - c_K^n = \Delta t \left(0.07(10^{-4} - c_K^{n+1}) - g_s 10^{-4} f_K^n r_K^n (v_K^{n+1} - 7.7 + 13.0287 \ln(c_K^{n+1})) \right) \quad (3.15)$$

where $F_{K,\sigma}^{n+1}$ is an approximation of $\int_{\sigma} -\lambda(x) \nabla v(t_{n+1}, x) \cdot \mathbf{n}_{K,\sigma} d\gamma$. We introduce the auxiliary unknowns $(v_{\sigma}^{n+1})_{\sigma \in \mathcal{E}}$ over the interfaces. They are used as an intermediate to obtain a conservative expression of the fluxes and are therefore eliminated in order to write the problem in terms of the primary unknowns $(v_K^{n+1})_{K \in \mathcal{T}_h}$. So, the approximation is first written with respect to the discrete unknowns $(v_K^{n+1})_{K \in \mathcal{T}_h}$ and $(v_{\sigma}^{n+1})_{\sigma \in \mathcal{E}}$. For $K \in \mathcal{T}_h$ and $\sigma \in \mathcal{E}_K$, let

$$\lambda_K = \frac{1}{|K|} \int_K \lambda(x) dx.$$

- On the external interfaces the Neumann boundary condition (3.3) on v is taken into account by fixing

$$F_{K,\sigma}^{n+1} = 0, \quad \forall K \in \mathcal{T}_h, \forall \sigma \in \mathcal{E}_K \cap \mathcal{E}_{ext}.$$

- On the internal interfaces, we approximate the flux as follows:

A natural expression for $F_{K,\sigma}^{n+1}$ is

$$F_{K,\sigma}^{n+1} = -|\sigma| \lambda_K \frac{v_{\sigma}^{n+1} - v_K^{n+1}}{d_{K,\sigma}}.$$

Using conservativity of flux, i.e. $F_{K,\sigma}^{n+1} = -F_{L,\sigma}^{n+1}$ if $\sigma = \sigma_{K,L}$, yields the value of v_{σ}^{n+1} , if $x_L \notin \sigma$:

$$v_{\sigma}^{n+1} = \frac{1}{\frac{\lambda_K}{d_{K,\sigma}} + \frac{\lambda_L}{d_{L,\sigma}}} \left(\frac{\lambda_K}{d_{K,\sigma}} v_K^{n+1} + \frac{\lambda_L}{d_{L,\sigma}} v_L^{n+1} \right).$$

Hence, the value of $F_{K,\sigma}^{n+1}$;

$$F_{K,\sigma}^{n+1} = -\tau_{\sigma} (v_L^{n+1} - v_K^{n+1}), \text{ if } \sigma \in \mathcal{E}_{int}, \sigma = \sigma_{K,L}, \quad (3.16)$$

where

$$\tau_{\sigma} = |\sigma| \frac{\lambda_K \lambda_L}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}}.$$

The discrete solution of the scheme (3.13)-(3.15) is a tuple $\mathbf{U}_{\mathcal{D}} = (v_{\mathcal{D}}, \mathbf{w}_{\mathcal{D}}, c_{\mathcal{D}})$, of functions that are piecewise constant over Ω_T given by:

$$\forall n \in \{0, \dots, N-1\}, \forall K \in \mathcal{T}_h, v_{\mathcal{D}}|_{(t_n, t_{n+1}] \times K} = v_K^{n+1}, \mathbf{w}_{\mathcal{D}}|_{(t_n, t_{n+1}] \times K} = \mathbf{w}_K^{n+1}, c_{\mathcal{D}}|_{(t_n, t_{n+1}] \times K} = c_K^{n+1}.$$

Let us show that the finite volume scheme (3.13)-(3.15) can be written in a discrete variational formulation.

Proposition 3.3.1. *The finite volume scheme (3.13)-(3.15) is equivalent to the variational discrete formulation:*

$$\int_{\Omega} \frac{v_h^{n+1} - v_h^n}{\Delta t} \phi_h dx + \frac{1}{d} \int_{\Omega} M_h \nabla_h v_h^{n+1} \cdot \nabla_h \phi_h dx = - \int_{\Omega} (I_{\text{ion}})_h^{n,n+1} \phi_h dx, \quad (3.17)$$

$$\int_{\Omega} \frac{w_{j,h}^{n+1} - w_{j,h}^n}{\Delta t} \xi_h dx = \int_{\Omega} R_{j,h}^{n,n+1} \xi_h dx, \quad (3.18)$$

for $j = 1, \dots, 6$,

$$\int_{\Omega} \frac{c_h^{n+1} - c_h^n}{\Delta t} \psi_h dx = \int_{\Omega} F_h^{n+1} \psi_h dx, \quad (3.19)$$

for all ϕ_h, ψ_h, ξ_h in $X(\mathcal{T})$ and $L^2(\Omega)$, where the function M_h is defined to be constant by diamond and the functions $(I_{\text{ion}})_h^{n,n+1}$, $R_{k,h}^{n,n+1}$, and $F_h^{n,n+1}$ are constant by control volume as:

$$(I_{\text{ion}})_h^{n,n+1} \Big|_K = I_{\text{Pot}}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{\text{Na}}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n),$$

$$R_{j,h}^{n,n+1} \Big|_K = \alpha_j(v_K^n)(1 - w_{j,K}^{n+1}) - \beta_j(v_K^n)w_{j,K}^{n+1},$$

and

$$F_h^{n+1} \Big|_K = 0.07(10^{-4} - c_K^{n+1}) - g_s 10^{-4} f_K^{n+1} r_K^{n+1} (v_K^{n+1} - 7.7 + 13.0287 \ln(c_K^{n+1})).$$

Proof. We will only detail the proof of (3.17). The proofs of (3.18) and (3.19) are similar. Multiplying the discrete equation (3.13) by ϕ_K and taking sums over K , one gets

$$\begin{aligned} & \sum_{K \in \mathcal{T}_h} |K| \frac{v_K^{n+1} - v_K^n}{\Delta t} \phi_K - \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) \phi_K \\ &= - \sum_{K \in \mathcal{T}_h} |K| \left(I_{\text{Pot}}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{\text{Na}}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\ & \quad \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) \phi_K. \end{aligned}$$

From the definition of the discrete functions, the first term is written as:

$$\sum_{K \in \mathcal{T}_h} |K| \frac{v_K^{n+1} - v_K^n}{\Delta t} \phi_K = \int_{\Omega} \frac{v_h^{n+1} - v_h^n}{\Delta t} \phi_h dx.$$

Summing by parts the second term and using the definition of the discrete gradient, one has:

$$\begin{aligned} & - \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) \phi_K \\ &= \sum_{\sigma_{K,L} \in \mathcal{E}} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) (\phi_L - \phi_K) \\ &= \sum_{\sigma_{K,L} \in \mathcal{E}} \frac{d_{KL}^2}{d^2} |\sigma_{K,L}| \frac{\lambda_L \lambda_K}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}} \frac{d(v_L^{n+1} - v_K^{n+1})}{d_{KL}} \mathbf{n}_{KL} \cdot \frac{d(\phi_L - \phi_K)}{d_{KL}} \mathbf{n}_{KL} \\ &= \frac{1}{d} \sum_{\sigma_{K,L} \in \mathcal{E}} |T_{K,L}| M_{K,L} \nabla_h v_h^{n+1} \Big|_{T_{K,L}} \cdot \nabla_h \phi_h \Big|_{T_{K,L}} \\ &= \frac{1}{d} \int_{\Omega} M_h \nabla_h v_h^{n+1} \cdot \nabla_h \phi_h dx \end{aligned}$$

where $M_{K,L} := \frac{\lambda_L \lambda_K}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}} d_{KL}$ and $M_h|_{T_{K,L}} = M_{KL}$ and $\nabla_h v_h^{n+1}|_{T_{K,L}}$ denotes the restriction of $\nabla_h v_h^{n+1}$ to the diamond $T_{K,L}$. Also, the third term can be easily written as

$$\begin{aligned} & - \sum_{K \in \mathcal{T}_h} |K| \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\ & \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) \phi_K \\ = & - \int_{\Omega} (I_{ion})_h^{n,n+1} \phi_h dx. \end{aligned}$$

□

3.3.3 Convergence of the Discrete Scheme

In this section, we study the convergence of the discrete scheme presented in the previous section. First, we state the convergence theorem. Then we prove the theorem using a priori estimates on the discrete solutions followed by a compactness argument.

Theorem 3.3.2. *Assume $v_0 \in L^\infty(\Omega)$, $\mathbf{w}_0 \in H^1(\Omega)^6$ and $c_0 \in H^1(\Omega)$, and that they satisfy (3.7). Furthermore, assume that the properties of the model stated in Section 2 hold. Then the finite volume solution $\mathbf{U}_{\mathcal{D}}$, generated by (3.13)-(3.15), converges along a subsequence to $\mathbf{U} = (v, \mathbf{w}, c)$ as $h, \Delta t \rightarrow 0$, where \mathbf{U} is a weak solution of (3.1)-(3.3) as in Definition 3.3.1. Furthermore, the limit function c is in $L^2(0, T; H^1(\Omega))$ and $\mathbf{w} \in L^2(0, T; H^1(\Omega)^6)$.*

The remaining part of this section is devoted to the proof of the aforementioned theorem.

Existence of Solution of the Discrete Problem

The existence of solution to the scheme (3.13)-(3.15) can be obtained with the use of the following classical lemma [Lio69].

Lemma 3.3.3. *Let \mathcal{A} be a finite dimensional Hilbert space with scalar product $[\cdot, \cdot]$ and norm $\|\cdot\|$, and let \mathcal{P} be a continuous mapping from \mathcal{A} into itself such that*

$$[\mathcal{P}(\xi), \xi] > 0 \text{ for } \|\xi\| = r > 0.$$

Then there exists $\xi \in \mathcal{A}$ with $\|\xi\| \leq r$ such that

$$\mathcal{P}(\xi) = 0.$$

The next proposition establishes the existence and uniqueness for the finite volume scheme.

Proposition 3.3.4. *System (3.13)-(3.15) admits a unique solution provided that*

$$\Delta t < \frac{1}{K_I}.$$

Proof. We show existence of a discrete solution using induction over n . We assume that $(v_h^n, \mathbf{w}_h^n, c_h^n)$ exists and we prove the existence of $(v_h^{n+1}, \mathbf{w}_h^{n+1}, c_h^{n+1})$.

Using Equation (3.14), we get for $j = 1, \dots, 6$ the explicit expression of $w_{j,K}^{n+1}$ as:

$$w_{j,K}^{n+1} = \frac{w_{j,K}^n + \Delta t \alpha_j(v_K^n)}{1 + \Delta t (\alpha_j(v_K^n) + \beta_j(v_K^n))},$$

and $w_{j,K}^{n+1}$ can be obtained since $\alpha_j(v)$ and $\beta_j(v)$ are strictly positive. Hence, there exists a unique solution \mathbf{w}_h^{n+1} to system (3.14). To prove the existence of solutions for system (3.13), we make use of Lemma 3.3.3. Consider the Hilbert space H_h^1 endowed with the norm

$$\|u_h\|_{H_h^1}^2 := \|u_h\|_{L^2(\Omega)}^2 + |u_h|_{1, \mathcal{T}_h}.$$

Define the mapping \mathcal{P} from the space H_h^1 to itself by:

$$\begin{aligned} [\mathcal{P}(v_h^{n+1}), \phi_h] &= \frac{1}{\Delta t} \left((v_h^{n+1}, \phi_h) - (v_h^n, \phi_h) \right) + \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_K^{n+1} - v_L^{n+1}) (\phi_K - \phi_L) \\ &+ \sum_{K \in \mathcal{T}_h} |K| I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \phi_K. \end{aligned}$$

The continuity of the mapping \mathcal{P} follows directly upon the use of the discrete Hölder's inequality and the continuity of the function I_{ion} . We need to show that

$$[\mathcal{P}(v_h^{n+1}), v_h^{n+1}] > 0, \quad \text{for } \|v_h^{n+1}\|_{H_h^1} = r > 0,$$

for a sufficiently large r . Using property (3.6), one has

$$I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) v_K^{n+1} \geq I_{\text{ion}}(0, 0, c_K^n) v_K^{n+1} - K_I \left((v_K^{n+1})^2 + \sum_{j=1}^6 (w_{j,K}^{n+1})^2 \right). \quad (3.20)$$

Using inequality (3.20) along with (3.4) and Cauchy-Schwartz' inequality, we obtain

$$\begin{aligned} [\mathcal{P}(v_h^{n+1}), v_h^{n+1}] &\geq \frac{1}{\Delta t} \|v_h^{n+1}\|_{L^2(\Omega)}^2 + m_0 |v_h^{n+1}|_{1, \mathcal{T}_h}^2 - \frac{1}{\Delta t} \|v_h^n\|_{L^2(\Omega)} \|v_h^{n+1}\|_{L^2(\Omega)} \\ &- K_I \left(\|v_h^{n+1}\|_{L^2(\Omega)}^2 + \|\mathbf{w}_h^{n+1}\|_{L^2(\Omega)^6}^2 \right) - \|I_{\text{ion}}(0, 0, c_h^n)\|_{L^2(\Omega)} \|v_h^{n+1}\|_{L^2(\Omega)}. \end{aligned}$$

The last inequality implies that

$$\begin{aligned} [\mathcal{P}(v_h^{n+1}), v_h^{n+1}] &\geq \min \left\{ \left(\frac{1}{\Delta t} - K_I \right), m_0 \right\} \|v_h^{n+1}\|_{H_h^1}^2 - K_I \|\mathbf{w}_h^{n+1}\|_{L^2(\Omega)^6}^2 \\ &- \left(\frac{1}{\Delta t} \|v_h^n\|_{L^2(\Omega)} + \|I_{\text{ion}}(0, 0, c_h^n)\|_{L^2(\Omega)} \right) \|v_h^{n+1}\|_{H_h^1}. \end{aligned}$$

Finally, for given v_h^n , \mathbf{w}_h^n and c_h^n we deduce that, for $\Delta t < \frac{1}{K_I}$, $[\mathcal{P}(v_h^{n+1}), v_h^{n+1}] > 0$ for $\|v_h^{n+1}\|_{H_h^1} = r$, for large enough r . Hence, system (3.13) has at least one solution. The uniqueness of solution can be proved by contradiction in a standard way as in [BK09].

Suppose that there exists $n \in \{0, \dots, N-1\}$ such that $v_{1,K}^n = v_{2,K}^n$ for all $K \in \mathcal{T}_h$ but $v_{1,K}^{n+1} \neq$

$v_{2,K}^{n+1}$ for some $K \in \mathcal{T}_h$. Subtracting (3.13) for $\{v_{1,K}^n\}_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$ and $\{v_{2,K}^n\}_{K \in \mathcal{T}_h, n \in \{0, \dots, N-1\}}$, we get

$$\begin{aligned} & |K| \frac{v_{1,K}^{n+1} - v_{2,K}^{n+1}}{\Delta t} - \sum_{L \in N(K)} \tau_{\sigma_{K,L}} \left((v_{1,L}^{n+1} - v_{2,L}^{n+1}) - (v_{1,K}^{n+1} - v_{2,K}^{n+1}) \right) \\ & + |K| \left(I_{\text{ion}}(v_{1,K}^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) - I_{\text{ion}}(v_{2,K}^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right) = 0. \end{aligned}$$

Multiplying this last equation by $\Delta t(v_{1,K}^{n+1} - v_{2,K}^{n+1})$ then summing over all $K \in \mathcal{T}_h$ and $n \in \{0, \dots, N-1\}$ yields

$$U_1 + U_2 + U_3 = 0,$$

where

$$U_1 = \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K| |v_{1,K}^{n+1} - v_{2,K}^{n+1}|^2,$$

$$U_2 = \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} \left| (v_{1,L}^{n+1} - v_{2,L}^{n+1}) - (v_{1,K}^{n+1} - v_{2,K}^{n+1}) \right|^2,$$

and

$$U_3 = \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| \left(I_{\text{ion}}(v_{1,K}^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) - I_{\text{ion}}(v_{2,K}^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right) (v_{1,K}^{n+1} - v_{2,K}^{n+1}).$$

Using (3.6), we obtain

$$U_3 \geq -K_I \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |v_{1,K}^{n+1} - v_{2,K}^{n+1}|^2.$$

Furthermore, noting that $U_2 > 0$, we have

$$\sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K| |v_{1,K}^{n+1} - v_{2,K}^{n+1}|^2 \leq K_I \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |v_{1,K}^{n+1} - v_{2,K}^{n+1}|^2. \quad (3.21)$$

Since $\sum_{K \in \mathcal{T}_h} |K| |v_{1,K}^{n+1} - v_{2,K}^{n+1}|^2 \neq 0$, (3.21) implies that

$$\frac{1}{K_I} \leq \Delta t, ,$$

which contradicts the choice of $\Delta t < \frac{1}{K_I}$ used in the existence proof.

Now given v_K^{n+1} and \mathbf{w}_K^{n+1} , we can rewrite Equation (3.15) as:

$$\begin{aligned} & (1 + 0.07\Delta t)c_K^{n+1} + 13.0287 \times 10^{-4} g_s f_K^{n+1} r_K^{n+1} \ln(c_K^{n+1}) \\ & = c_K^n + 10^{-4} \Delta t \left(0.07 - g_s f_K^{n+1} r_K^{n+1} (v_K^{n+1} - 7.7) \right). \end{aligned} \quad (3.22)$$

Since the function $x \mapsto (1 + 0.07\Delta t)x + 13.0287 \times 10^{-4} g_s f_K^{n+1} r_K^{n+1} \ln(x)$, which is defined for $x > 0$ onto \mathbb{R} , is bijective. Thus, Equation (3.22) admits a unique solution c_K^{n+1} . Therefore, the existence and uniqueness of solution of the discrete system is obtained. \square

A Priori Analysis of the Discrete Solutions

Confinement of $v_{\mathcal{D}}, w_{\mathcal{D}}, c_{\mathcal{D}}$

Lemma 3.3.5. *Let $(v_{\mathcal{D}}, w_{\mathcal{D}}, c_{\mathcal{D}})$ be the discrete solution of (3.13)-(3.15). Then for all $K \in \mathcal{T}_h$, and $n \in \{0, \dots, N-1\}$, we have: $0 \leq w_{j,K}^{n+1} \leq 1$, for $j = 1, \dots, 6$, $c_m \leq c_K^{n+1} \leq c_M$ and $v_m \leq v_K^{n+1} \leq v_M$.*

Proof. We use induction over n . Due to assumption (3.7), the assertion is true for $n = 0$. We assume it true for n , and we prove it true for $n + 1$.

In the following, the index j is skipped in order to simplify the notation. Define

$$\chi(x) = \begin{cases} 1 - x & \text{if } x \leq 1, \\ 0 & \text{if } x > 1. \end{cases}$$

we write the equation (3.14) as:

$$w_K^{n+1} - w_K^n = \Delta t \left(\alpha(v_K^n) \chi(w_K^{n+1}) - \beta(v_K^n) w_K^{n+1} \right). \quad (3.23)$$

Multiplying first (3.23) by $-(w_K^{n+1})^- := \min(w_K^{n+1}, 0)$, one obtains:

$$\begin{aligned} |(w_K^{n+1})^-|^2 &= -w_K^n (w_K^{n+1})^- + \left[-\alpha(v_K^n) \chi(w_K^{n+1}) (w_K^{n+1})^- + \beta(v_K^n) w_K^{n+1} (w_K^{n+1})^- \right] \Delta t \\ &= -w_K^n (w_K^{n+1})^- + \left[-\alpha(v_K^n) \chi(w_K^{n+1}) (w_K^{n+1})^- - \beta(v_K^n) \left((w_K^{n+1})^- \right)^2 \right] \Delta t \\ &\leq 0. \end{aligned}$$

The last inequality implies that $(w_K^{n+1})^- = 0$ and $w_K^{n+1} \geq 0$. Therefore, $w_K^{n+1} \geq 0$ for all $K \in \mathcal{T}_h$.

Using the same reasoning, multiply equation (3.23) by $(w_K^{n+1} - 1)^+ := \max(0, w_K^{n+1} - 1)$ to obtain

$$|(w_K^{n+1} - 1)^+|^2 = (w_K^n - 1) (w_K^{n+1} - 1)^+ + \left[\alpha(v_K^n) \chi(w_K^{n+1}) (w_K^{n+1} - 1)^+ - \beta(v_K^n) w_K^{n+1} (w_K^{n+1} - 1)^+ \right] \Delta t.$$

Suppose that $w_K^{n+1} > 1$. By definition of the function χ , one can easily check that $\chi(w_K^{n+1}) (w_K^{n+1} - 1)^+ = 0$. Moreover, one has $w_K^{n+1} (w_K^{n+1} - 1)^+ \geq 0$, so

$$-\beta(v_K^n) w_K^{n+1} (w_K^{n+1} - 1)^+ \leq 0.$$

Making use of the inductive hypothesis, one also has $w_K^n - 1 \leq 0$. As a result, there holds $|(w_K^{n+1} - 1)^+|^2 \leq 0$, which is a contradiction to the assumption that $w_K^{n+1} > 1$. Therefore, $w_K^{n+1} \leq 1$ for all $K \in \mathcal{T}_h$.

In order to prove that $v_m \leq v_L^{n+1} \leq v_M$ for all L , consider a fixed control volume K such that $v_K^{n+1} = \min_{L \in \mathcal{T}_h} (v_L^{n+1})$ and assume that $v_K^{n+1} < v_m$ trying to obtain a contradiction.

Denoting by $U_K^{n+1} := (v_K^{n+1} - v_m)$ and multiplying equation (3.13) by $-(U_K^{n+1})^- := \min(U_K^{n+1}, 0)$,

one obtains

$$\begin{aligned}
|K| \left((U_K^{n+1})^- \right)^2 &= -|K| U_K^n (U_K^{n+1})^- + \Delta t \sum_{\sigma \in \mathcal{E}_K \cap \mathcal{E}_{int}} F_{K,\sigma}^{n+1} (U_K^{n+1})^- + \Delta t |K| \left(I_{Pot}(v_K^{n+1}) \right. \\
&\quad + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \\
&\quad \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) (U_K^{n+1})^- \\
&\leq |K| \Delta t \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\
&\quad \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) (U_K^{n+1})^- \\
&:= I_1 + I_2 + I_3 + I_4,
\end{aligned}$$

where

$$\begin{aligned}
I_1 &:= |K| \Delta t I_{Pot}(v_K^{n+1}) (U_K^{n+1})^-, \\
I_2 &:= |K| \Delta t I_z(v_K^{n+1}, z_K^{n+1}) (U_K^{n+1})^-, \\
I_3 &:= |K| \Delta t I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) (U_K^{n+1})^-, \\
\text{and } I_4 &:= |K| \Delta t I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) (U_K^{n+1})^-.
\end{aligned}$$

We easily notice that if $v_K^{n+1} < v_m$, then

$$I_1 \leq 0 \text{ and } I_2 \leq 0.$$

Moreover,

$$\begin{aligned}
I_3 &= |K| \Delta t \left(g_{Na} (m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC} \right) (v_K^{n+1} - E_{Na}) (U_K^{n+1})^- \\
&= |K| \Delta t \left(g_{Na} (m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC} \right) (U_K^{n+1} + v_m - E_{Na}) (U_K^{n+1})^- \\
&= |K| \Delta t \left[- (g_{Na} (m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC}) |(U_K^{n+1})^-|^2 + (g_{Na} (m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC}) \right. \\
&\quad \left. (v_m - E_{Na}) (U_K^{n+1})^- \right] \\
&\leq 0.
\end{aligned}$$

Also, we have

$$\begin{aligned}
I_4 &= |K| \Delta t g_s f_K^{n+1} r_K^{n+1} (v_K^{n+1} - 7.7 + 13.028 \ln(c_K^n)) (U_K^{n+1})^- \\
&= |K| \Delta t g_s f_K^{n+1} r_K^{n+1} (U_K^{n+1} + v_m - 7.7 + 13.028 \ln(c_K^n)) (U_K^{n+1})^- \\
&= |K| \Delta t \left[-g_s f_K^{n+1} r_K^{n+1} \left((U_K^{n+1})^- \right)^2 + g_s f_K^{n+1} r_K^{n+1} (v_m - 7.7 + 13.028 \ln(c_K^n)) (U_K^{n+1})^- \right] \\
&\leq 0.
\end{aligned}$$

We conclude therefore that $(U_K^{n+1})^- = 0$, and $v_K^{n+1} \geq v_m$. Similarly, we can prove that $v_K^{n+1} \leq v_M$, by using (3.13) over the control volume K such that: $v_K^{n+1} = \max_{L \in \mathcal{T}_h} (v_L^{n+1})$, then multiplying the equation by $(v_K^{n+1} - v_M)^+$.

Now, we show that $c_m \leq c_K^{n+1} \leq c_M$.

Define, first, the function

$$F(v, f, r, c) = 0.07(10^{-4} - c) - 10^{-4}I_s(v, f, r, c).$$

Then assume that $c_K^{n+1} < c_m$ and multiply (3.15) by $-(c_K^{n+1} - c_m)^- := \min((c_K^{n+1} - c_m), 0)$, to get:

$$-c_K^{n+1}(c_K^{n+1} - c_m)^- = -c_K^n(c_K^{n+1} - c_m)^- - \Delta t F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1})(c_K^{n+1} - c_m)^-,$$

or equivalently

$$[(c_K^{n+1} - c_m)^-]^2 = -(c_K^n - c_m)(c_K^{n+1} - c_m)^- - \Delta t F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1})(c_K^{n+1} - c_m)^-.$$

Since $c_K^n \geq c_m$, then

$$\begin{aligned} [(c_K^{n+1} - c_m)^-]^2 &\leq -\Delta t F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1})(c_K^{n+1} - c_m)^- \\ &= -\Delta t [F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1}) - F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_m)](c_K^{n+1} - c_m)^- \\ &\quad - \Delta t F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_m)(c_K^{n+1} - c_m)^-, \end{aligned}$$

Noting that $\frac{\partial F}{\partial c} < 0$, one has

$$F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1}) - F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_m) \geq 0.$$

Consequently, one gets

$$\begin{aligned} [(c_K^{n+1} - c_m)^-]^2 &\leq -\Delta t F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_m)(c_K^{n+1} - c_m)^- \\ &\leq 0, \end{aligned}$$

where the last inequality follows since $F(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_m) \geq 0$ for $0 \leq v_K^{n+1} \leq 1$. So $(c_K^{n+1} - c_m)^- = 0$ and $c_K^{n+1} \geq c_m$ which contradicts the assumption that $c_K^{n+1} < c_m$. Hence $c_K^{n+1} \geq c_m$. We repeat the argument by multiplying (3.15) by $(c_K^{n+1} - c_M)^+$ to obtain $c_K^{n+1} \leq c_M$. \square

Discrete A Priori Estimates

Lemma 3.3.6. (Estimates on $v_{\mathcal{D}}$ and its discrete gradient). *Let $(v_{\mathcal{D}}, \mathbf{w}_{\mathcal{D}}, c_{\mathcal{D}})$ be a solution of the discrete finite volume scheme (3.13)-(3.15). Then there exists a constant $C_1 > 0$ depending on $\Omega, T, v_0, \mathbf{w}_0, c_0$ such that*

$$\max_{n \in \{1, \dots, N\}} \|v_h^n\|_{L^2(\Omega)}^2 + \sum_{n=0}^{N-1} \Delta t \|\nabla_h v_h^{n+1}\|_{L^2(\Omega)}^2 \leq C_1. \quad (3.24)$$

Proof. We first note that by the confinement of $v_K^{n+1}, \mathbf{w}_K^{n+1}$ and c_K^{n+1} obtained in the previous section, there exists a constant $c_3 > 0$ such that:

$$|I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)| \leq c_3.$$

Then we rewrite equation (3.13) as:

$$|K|(v_K^{n+1} - v_K^n) - \Delta t \sum_{L \in N(K)} \tau_{\sigma_{K,L}}(v_L^{n+1} - v_K^{n+1}) = -\Delta t |K| I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n). \quad (3.25)$$

Multiplying (3.25) by v_K^{n+1} and taking the sum over $K \in \mathcal{T}_h$ and $n \in \{0, \dots, N-1\}$, we have:

$$\begin{aligned} \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K|(v_K^{n+1} - v_K^n)v_K^{n+1} - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}}(v_L^{n+1} - v_K^{n+1})v_K^{n+1} \\ = - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)v_K^{n+1}, \end{aligned}$$

or

$$T_1 + T_2 = T_3,$$

where

$$\begin{aligned} T_1 &:= \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K|(v_K^{n+1} - v_K^n)v_K^{n+1}, \\ T_2 &:= - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}}(v_L^{n+1} - v_K^{n+1})v_K^{n+1}, \\ T_3 &:= - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)v_K^{n+1}. \end{aligned}$$

We use the inequality $(a - b)a \geq \frac{1}{2}a^2 - \frac{1}{2}b^2$, to get:

$$T_1 \geq \frac{1}{2} \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K|((v_K^{n+1})^2 - (v_K^n)^2).$$

Having a telescoping series on the RHS of the last inequality, we can rewrite it as:

$$T_1 \geq \frac{1}{2} \sum_{K \in \mathcal{T}_h} |K|((v_K^N)^2 - (v_K^0)^2),$$

or equivalently,

$$T_1 \geq \frac{1}{2} \sum_{K \in \mathcal{T}_h} |K|(v_K^N)^2 - \frac{1}{2} \sum_{K \in \mathcal{T}_h} |K|(v_K^0)^2.$$

Now for the diffusive term T_2 , we use the discrete integration by parts formula, to obtain:

$$T_2 = \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L} \in \mathcal{E}_{\text{int}}} \tau_{\sigma_{K,L}}(v_L^{n+1} - v_K^{n+1})^2 \geq 0.$$

Moreover, since $v_m \leq v_K^{n+1} \leq v_M$ and $|I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)| \leq c_3$, there exists a positive constant c_4 depending on T and Ω such that:

$$|T_3| \leq c_4.$$

As a result of the previous discussion, we have:

$$\frac{1}{2} \sum_{K \in \mathcal{T}_h} |K| (v_K^N)^2 + \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L} \in \mathcal{E}_{int}} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1})^2 \leq c_4 + \frac{1}{2} \sum_{K \in \mathcal{T}_h} |K| (v_K^0)^2,$$

so there exists $c_5 > 0$ depending on Ω , T and v_0 such that:

$$\frac{1}{2} \sum_{K \in \mathcal{T}_h} |K| (v_K^N)^2 + \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L} \in \mathcal{E}_{int}} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1})^2 \leq c_5. \quad (3.26)$$

From the last inequality, we have:

$$\frac{1}{2} \sum_{K \in \mathcal{T}_h} |K| (v_K^N)^2 \leq c_5,$$

and this inequality is also true if we replace N by $n_0 \in \{1, \dots, N\}$, so

$$\sum_{K \in \mathcal{T}_h} |K| (v_K^{n_0})^2 \leq 2c_5$$

for any $n_0 \in \{1, \dots, N\}$ and consequently:

$$\max_{n \in \{1, \dots, N\}} \sum_{K \in \mathcal{T}_h} |K| (v_K^n)^2 \leq 2c_5.$$

Also by equation (3.26), we have

$$\sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L} \in \mathcal{E}_{int}} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1})^2 \leq c_5,$$

where by the regularity of the mesh and the definition of the transmissibilities, there exists a constant $\mathcal{C} > 0$ such that

$$\sum_{n=0}^{N-1} \Delta t |v|_{1,\mathcal{T}}^2 \leq \mathcal{C} \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L} \in \mathcal{E}_{int}} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1})^2.$$

As a result, estimate (3.24) follows. □

Lemma 3.3.7. *(Estimate on the discrete evolutive term of the potential difference v). Let $(v_{\mathcal{D}}, \mathbf{w}_{\mathcal{D}}, c_{\mathcal{D}})$ be a solution of (3.13)-(3.15). There exists a constant $C_2 > 0$ depending on Ω , T , v_0 , \mathbf{w}_0 , c_0 such that the following estimate holds:*

$$\sum_{n=0}^{N-1} \Delta t \int_{\Omega} \left| \frac{v_h^{n+1} - v_h^n}{\Delta t} \right|^2 dx \leq C_2. \quad (3.27)$$

Proof. Let $\phi_h = v_h^{n+1} - v_h^n$ as test function in (3.17), expanding the discrete gradient over v_h^{n+1} and v_h^n , on gets

$$\Delta t \int_{\Omega} \left| \frac{v_h^{n+1} - v_h^n}{\Delta t} \right|^2 dx = \frac{1}{d} \int_{\Omega} (M_h \nabla_h v_h^{n+1} \cdot \nabla_h v_h^{n+1} - M_h \nabla_h v_h^{n+1} \cdot \nabla_h v_h^n) dx - \int_{\Omega} (I_{\text{ion}})_h^{n,n+1} (v_h^{n+1} - v_h^n).$$

Then using Cauchy-Schwartz' and Young's inequalities and making use of (3.4), we can find a constant $C > 0$ such that:

$$\begin{aligned} & \Delta t \int_{\Omega} \left| \frac{v_h^{n+1} - v_h^n}{\Delta t} \right|^2 dx \\ & \leq C \left[\|\nabla_h v_h^{n+1}\|_{L^2(\Omega)}^2 + \|\nabla_h v_h^n\|_{L^2(\Omega)}^2 + \|(I_{\text{ion}})_h^{n,n+1}\|_{L^2(\Omega)} (\|v_h^{n+1}\|_{L^2(\Omega)} + \|v_h^n\|_{L^2(\Omega)}) \right]. \end{aligned}$$

Finally taking sum over n and making use of $|(I_{\text{ion}})_h^{n,n+1}| \leq c_3$, and estimate (3.24), one obtains (3.27) \square

Remark 8. We note that since $c_{\mathcal{D}}$ and $w_{\mathcal{D}}$ satisfy the maximum principle stated in the previous subsection, we only need to prove in the following lemmata the regularity of their discrete gradients.

Lemma 3.3.8. (Estimate on the discrete gradient of $w_{\mathcal{D}}$). Let $(v_{\mathcal{D}}, w_{\mathcal{D}}, c_{\mathcal{D}})$ be a solution of the discrete finite volume scheme (3.13)-(3.15). Then there exists a constant $C_3 > 0$ depending on Ω, T, v_0, w_0, c_0 such that for $j = 1, \dots, 6$, there holds

$$\sum_{n=0}^{N-1} \Delta t \|\nabla_h w_{j,h}^{n+1}\|_{L^2(\Omega)}^2 \leq C_3. \quad (3.28)$$

Proof. In order to prove estimate (3.28), we drop the index j for simplicity of notation and we consider equation (3.14) separately on the control volumes K and L , then we subtract the two equations, to get for each $L \in N(K)$:

$$\begin{aligned} \frac{w_K^{n+1} - w_L^{n+1}}{\Delta t} - \frac{w_K^n - w_L^n}{\Delta t} &= \left(\alpha(v_K^n) - \alpha(v_L^n) \right) (1 - w_K^{n+1}) - \left(\alpha(v_L^n) + \beta(v_L^n) \right) (w_K^{n+1} - w_L^{n+1}) \\ &\quad - \left(\beta(v_K^n) - \beta(v_L^n) \right) w_K^{n+1} \end{aligned}$$

Multiplying both sides of the equation by $w_K^{n+1} - w_L^{n+1}$, then noting that $1 - w_K^{n+1} \leq 1$, $w_K^{n+1} \leq 1$ and $(\alpha(v_L^n) + \beta(v_L^n)) \geq 0$, we get

$$\begin{aligned} (w_K^{n+1} - w_L^{n+1}) \left(\frac{w_K^{n+1} - w_L^{n+1}}{\Delta t} - \frac{w_K^n - w_L^n}{\Delta t} \right) &\leq \left| \alpha(v_K^n) - \alpha(v_L^n) \right| |w_K^{n+1} - w_L^{n+1}| \\ &\quad + \left| \beta(v_K^n) - \beta(v_L^n) \right| |w_K^{n+1} - w_L^{n+1}|, \end{aligned}$$

and by Young's inequality with $\varepsilon = \frac{1}{2}$, we get:

$$\begin{aligned} (w_K^{n+1} - w_L^{n+1}) \left(\frac{w_K^{n+1} - w_L^{n+1}}{\Delta t} - \frac{w_K^n - w_L^n}{\Delta t} \right) &\leq \frac{\left| \alpha(v_K^n) - \alpha(v_L^n) \right|^2}{2} + \frac{\left| \beta(v_K^n) - \beta(v_L^n) \right|^2}{2} \\ &\quad + |w_K^{n+1} - w_L^{n+1}|^2. \end{aligned}$$

Now using the inequality $a(a - b) \geq \frac{1}{2}(a^2 - b^2)$ on the LHS of the above inequality we obtain:

$$\frac{1}{2} \frac{(w_K^{n+1} - w_L^{n+1})^2 - (w_K^n - w_L^n)^2}{\Delta t} \leq \frac{|\alpha(v_K^n) - \alpha(v_L^n)|^2}{2} + \frac{|\beta(v_K^n) - \beta(v_L^n)|^2}{2} + |w_K^{n+1} - w_L^{n+1}|^2.$$

By the regularity of α_j and β_j and the boundedness of v_K^n , there exists a constant $c_6 > 0$ such that:

$$\frac{(w_K^{n+1} - w_L^{n+1})^2 - (w_K^n - w_L^n)^2}{\Delta t} \leq c_6(v_K^n - v_L^n)^2 + 2|w_K^{n+1} - w_L^{n+1}|^2.$$

By the discrete differential form of Gronwall's inequality (see for instance [Emm99]), we obtain:

$$(w_K^n - w_L^n)^2 \leq (1 - 2\Delta t)^{-n} \left((w_K^0 - w_L^0)^2 + c_6 \Delta t \sum_{j=0}^{n-1} (1 - 2\Delta t)^j (v_K^j - v_L^j)^2 \right).$$

We note that for $\Delta t \leq 1/2$, we get

$$(w_K^n - w_L^n)^2 \leq e^{2T} \left((w_K^0 - w_L^0)^2 + c_6 \Delta t \sum_{j=0}^{n-1} (v_K^j - v_L^j)^2 \right).$$

Multiplying both sides by $\frac{|\sigma_{K,L}|}{d_{K,L}}$ and taking sums, we obtain:

$$\sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \frac{|\sigma_{K,L}|}{d_{K,L}} (w_K^n - w_L^n)^2 \leq e^{2T} \left(\frac{1}{d} |w_h^0|_{1, \mathcal{T}_h}^2 + c_6 \sum_{j=0}^{n-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \frac{|\sigma_{K,L}|}{d_{K,L}} (v_K^j - v_L^j)^2 \right).$$

Now using (3.24), we get:

$$\sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \frac{|\sigma_{K,L}|}{d_{K,L}} (w_K^n - w_L^n)^2 \leq e^{2T} \left(\frac{1}{d} |w_h^0|_{1, \mathcal{T}_h}^2 + c_6 C_1 \right).$$

leading to

$$\sum_{n=1}^N \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \frac{|\sigma_{K,L}|}{d_{K,L}} (w_K^n - w_L^n)^2 \leq T e^{2T} \left(\frac{1}{d} |w_h^0|_{1, \mathcal{T}_h}^2 + c_6 C_1 \right).$$

Thus estimate (3.28) is obtained. \square

Lemma 3.3.9. (Estimate on the discrete evolutive term of \mathbf{w}_D). *Let (v_D, \mathbf{w}_D, c_D) be a solution of the discrete finite volume scheme (3.50)-(3.52). Then there exists a constant $C_4 > 0$ depending on $\Omega, T, v_0, \mathbf{w}_0, c_0$ such that*

$$\sum_{n=0}^{N-1} \Delta t \int_{\Omega} \left| \frac{w_{j,h}^{n+1} - w_{j,h}^n}{\Delta t} \right|^2 dx \leq C_4. \quad (3.29)$$

Proof. Using (3.18) with $\xi_h = w_{j,h}^{n+1} - w_{j,h}^n$ along with Cauchy-Schwartz' and Young's inequalities in addition to the maximum principle obtained above, one can obtain estimate (3.29) in a straightforward way. \square

Lemma 3.3.10. (Estimate on the discrete gradient of $c_{\mathcal{D}}$). *Let $(v_{\mathcal{D}}, \mathbf{w}_{\mathcal{D}}, c_{\mathcal{D}})$ be a solution of the discrete finite volume scheme (3.13)-(3.15). Then there exists a constant $C_5 > 0$ depending on $\Omega, T, v_0, \mathbf{w}_0, c_0$ such that*

$$\sum_{n=0}^{N-1} \Delta t \|\nabla_h c_h^{n+1}\|_{L^2(\Omega)}^2 \leq C_5. \quad (3.30)$$

Proof. We proceed as in the previous lemma and we consider equation (3.15) repeatedly on the control volumes K and L , then we subtract the resulting equations to get for each $L \in N(K)$:

$$\begin{aligned} \frac{c_K^{n+1} - c_L^{n+1}}{\Delta t} - \frac{c_K^n - c_L^n}{\Delta t} &= -0.07(c_K^{n+1} - c_L^{n+1}) - g_s 10^{-4} \left(-7.7(f_K^{n+1} r_K^{n+1} - f_L^{n+1} r_L^{n+1}) \right. \\ &\quad \left. + 13.0287(f_K^{n+1} r_K^{n+1} \ln(c_K^{n+1}) - f_L^{n+1} r_L^{n+1} \ln(c_L^{n+1})) \right. \\ &\quad \left. + f_K^{n+1} r_K^{n+1} v_K^{n+1} - f_L^{n+1} r_L^{n+1} v_L^{n+1} \right). \end{aligned}$$

For simplicity, we write the above equation as:

$$\begin{aligned} \frac{c_K^{n+1} - c_L^{n+1}}{\Delta t} - \frac{c_K^n - c_L^n}{\Delta t} &= -0.07(c_K^{n+1} - c_L^{n+1}) - \left(H(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1}) \right. \\ &\quad \left. - H(v_L^{n+1}, f_L^{n+1}, r_L^{n+1}, c_L^{n+1}) \right), \end{aligned}$$

where

$$H(v, f, r, c) = g_s 10^{-4} f r (v - 7.7 + 13.0287 \ln(c)).$$

Multiplying both sides by $(c_K^{n+1} - c_L^{n+1})$ then applying Young's inequality, we get:

$$\begin{aligned} &(c_K^{n+1} - c_L^{n+1}) \left(\frac{c_K^{n+1} - c_L^{n+1}}{\Delta t} - \frac{c_K^n - c_L^n}{\Delta t} \right) \\ &\leq 0.57(c_K^{n+1} - c_L^{n+1})^2 + \frac{1}{2} \left(H(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^{n+1}) - H(v_L^{n+1}, f_L^{n+1}, r_L^{n+1}, c_L^{n+1}) \right)^2. \end{aligned}$$

Using the regularity of H and the maximum principle (in particular, $c_K^n \geq c_m > 0$), we can find a constant $C_H > 0$ such that:

$$\begin{aligned} &(c_K^{n+1} - c_L^{n+1}) \left(\frac{c_K^{n+1} - c_L^{n+1}}{\Delta t} - \frac{c_K^n - c_L^n}{\Delta t} \right) \\ &\leq 0.57(c_K^{n+1} - c_L^{n+1})^2 + \frac{C_H}{2} \left((v_K^{n+1} - v_L^{n+1})^2 + (f_K^{n+1} - f_L^{n+1})^2 + (r_K^{n+1} - r_L^{n+1})^2 \right. \\ &\quad \left. + (c_K^{n+1} - c_L^{n+1})^2 \right), \end{aligned}$$

and by the inequality $a(a - b) \geq 1/2(a^2 - b^2)$, we get:

$$\begin{aligned} &\frac{(c_K^{n+1} - c_L^{n+1})^2 - (c_K^n - c_L^n)^2}{\Delta t} \\ &\leq 1.14(c_K^{n+1} - c_L^{n+1})^2 + C_H \left((v_K^{n+1} - v_L^{n+1})^2 + (f_K^{n+1} - f_L^{n+1})^2 + (r_K^{n+1} - r_L^{n+1})^2 \right. \\ &\quad \left. + (c_K^{n+1} - c_L^{n+1})^2 \right). \end{aligned}$$

So we have

$$\begin{aligned} & \frac{(c_K^{n+1} - c_L^{n+1})^2 - (c_K^n - c_L^n)^2}{\Delta t} \\ & \leq (1.14 + C_H)(c_K^{n+1} - c_L^{n+1})^2 + C_H \left((v_K^{n+1} - v_L^{n+1})^2 + (f_K^{n+1} - f_L^{n+1})^2 + (r_K^{n+1} - r_L^{n+1})^2 \right). \end{aligned}$$

Estimate (3.30) follows easily from this last inequality by using Gronwall's inequality provided that $\Delta t \leq \frac{1}{1.14 + C_H}$ by a similar argument to the one used in the case of proving (3.28).

Therefore the proof of the lemma is complete. \square

Lemma 3.3.11. (Estimate on the discrete evolutive term of c_D). *Let (v_D, w_D, c_D) be a solution of the discrete finite volume scheme (3.13)-(3.15). Then there exists a constant $C_6 > 0$ depending on Ω, T, v_0, w_0, c_0 such that*

$$\sum_{n=0}^{N-1} \Delta t \int_{\Omega} \left| \frac{c_h^{n+1} - c_h^n}{\Delta t} \right|^2 dx \leq C_6. \quad (3.31)$$

Proof. Using (3.19) with $\psi_h = c_h^{n+1} - c_h^n$, one can obtain estimate (3.31) straightforwardly. \square

Compactness Estimates on the Discrete Solution

We state and prove now some estimates on the time and space translates of the discrete solutions v_h, w_h, c_h that are needed in the application of the compactness argument.

Lemma 3.3.12. *There exists a constant C dependent on Ω, T, v_0, w_0, c_0 such that:*

$$\forall y \in \mathbb{R}^d, \iint_{\Omega' \times (0, T)} |v_h(x + y, t) - v_h(x, t)|^2 dx dt \leq C|y|(|y| + 2h), \quad (3.32)$$

where $\Omega' := \{x \in \Omega : [x, x + y] \subset \Omega\}$, and

$$\forall \tau \in (0, T), \iint_{\Omega \times (0, T - \tau)} |v_h(x, t + \tau) - v_h(x, t)|^2 dx dt \leq C\tau. \quad (3.33)$$

Proof. We start by proving (3.32):

Let $y \in \mathbb{R}^d, x \in \Omega'$. Define on Ω' the function:

$$\chi_{\sigma_{K,L}}(x) = \begin{cases} 1 & \text{if } [x, x + y] \text{ intersects } \sigma_{K,L}, K \text{ and } L, \\ 0 & \text{otherwise.} \end{cases}$$

Next, define $c_{\sigma_{K,L}} = \left| \frac{y}{|y|} \mathbf{n}_{K,L} \right|$ and observe that

$$\int_{\Omega'} \chi_{\sigma_{K,L}} dx \leq |\sigma_{K,L}| |y| c_{\sigma_{K,L}}.$$

Writing

$$|v_h(x + y, t) - v_h(x, t)| \leq \sum_{\sigma_{K,L}} \chi_{\sigma_{K,L}}(x) |v_L^{n+1} - v_K^{n+1}|,$$

and applying Cauchy-Schwartz' inequality, one gets:

$$|v_h(x+y, t) - v_h(x, t)|^2 \leq \sum_{\sigma_{K,L}} \chi_{\sigma_{K,L}} d_{K,L}(x) \sum_{\sigma_{K,L}} \frac{|v_L^{n+1} - v_K^{n+1}|^2}{d_{K,L}} \chi_{\sigma_{K,L}}$$

Noting that $\sum_{\sigma_{K,L}} \chi_{\sigma_{K,L}} d_{K,L} \leq |y| + 2h$, there holds:

$$\begin{aligned} \iint_{(0,T) \times \Omega'} |v_h(x+y, t) - v_h(x, t)|^2 dx dt &\leq (|y| + 2h) \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L}} \frac{|v_L^{n+1} - v_K^{n+1}|^2}{d_{K,L}} \int_{\Omega'} \chi_{\sigma_{K,L}} dx \\ &\leq |y|(|y| + 2h) \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{K,L}} \frac{|v_L^{n+1} - v_K^{n+1}|^2}{d_{K,L}} |\sigma_{K,L}|. \end{aligned}$$

Using (3.24), one deduces (3.32). The proof of (3.33) is similar, and the details can be found in [EGH00] or in the proof of Lemma 6.1 in [BK09]. \square

Similar estimates can be shown on the gating variables w and the concentration variable c , as stated in the following lemmata:

Lemma 3.3.13. *There exists a constant C dependent on Ω, T, v_0, w_0, c_0 such that:*

$$\forall y \in \mathbb{R}^d, \iint_{\Omega' \times (0,T)} |w_h(x+y, t) - w_h(x, t)|^2 dx dt \leq C|y|(|y| + 2h), \quad (3.34)$$

where $\Omega' := \{x \in \Omega : [x, x+y] \subset \Omega\}$, and

$$\forall \tau \in (0, T), \iint_{\Omega \times (0, T-\tau)} |w_h(x, t+\tau) - w_h(x, t)|^2 dx dt \leq C\tau. \quad (3.35)$$

Lemma 3.3.14. *There exists a constant C dependent on Ω, T, v_0, w_0, c_0 such that:*

$$\forall y \in \mathbb{R}^d, \iint_{\Omega' \times (0,T)} |c_h(x+y, t) - c_h(x, t)|^2 dx dt \leq C|y|(|y| + 2h), \quad (3.36)$$

where $\Omega' := \{x \in \Omega : [x, x+y] \subset \Omega\}$, and

$$\forall \tau \in (0, T), \iint_{\Omega \times (0, T-\tau)} |c_h(x, t+\tau) - c_h(x, t)|^2 dx dt \leq C\tau. \quad (3.37)$$

Convergence of the Finite Volume Scheme

As a consequence of (3.32), (3.33), (3.34), (3.35), (3.36), (3.37) and Kolmogorov's theorem, we have the following result:

Lemma 3.3.15. *There exists a subsequence of $U_{\mathcal{D}} = (v_{\mathcal{D}}, w_{\mathcal{D}}, c_{\mathcal{D}})$, not relabeled, such that as $\Delta t, h \rightarrow 0$,*

- $v_{\mathcal{D}} \rightarrow v$ strongly in $L^2(\Omega_T)$,
- $w_{\mathcal{D}} \rightarrow w$ strongly in $L^2(\Omega_T)^6$,

— $c_{\mathcal{D}} \rightarrow c$ strongly in $L^2(\Omega_T)$.

Our goal now is to prove that the limit functions v, \mathbf{w}, c constitute a weak solution of the monodomain model as in Definition 3.4.1. We start by considering (3.13): let T be a fixed positive constant and $\varphi \in D([0, T] \times \bar{\Omega})$, multiply (3.13) by $\Delta t \varphi(t_n, x_K)$ and sum over $K \in \mathcal{T}_h$ and $n \in \{0, \dots, N-1\}$ to get:

$$\begin{aligned} & \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K| (v_K^{n+1} - v_K^n) \varphi(t_n, x_K) - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) \varphi(t_n, x_K) \\ = & - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\ & \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) \varphi(t_n, x_K); \end{aligned}$$

or

$$T_1 + T_2 = T_3 + T_4 + T_5 + T_6.$$

Using summation by parts in time and keeping in mind that $\varphi(T, x_K) = 0$, notice that T_1 can be written as:

$$\begin{aligned} T_1 &= \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K| (v_K^{n+1} - v_K^n) \varphi(t_n, x_K) \\ &= - \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} |K| v_K^{n+1} (\varphi(t_{n+1}, x_K) - \varphi(t_n, x_K)) - \sum_{K \in \mathcal{T}_h} |K| v_K^0 \varphi(0, x_K) \\ &= - \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} v_K^{n+1} \partial_t \varphi(t, x_K) dx dt - \sum_{K \in \mathcal{T}_h} \int_K v_K^0 \varphi(0, x_K) dx \\ &:= -T_{1,1} - T_{1,2} \end{aligned}$$

Consider first $T_{1,2}$, and observe that:

$$\begin{aligned} \left| T_{1,2} - \sum_{K \in \mathcal{T}_h} \int_K v_K^0 \varphi(0, x) dx \right| &\leq \sum_K \int_K |v_K^0| |\varphi(0, x_K) - \varphi(0, x)| dx \\ &\leq Ch, \end{aligned}$$

where the last inequality follows from the boundedness of v_K^0 , the regularity of φ and Taylor's theorem. Hence, one concludes that:

$$\left| T_{1,2} - \int_{\Omega} v_h^0 \varphi(0, x) dx \right| \rightarrow 0 \text{ as } h \rightarrow 0.$$

Second, let $T_{1,1}^* := \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} \int_K v_K^{n+1} \partial_t \varphi(t, x) dx dt$, and observe that:

$$\begin{aligned} T_{1,1} - T_{1,1}^* &= \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} v_K^{n+1} \int_{t_n}^{t_{n+1}} \int_K (\partial_t \varphi(t, x_K) - \partial_t \varphi(t, x)) dx dt \\ &\leq c_7 h \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| v_K^{n+1}, \text{ (by regularity of } \varphi \text{ and Taylor),} \\ &\leq c_8 h, \end{aligned}$$

where c_7 and c_8 are positive constants and c_8 depends on h , Δt and v_M . As a result, one has:

$$|T_{1,1} - T_{1,1}^*| \rightarrow 0 \text{ as } h \rightarrow 0.$$

Now, consider

$$T_2 := - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) \varphi(t_n, x_K)$$

and rewrite it as:

$$T_2 = \frac{1}{2} \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} \tau_{\sigma_{K,L}} (v_L^{n+1} - v_K^{n+1}) (\varphi(t_n, x_L) - \varphi(t_n, x_K)).$$

Noting that

$$\tau_{\sigma_{K,L}} = |\sigma_{K,L}| \frac{\lambda_K \lambda_L}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}} = M_{KL} \frac{|\sigma_{K,L}|}{d_{K,L}},$$

where $M_{KL} = \frac{\lambda_K \lambda_L}{\lambda_K d_{L,\sigma} + \lambda_L d_{K,\sigma}}$, T_2 can be written as:

$$\begin{aligned} T_2 &= \frac{1}{2} \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} M_{KL} |\sigma_{K,L}| (v_L^{n+1} - v_K^{n+1}) \frac{(\varphi(t_n, x_L) - \varphi(t_n, x_K))}{d_{K,L}} \\ &= \frac{1}{2} \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} |\sigma_{K,L}| (v_L^{n+1} - v_K^{n+1}) \int_{t_n}^{t_{n+1}} M_{KL} \frac{(\varphi(t_n, x_L) - \varphi(t_n, x_K))}{d_{K,L}} dt. \end{aligned}$$

Continuing, define:

$$T_2^* = - \int_0^T \int_{\Omega} v_{\mathcal{D}} \nabla \cdot (\lambda \nabla \varphi) dx dt$$

and observe that

$$T_2^* \rightarrow - \int_0^T \int_{\Omega} v \nabla \cdot (\lambda \nabla \varphi) dx dt = \int_0^T \int_{\Omega} \lambda \nabla v \cdot \nabla \varphi dx dt \text{ as } h \rightarrow 0.$$

Furthermore, note that:

$$\begin{aligned} T_2^* &= - \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} v_K^{n+1} \int_{t_n}^{t_{n+1}} \int_{\sigma_{K,L}} \lambda \nabla \varphi \cdot \mathbf{n}_{K,L} d\gamma dt \\ &= \frac{1}{2} \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} (v_L^{n+1} - v_K^{n+1}) \int_{t_n}^{t_{n+1}} \int_{\sigma_{K,L}} \lambda \nabla \varphi \cdot \mathbf{n}_{K,L} d\gamma dt. \end{aligned}$$

Hence,

$$\begin{aligned} T_2 - T_2^* &= \frac{1}{2} \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \sum_{L \in N(K)} |\sigma_{K,L}| (v_L^{n+1} - v_K^{n+1}) \\ &\quad \left(\int_{t_n}^{t_{n+1}} M_{KL} \frac{(\varphi(t_n, x_L) - \varphi(t_n, x_K))}{d_{K,L}} dt - \frac{1}{|\sigma_{K,L}|} \int_{t_n}^{t_{n+1}} \int_{\sigma_{K,L}} \lambda \nabla \varphi \cdot \mathbf{n}_{K,L} d\gamma dt \right). \end{aligned}$$

Since the straight line (x_K, x_L) is orthogonal to $\sigma_{K,L}$, there holds:

$$\frac{x_L - x_K}{d_{K,L}} = \mathbf{n}_{K,L}.$$

This implies from the regularity of φ that

$$\frac{(\varphi(t_n, x_L) - \varphi(t_n, x_K))}{d_{K,L}} = \nabla\varphi \cdot \mathbf{n}_{K,L},$$

for some $x \in \{(1-s)x_K + sx_L, s \in (0, 1)\}$, so:

$$\left| \int_{t_n}^{t_{n+1}} M_{KL} \frac{(\varphi(t_n, x_L) - \varphi(t_n, x_K))}{d_{K,L}} dt - \frac{1}{|\sigma_{K,L}|} \int_{t_n}^{t_{n+1}} \int_{\sigma_{K,L}} \lambda \nabla\varphi \cdot \mathbf{n}_{K,L} d\gamma dt \right| \leq c_9 \Delta t h, \quad (3.38)$$

for some constant $c_9 > 0$. Using (3.38) and (3.24), one deduces

$$\lim_{h \rightarrow 0} T_2 = \iint_{\Omega_T} \lambda \nabla v \cdot \nabla \varphi dx dt.$$

Next, to show that:

$$T_3 := - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_{Pot}(v_K^{n+1}) \varphi(t_n, x_K) \rightarrow \iint_{\Omega_T} -I_{Pot}(v) \varphi := L_3.$$

First rewrite T_3 and L_3 as:

$$T_3 = - \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} \int_K I_{Pot}(v_K^{n+1}) \varphi(t_n, x_K),$$

and

$$L_3 = \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} \int_K -I_{Pot}(v) \varphi(t, x) dx dt.$$

Then note that $|T_3 - L_3|$ can be written as:

$$\begin{aligned} |T_3 - L_3| &= \left| \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} I_{Pot}(v_K^{n+1}) \int_{t_n}^{t_{n+1}} \int_K (\varphi(t_n, x_K) - \varphi(t, x)) \right. \\ &\quad \left. + \int_{t_n}^{t_{n+1}} \int_K (I_{Pot}(v_K^{n+1}) \varphi(t, x) - I_{Pot}(v) \varphi(t, x)) \right| \end{aligned}$$

For all $x \in K$ and $t \in [t_n, t_{n+1}]$, there holds

$$|\varphi(t_n, x_K) - \varphi(t, x)| \leq c_{10}(\Delta t + h),$$

for some $c_{10} > 0$. Moreover, $|\varphi(t, x)| \leq c_{11}$ for some $c_{11} > 0$. Therefore,

$$|T_3 - L_3| \leq c_{10}(\Delta t + h) \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |I_{Pot}(v_K^{n+1})| + c_{11} \iint_{\Omega_T} |I_{Pot}(v_D) - I_{Pot}(v)| dx dt.$$

Since $|I_{Pot}(v_K^{n+1})| \leq c_1$, we get

$$|T_3 - L_3| \leq c_1 c_{10} (\Delta t + h) T |\Omega| + c_{11} \iint_{\Omega_T} |I_{Pot}(v_h) - I_{Pot}(v)| dx dt.$$

On the other hand, since $v_h \rightarrow v$ a.e. in Ω_T and I_{Pot} is continuous, then $I_{Pot}(v_h) \rightarrow I_{Pot}(v)$ a.e. in Ω_T . Moreover, since $I_{Pot}(v_h) \in L^\infty(\Omega_T)$, then by Lebesgue's dominated convergence we get the convergence of $I_{Pot}(v_h)$ to $I_{Pot}(v)$ in $L^1(\Omega_T)$. As a result, we conclude that $T_3 \rightarrow L_3$. Similarly, to show that

$$T_4 := - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_z(v_K^{n+1}, z_K^{n+1}) \varphi(t_n, x_K) \rightarrow \iint_{\Omega_T} -I_z(v, z) \varphi := L_4,$$

T_4 and L_4 are written as:

$$T_4 = - \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} \int_K I_z(v_K^{n+1}, z_K^{n+1}) \varphi(t_n, x_K),$$

and

$$L_4 = \sum_{n=0}^{n-1} \sum_{K \in \mathcal{T}_h} \int_{t_n}^{t_{n+1}} \int_K -I_z(v, z) \varphi(t, x) dx dt.$$

Then note that $|T_4 - L_4|$ is given by:

$$\begin{aligned} |T_4 - L_4| &= \left| \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} I_z(v_K^{n+1}, z_K^{n+1}) \int_{t_n}^{t_{n+1}} \int_K (\varphi(t_n, x_K) - \varphi(t, x)) \right. \\ &\quad \left. + \int_{t_n}^{t_{n+1}} \int_K (I_z(v_K^{n+1}, z_K^{n+1}) \varphi(t, x) - I_z(v, z) \varphi(t, x)) \right|. \end{aligned}$$

Therefore,

$$|T_4 - L_4| \leq c_{10} (\Delta t + h) \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |I_z(v_K^{n+1}, z_K^{n+1})| + c_{11} \iint_{\Omega_T} |I_z(v_D, z_D) - I_z(v, z)| dx dt.$$

By a similar discussion to the one done in the case of T_3 , we get $T_4 \rightarrow L_4$.

Also, in order to show that

$$T_5 := - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \varphi(t_n, x_K) \rightarrow \iint_{\Omega_T} -I_{Na}(v, m, o, l) \varphi := L_5,$$

note that $|T_5 - L_5|$ can be written as:

$$\begin{aligned} |T_5 - L_5| &= \left| \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \int_{t_n}^{t_{n+1}} \int_K (\varphi(t_n, x_K) - \varphi(t, x)) \right. \\ &\quad \left. + \int_{t_n}^{t_{n+1}} \int_K (I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \varphi(t, x) - I_{Na}(v, m, o, l) \varphi(t, x)) \right|. \end{aligned}$$

Therefore,

$$\begin{aligned} |T_5 - L_5| &\leq c_{10}(\Delta t + h) \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1})| \\ &\quad + c_{11} \iint_{\Omega_T} |I_{Na}(v_{\mathcal{D}}, m_{\mathcal{D}}, o_{\mathcal{D}}, l_{\mathcal{D}}) - I_{Na}(v, m, o, l)| dx dt. \end{aligned}$$

Consequently, $T_5 \rightarrow L_5$ as above.

Moreover, in order to get

$$T_6 := - \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \varphi(t_n, x_K) \rightarrow \iint_{\Omega_T} -I_s(v, f, r, c) \varphi := L_6.$$

write $|T_6 - L_6|$ as:

$$\begin{aligned} |T_6 - L_6| &= \left| \sum_{n=0}^{N-1} \sum_{K \in \mathcal{T}_h} I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \int_{t_n}^{t_{n+1}} \int_K \left(\varphi(t_n, x_K) - \varphi(t, x) \right) \right. \\ &\quad \left. + \int_{t_n}^{t_{n+1}} \int_K \left(I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \varphi(t, x) - I_s(v, f, r, c) \varphi(t, x) \right) \right|. \end{aligned}$$

Therefore,

$$\begin{aligned} |T_6 - L_6| &\leq c_{10}(\Delta t + h) \sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{T}_h} |K| |I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n)| \\ &\quad + c_{11} \iint_{\Omega_T} |I_s(v_{\mathcal{D}}, f_{\mathcal{D}}, r_{\mathcal{D}}, c_{\mathcal{D}}) - I_s(v, f, r, c)| dx dt. \end{aligned}$$

And one obtains $T_6 \rightarrow L_6$ by a similar classical argument as above. Reasoning along the same lines, one also concludes that (3.9) and (3.10) hold.

3.4 Numerical Analysis of CVFE Scheme

In this section, we investigate a positive nonlinear control volume finite element (CVFE) scheme, based on Godunov's flux approximation of the diffusion term, for System (3.1)-(3.3) using an anisotropic diffusion tensor. Such schemes were proposed in [CG16] for solving degenerate anisotropic parabolic diffusion equations modeling flows in porous media and in [CIS17] for a degenerate nonlinear chemotaxis model. In this scheme, degrees of freedom are assigned to vertices of a primal triangular mesh, as in finite element methods. The diffusion term which involves an anisotropic tensor is discretized on a dual mesh using the diffusion fluxes provided by the conforming finite element reconstruction on the primal mesh. The scheme ensures the validity of the discrete maximum principle without any restriction on the transmissibility coefficients. By using a compactness argument, we obtain the convergence of the discrete solution and as a consequence, we get the existence of a weak solution of the original model. Finally, we illustrate the efficiency of the proposed scheme by exhibiting some numerical results.

3.4.1 Mathematical Assumptions

We consider a bounded, open, polygonal, connected domain $\Omega \subset \mathbb{R}^d$, $d = 2$, with boundary $\partial\Omega$, a fixed final time $T > 0$, and we set $\Omega_T = (0, T) \times \Omega$. Assumptions (H.2)-(H.4) used in the previous section are also used herein, but assumption (H.1) is modified to:

(H.1)' Assuming an anisotropic medium, the conductivity is represented by the tensor $\Lambda(x)$ which is a bounded, uniformly positive symmetric tensor on Ω , that is, for all $\xi \in \mathbb{R}^d$:

$$\Lambda : \Omega \rightarrow \mathbb{R}^{d \times d}, \text{ and } \exists m_0, M_0 \text{ such that } 0 < m_0 |\xi|^2 \leq \Lambda \xi \cdot \xi \leq M_0 |\xi|^2, \text{ for a.e. } x \in \Omega. \quad (3.39)$$

For simplicity of the calculations herein, we introduce a rescaling \tilde{v} of the potential difference v given by the relation:

$$\tilde{v} = \frac{v - v_m}{v_M - v_m},$$

and we denote by

$$\tilde{I}_{\text{ion}}(\tilde{v}, \mathbf{w}, c) := \frac{1}{v_M - v_m} I_{\text{ion}}((v_M - v_m)\tilde{v} + v_m, \mathbf{w}, c),$$

$$\tilde{\alpha}_j(\tilde{v}) := \alpha_j((v_M - v_m)\tilde{v} + v_m),$$

$$\tilde{\beta}_j(\tilde{v}) := \beta_j((v_M - v_m)\tilde{v} + v_m),$$

and

$$\tilde{I}_{s,1}(\tilde{v}, f, r, c) := I_s((v_M - v_m)\tilde{v} + v_m, f, r, c).$$

So assumption (3.7) becomes:

$$\begin{aligned} 0 &\leq \tilde{v}_0 \leq 1 && \text{in } \Omega, \\ c_m &\leq c_0 \leq c_M && \text{in } \Omega, \\ 0 &\leq w_{0,j} \leq 1 && \text{in } \Omega, \text{ for } j = 1, \dots, 6. \end{aligned} \quad (3.40)$$

We further notice that the ionic function \tilde{I}_{ion} verifies for all $w_j \in [0, 1]$, $j = 1, \dots, 6$ and $c \in [c_m, c_M]$

$$\tilde{I}_{\text{ion}}(0, \mathbf{w}, c) \leq 0 \text{ and } \tilde{I}_{\text{ion}}(1, \mathbf{w}, c) \geq 0. \quad (3.41)$$

To summarize, we have the following system of equations:

$$\begin{aligned} \frac{\partial \tilde{v}}{\partial t} &= \nabla \cdot (\Lambda \nabla \tilde{v}) - \tilde{I}_{\text{ion}}(\tilde{v}, \mathbf{w}, c), && \text{for a.e. } (t, x) \in \Omega_T, \\ \frac{\partial w_j}{\partial t} &= \tilde{\alpha}_j(\tilde{v})(1 - w_j) - \tilde{\beta}_j(\tilde{v})w_j, && \text{for a.e. } (t, x) \in \Omega_T \text{ and } j = 1, \dots, 6, \\ \frac{\partial c}{\partial t} &= 0.07(10^{-4} - c) - 10^{-4} \tilde{I}_{s,1}(\tilde{v}, f, r, c), && \text{for a.e. } (t, x) \in \Omega_T, \\ \tilde{v}(0, x) &= \tilde{v}_0(x), && \text{for a.e. } x \in \Omega, \\ \mathbf{w}(0, x) &= \mathbf{w}_0(x), && \text{for a.e. } x \in \Omega, \\ c(0, x) &= c_0(x), && \text{for a.e. } x \in \Omega \\ \Lambda \nabla \tilde{v} \cdot \mathbf{n} &= 0 && \text{a.e. on } \partial\Omega \times (0, T). \end{aligned} \quad (3.42)$$

For simplicity of notation, we will omit in what follows the \sim symbol.

3.4.2 Weak Formulation

Before defining the discrete scheme, we need to provide a relevant definition of a weak solution for the monodomain model.

Definition 3.4.1. A weak solution of (3.42) is a vector $\mathbf{U} = (v, \mathbf{w}, c)$, of functions such that $v \in L^\infty(\Omega_T) \cap L^2(0, T; H^1(\Omega))$, $\mathbf{w} \in \left(L^\infty(\Omega_T)\right)^6$, $c \in L^\infty(\Omega_T)$, with $0 \leq v \leq 1$, $0 \leq w_j \leq 1$ for $j = 1, \dots, 6$, $0 < c_m \leq c \leq c_M$, and for all φ and $\xi \in \mathcal{D}([0, T] \times \bar{\Omega})$, there holds:

$$-\int_{\Omega} v_0(x)\varphi(0, x)dx + \iint_{\Omega_T} \left(-v\partial_t\varphi + \Lambda\nabla v \cdot \nabla\varphi\right)dxdt = \iint_{\Omega_T} -I_{\text{ion}}(v, \mathbf{w}, c)\varphi dxdt, \quad (3.43)$$

$$-\int_{\Omega} w_{0,j}(x)\xi(0, x)dx + \iint_{\Omega_T} -w_j\partial_t\xi dxdt = \iint_{\Omega_T} (\alpha_j(v)(1-w_j) - \beta_j(v)w_j)\xi dxdt, \quad (3.44)$$

for $j = 1, \dots, 6$, and

$$-\int_{\Omega} c_0(x)\xi(0, x)dx + \iint_{\Omega_T} -c\partial_t\xi dxdt = \iint_{\Omega_T} (0.07(10^{-4} - c) - 10^{-4}I_{s,1}(v, f, r, c))\xi dxdt. \quad (3.45)$$

3.4.3 Discrete Problem

Space Discretization

Following [CG16, CIS17], we give a precise definition of the CVFE scheme for the monodomain equations.

We recall that Ω is an open, bounded, connected polygonal domain in \mathbb{R}^d , $d = 2$, with boundary $\partial\Omega$. Let \mathcal{T} be a conforming triangulation of Ω . We assume that $\bigcup_{T \in \mathcal{T}} \bar{T} = \bar{\Omega}$. We denote by \mathcal{V}

the set of vertices (located at positions $(x_K)_{K \in \mathcal{V}}$) and by \mathcal{E} the set of edges of the triangulation \mathcal{T} . For $T \in \mathcal{T}$, \mathcal{E}_T denotes the subset of edges σ such that $\bigcup_{\sigma \in \mathcal{E}_T} \sigma = \partial T$. We also assume that

$$\mathcal{E} = \bigcup_{T \in \mathcal{T}} \mathcal{E}_T.$$

For $T \in \mathcal{T}$, x_T denotes the center of gravity of T , h_T the diameter of the triangle T , and ρ_T the diameter of the circle inscribed in T . Then we define the mesh diameter h and the mesh regularity $\theta_{\mathcal{T}}$ by

$$h = \max_{T \in \mathcal{T}} h_T, \quad \theta_{\mathcal{T}} = \max_{T \in \mathcal{T}} \frac{h_T}{\rho_T}.$$

For $K \in \mathcal{V}$, the subset of \mathcal{T} made of triangles that have K as a vertex are denoted by \mathcal{T}_K , and the set of edges having the vertex K at an extremity by \mathcal{E}_K . Furthermore, the subset \mathcal{V}_K of \mathcal{V} consists of vertices L that share a common edge with K .

Once the primal triangular discretization is constructed, we build a different space discretization of Ω called the dual barycentric discretization \mathcal{M} . To each $K \in \mathcal{V}$, we associate a control volume ω_K (of measure m_K) which vertices are the centers of gravity x_T of the triangles $T \in \mathcal{T}_K$ and the barycenters of the edges $\sigma \in \mathcal{E}_K$. We note that $\bar{\Omega} = \bigcup_{K \in \mathcal{V}} \bar{\omega}_K$.

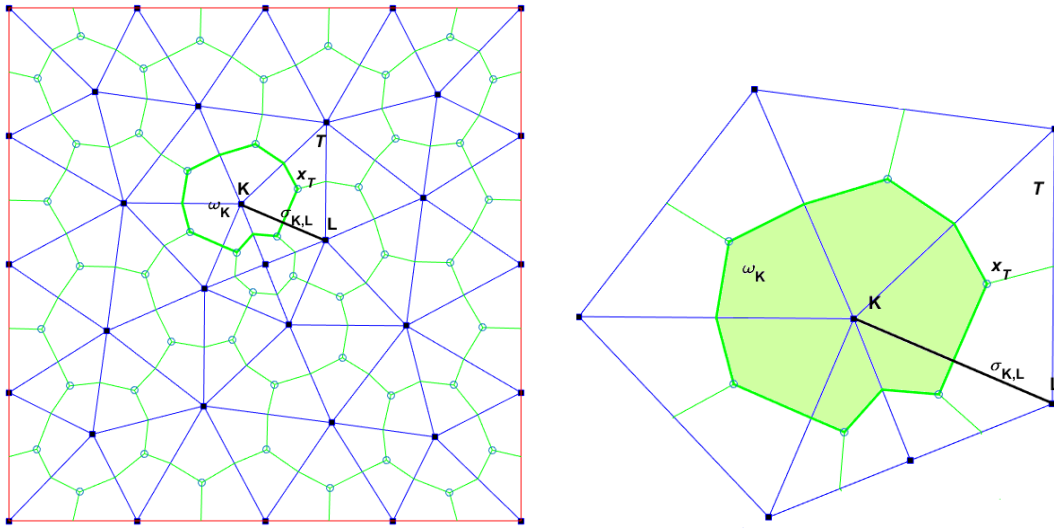


Figure 3.1 – Triangular mesh \mathcal{T} (in blue), dual mesh \mathcal{M} (in green)

Discrete Spaces

We construct two discrete functional spaces corresponding to the primal and dual meshes. The first one is the usual \mathbb{P}_1 -conforming finite element space denoted by:

$$V_{\mathcal{T}} = \{f \in C(\Omega); f|_T \in \mathbb{P}_1(\mathbb{R}^d), \forall T \in \mathcal{T}\}.$$

We also define the space $X_{\mathcal{M}}$ of piecewise constant functions on the dual cells by

$$X_{\mathcal{M}} = \{f : \Omega \rightarrow \bar{\mathbb{R}} \text{ measurable}; f|_{\omega_K} \in \mathbb{P}_0(\mathbb{R}^d), \forall K \in \mathcal{V}\}.$$

Given a vector $(v_K)_{K \in \mathcal{V}} \in \mathbb{R}^{\text{Card}(\mathcal{V})}$, there exists a unique $v_{\mathcal{T}} \in V_{\mathcal{T}}$ and a unique $v_{\mathcal{M}} \in X_{\mathcal{M}}$ such that

$$v_{\mathcal{T}}(x_K) = v_{\mathcal{M}}(x_K) = v_K, \quad \forall K \in \mathcal{V}.$$

In what follows, we denote by $(e_K)_{K \in \mathcal{V}}$ the canonical basis of $V_{\mathcal{T}}$, characterized by

$$e_K(x_L) = \delta_{KL}, \quad \forall K \in \mathcal{V}.$$

We remark that

$$\sum_{K \in \mathcal{V}} e_K(x) = 1, \quad \forall x \in \Omega.$$

Therefore

$$\sum_{K \in \mathcal{V}} \int_{\Omega} e_K(x) dx = |\Omega|,$$

and

$$\sum_{K \in \mathcal{V}} \nabla e_K(x) = 0, \text{ for a.e. } x \in \Omega. \quad (3.46)$$

We use the finite element approximations for v , w_j , $j = 1, \dots, 6$ and c , where:

$$v \approx v_{\mathcal{T}} = \sum_{L \in \mathcal{V}} v_L e_L, \quad w_j \approx w_{j,\mathcal{T}} = \sum_{L \in \mathcal{V}} w_{j,L} e_L, \quad \text{and } c \approx c_{\mathcal{T}} = \sum_{L \in \mathcal{V}} c_L e_L.$$

For all $(K, L) \in \mathcal{V}^2$, we define the transmissibility coefficient Λ_{KL} by

$$\Lambda_{KL} = - \int_{\Omega} \Lambda(x) \nabla e_K(x) \cdot \nabla e_L(x) dx = \Lambda_{LK}. \quad (3.47)$$

Due to (3.46), we have $\Lambda_{KK} = - \sum_{L \neq K} \Lambda_{KL} < 0$. As a result, we have

$$\int_{\Omega} \Lambda(x) \nabla v_{\mathcal{T}} \cdot \nabla \varphi_{\mathcal{T}} = \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (v_K - v_L) (\varphi_K - \varphi_L). \quad (3.48)$$

Time Discretization

The discretization of the time interval $(0, T)$ is given by a time step Δt , and a positive integer N chosen such that $N\Delta t = T$. We set $t_n = n\Delta t$ for $n \in \{0, \dots, N\}$.

Space-time Discretization

We define the space and time discrete spaces $V_{\mathcal{T}, \Delta t}$ and $X_{\mathcal{M}, \Delta t}$ as the set of piecewise constant functions in time with values in $V_{\mathcal{T}}$ and $X_{\mathcal{M}}$ respectively, i.e.:

$$f \in V_{\mathcal{T}, \Delta t} \Leftrightarrow f(t, x) = f(t_{n+1}, x) \in V_{\mathcal{T}}, \quad \forall t \in (t_n, t_{n+1}],$$

and

$$f \in X_{\mathcal{M}, \Delta t} \Leftrightarrow f(t, x) = f(t_{n+1}, x) \in X_{\mathcal{M}}, \quad \forall t \in (t_n, t_{n+1}].$$

For a given $(v_K^{n+1})_{n \in \{0, \dots, N-1\}, K \in \mathcal{V}} \in \mathbb{R}^{N \text{Card}(\mathcal{V})}$, we denote the unique elements $v_{\mathcal{T}, \Delta t} \in V_{\mathcal{T}, \Delta t}$ and $v_{\mathcal{M}, \Delta t} \in X_{\mathcal{M}, \Delta t}$ such that

$$v_{\mathcal{T}, \Delta t}(t, x_K) = v_{\mathcal{M}, \Delta t}(t, x_K) = v_K^{n+1}, \quad \forall K \in \mathcal{V}, \forall t \in (t_n, t_{n+1}].$$

The CVFE Scheme

In order to discretize the equations of (3.42), we formally integrate the equations over $(t_n, t_{n+1}) \times \omega_K$ and we use Green's theorem on the diffusive term. We obtain:

$$\begin{aligned} \int_{\omega_K} v(t_{n+1}, x) - v(t_n, x) dx &= \int_{t_n}^{t_{n+1}} \int_{\partial \omega_K} (\Lambda \nabla v) \cdot \mathbf{n} d\gamma dt - \int_{t_n}^{t_{n+1}} \int_{\omega_K} I_{ion}(v, m, o, l, f, r, z, c) dx dt, \\ \int_{\omega_K} w_j(t_{n+1}, x) - w_j(t_n, x) dx &= \int_{t_n}^{t_{n+1}} \int_{\omega_K} (\alpha_j(v)(1 - w_j) - \beta_j(v)w_j) dx dt, \quad \text{for } j = 1, \dots, 6, \\ \int_{\omega_K} c(t_{n+1}, x) - c(t_n, x) dx &= \int_{t_n}^{t_{n+1}} \int_{\omega_K} (0.07(10^{-4} - c) - 10^{-4} I_{s,1}(v, f, r, c)) dx dt. \end{aligned}$$

We use a time discretization in which the linear terms of the ODEs corresponding to the recovery variables are implicitly discretized whereas the nonlinear terms are considered explicitly. In order to ensure the maximum principle, the potential difference v in the ionic function and the logarithmic term of the ODE involving the concentration variable c are considered implicitly. We propose the following semi-implicit CVFE scheme:

We look for $(v_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$, $(\mathbf{w}_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$, and $(c_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$ solution of the nonlinear system: $\forall K \in \mathcal{V}$,

$$v_K^0 = \frac{1}{m_K} \int_{\omega_K} v_0(x) dx, \mathbf{w}_K^0 = \frac{1}{m_K} \int_{\omega_K} \mathbf{w}_0(x) dx, \text{ and } c_K^0 = \frac{1}{m_K} \int_{\omega_K} c_0(x) dx \quad (3.49)$$

and $\forall n \in \{0, \dots, N-1\}, \forall K \in \mathcal{V}$,

$$\begin{aligned} & \frac{m_K}{\Delta t} (v_K^{n+1} - v_K^n) + \sum_{\sigma_{KL} \in \mathcal{E}_K} \Lambda_{KL} (v_K^{n+1} - v_L^{n+1}) \\ &= -m_K \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_{Na}(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_s(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right), \end{aligned} \quad (3.50)$$

$$w_{j,K}^{n+1} - w_{j,K}^n = \Delta t \left(\alpha_j(v_K^n)(1 - w_{j,K}^{n+1}) - \beta_j(v_K^n) w_{j,K}^{n+1} \right), \text{ for } j = 1, \dots, 6, \quad (3.51)$$

$$c_K^{n+1} - c_K^n = \Delta t \left(0.07(10^{-4} - c_K^{n+1}) - g_s 10^{-4} f_K^{n+1} r_K^{n+1} (v_K^{n+1} - 7.7 + 13.0287 \ln(c_K^{n+1})) \right), \quad (3.52)$$

where the transmissibility coefficient Λ_{KL} is defined by (3.47). However, for general triangulations and/or for anisotropic tensors Λ , this discretization does not guarantee the monotonicity of the discrete diffusion operator and hence obtaining the discrete maximum principle [CG16]. For this reason, we introduce the functions $\eta(v)$, $p(v)$, $\Gamma(v)$ and $\phi(v)$ defined by:

$$\eta(v) = \begin{cases} v(1-v), & \text{if } 0 \leq v \leq 1, \\ 0, & \text{if } v \leq 0 \text{ or } v > 1, \end{cases} \quad (3.53)$$

$$p(v) = \ln\left(\frac{v}{1-v}\right), \text{ if } 0 < v < 1, \quad (3.54)$$

$$\Gamma(v) = v \ln(v) + (1-v) \ln(1-v) + 1, \text{ if } 0 < v < 1, \quad (3.55)$$

$$\phi(v) = 2 \arcsin \sqrt{v}, \text{ if } 0 \leq v \leq 1. \quad (3.56)$$

We use herein the convention

$$\eta(v)p(v) = 0 \quad v \leq 0 \text{ and } v \geq 1.$$

Note that, by the mean value theorem, there holds for $x, y \in (0, 1)$,

$$\frac{p(x) - p(y)}{x - y} = p'(b) = \frac{1}{\eta(b)}, \text{ for some } b \in (x, y)$$

and then

$$x - y = \eta(b)(p(x) - p(y)).$$

The discrete equation (3.50) is now replaced by

$$\begin{aligned} & \frac{m_K}{\Delta t} (v_K^{n+1} - v_K^n) + \sum_{\sigma_{KL} \in \mathcal{E}_K} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) \\ &= -m_K \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_{Na}(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_s(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right) \end{aligned} \quad (3.57)$$

where, denoting by $J_{KL}^{n+1} = [\min(v_K^{n+1}, v_L^{n+1}), \max(v_K^{n+1}, v_L^{n+1})]$, we have set

$$\eta_{KL}^{n+1} = \begin{cases} \max_{s \in J_{KL}^{n+1}} \eta(s) & \text{if } \Lambda_{KL} \geq 0, \\ \min_{s \in J_{KL}^{n+1}} \eta(s) & \text{if } \Lambda_{KL} < 0. \end{cases} \quad (3.58)$$

Remark 9. Note that due to the use of the function p in the scheme, (3.57) does not make sense unless

$$0 < v_K^{n+1} < 1 \quad \forall K \in \mathcal{V}, \forall n \geq 0.$$

This will be assumed in the a priori estimates and proved later in Lemma 3.5.10 and Lemma 3.5.11.

Main result

Let $(\mathcal{T}_m)_{m \geq 1}$ be a sequence of triangulations of Ω such that

$$h_m = \max_{T \in \mathcal{T}_m} \text{diam}(T) \rightarrow 0 \text{ as } m \rightarrow \infty,$$

and assume that the sequence of triangulations has a bounded regularity, in other words, there exists a constant $\theta > 0$ such that

$$\theta_{\mathcal{T}_m} \leq \theta, \quad \forall m \geq 1.$$

A sequence of barycentric dual meshes $(\mathcal{M}_m)_{m \geq 1}$ is also constructed. Furthermore, for an increasing sequence of integers $(N_m)_{m \geq 1}$, define the corresponding sequence of time steps $(\Delta t_m)_{m \geq 1}$ such that $\Delta t_m \rightarrow 0$ as $m \rightarrow \infty$. The main purpose of this work is to prove the following theorem.

Theorem 3.4.1. *There exists a sequence $(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m})_m$ of solutions to the scheme (3.57), (3.51), (3.52), such that $0 < v_{\mathcal{M}_m, \Delta t_m} < 1$, $0 \leq w_{j, \mathcal{M}_m, \Delta t_m} \leq 1$ for $j = 1, \dots, 6$, $c_m \leq c_{\mathcal{M}_m, \Delta t_m} \leq c_M$ and*

$$v_{\mathcal{M}_m, \Delta t_m} \rightarrow v, \quad \mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w}, \quad \text{and } c_{\mathcal{M}_m, \Delta t_m} \rightarrow c \text{ a.e. in } \Omega_T \text{ as } m \rightarrow \infty,$$

where the triplet (v, \mathbf{w}, c) is a weak solution to System (3.42) as in Definition 3.4.1.

The rest of the chapter is devoted to the proof of the above theorem which is organized as follows: in Section 3.5, some discrete properties, the discrete maximum principle, some a priori estimates and the existence of the discrete solution are obtained. The compactness estimates and the passage to the limit are established in Section 3.6. Furthermore, the identification of the limit functions as a weak solution is proved in Section 3.7. Finally, in Section 3.8, some numerical tests are shown.

3.5 Discrete properties and existence of a discrete solution

Discrete Maximum Principle

Lemma 3.5.1. *Let $(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N-1\}}$ be a solution of the CVFE scheme (3.57), (3.51), (3.52). Then for all $K \in \mathcal{V}$, and $n \in \{0, \dots, N-1\}$, we have: $0 \leq w_{j,K}^{n+1} \leq 1$, $j = 1, \dots, 6$, $c_m \leq c_K^{n+1} \leq c_M$ and $0 \leq v_K^{n+1} \leq 1$.*

Proof. We use induction over n . Due to assumption (3.40), the assertion is true for $n = 0$. We assume it true for n , and we prove it true for $n + 1$.

The confinement of $w_{j,K}^{n+1}$ for $j = 1, \dots, 6$ and c_K^{n+1} is obtained analogously to Lemma 3.3.5 and the proof is skipped herein.

In order to prove that $0 \leq v_K^{n+1} \leq 1$, consider a fixed dual control volume ω_K such that $v_K^{n+1} = \min_{L \in \mathcal{V}}(v_L^{n+1})$ and assume that $v_K^{n+1} < 0$ trying to obtain a contradiction.

Multiplying equation (3.57) by $-(v_K^{n+1})^- := \min(v_K^{n+1}, 0)$, we obtain

$$\begin{aligned} m_K \left| (v_K^{n+1})^- \right|^2 &= -m_K v_K^n (v_K^{n+1})^- + \Delta t \sum_{\sigma \in \mathcal{E}_K} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) (v_K^{n+1})^- \\ &\quad + m_K \Delta t \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\ &\quad \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) (v_K^{n+1})^- \end{aligned}$$

In view of the definition of η_{KL}^{n+1} given in (3.58), and of the fact that $\eta(v) = 0$ if $v \leq 0$, we have $\eta_{KL}^{n+1} = 0$ if $\Lambda_{KL} \leq 0$. Therefore, the second term on the left hand side of the above equation is reduced to:

$$\Delta t \sum_{\sigma \in \mathcal{E}_K} (\Lambda_{KL})^+ \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) (v_K^{n+1})^-,$$

and by monotonicity of p , we have

$$p(v_K^{n+1}) - p(v_L^{n+1}) \leq 0.$$

Thus, we get

$$\begin{aligned} m_K \left| (v_K^{n+1})^- \right|^2 &\leq m_K \Delta t \left(I_{Pot}(v_K^{n+1}) + I_z(v_K^{n+1}, z_K^{n+1}) + I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) \right. \\ &\quad \left. + I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n) \right) (v_K^{n+1})^-. \end{aligned} \quad (3.59)$$

Let us show that

$$m_K \left| (v_K^{n+1})^- \right|^2 \leq 0.$$

Recalling that the expressions of I_{Pot} and I_z (after rescaling v) are given by:

$$I_{Pot}(v) = \frac{1}{v_M - v_m} \left(1.4 \frac{e^{0.04((v_M - v_m)v)} - 1}{e^{0.08((v_M - v_m)v - 32)} + e^{0.04((v_M - v_m)v - 32)}} + 0.07 \frac{(v_M - v_m)v - 62}{1 - e^{-0.04((v_M - v_m)v - 62)}} \right)$$

and

$$I_z(v, z) = \frac{1}{v_M - v_m} \left(0.8z \frac{e^{0.04((v_M - v_m)v - 8)} - 1}{e^{0.04((v_M - v_m)v - 50)}} \right),$$

one can easily verify that if $v_K^{n+1} < 0$, then $I_{Pot} \leq 0$ and $I_z \leq 0$. Moreover, the third term on the right hand side of (3.59) can be rearranged as follows

$$\begin{aligned} &I_{Na}(v_K^{n+1}, m_K^{n+1}, o_K^{n+1}, l_K^{n+1}) (v_K^{n+1})^- \\ &= \frac{1}{v_M - v_m} [(g_{Na}(m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC}) ((v_M - v_m)v_K^{n+1} + v_m - E_{Na})(v_K^{n+1})^-] \\ &= -(g_{Na}(m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC}) |(v_K^{n+1})^-|^2 \\ &\quad + \frac{1}{v_M - v_m} (g_{Na}(m_K^{n+1})^3 o_K^{n+1} l_K^{n+1} + g_{NaC}) (v_m - E_{Na})(v_K^{n+1})^- \\ &\leq 0. \end{aligned}$$

Also, one can write $I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n)(v_K^{n+1})^-$ as

$$\begin{aligned} I_s(v_K^{n+1}, f_K^{n+1}, r_K^{n+1}, c_K^n)(v_K^{n+1})^- &= \frac{1}{v_M - v_m} g_s f_K^{n+1} r_K^{n+1} ((v_M - v_m) v_K^{n+1} \\ &\quad + v_m - 7.7 + 13.028 \ln(c_K^n))(v_K^{n+1})^- \\ &= -g_s f_K^{n+1} r_K^{n+1} \left| (v_K^{n+1})^- \right|^2 \\ &\quad + \frac{1}{v_M - v_m} g_s f_K^{n+1} r_K^{n+1} (v_m - 7.7 + 13.028 \ln(c_K^n))(v_K^{n+1})^- \\ &\leq 0, \end{aligned}$$

where the last inequality is a consequence of the hypothesis $c_m \leq c_K^n \leq c_M$ and the positivity of f_K^{n+1} and r_K^{n+1} . We conclude therefore that $(v_K^{n+1})^- = 0$ which contradicts the assumption that $v_K^{n+1} < 0$. Hence, $v_K^{n+1} \geq 0$. Similarly, one can prove that $v_K^{n+1} \leq 1$, by using (3.57) over the dual control volume ω_K such that: $v_K^{n+1} = \max_{L \in \mathcal{V}}(v_L^{n+1})$, then multiplying equation (3.57) by $(v_K^{n+1} - 1)^+ := \max(0, v_K^{n+1} - 1)$. \square

Discrete properties

Lemma 3.5.2. *Let $(v_K^{n+1})_{K,n} \in \mathbb{R}^{N \text{Card}(\mathcal{V})}$, then denoting by $\phi_{\mathcal{T}, \Delta t}$ the unique function in $V_{\mathcal{T}, \Delta t}$ with nodal values $\phi(v_K^{n+1})$, there holds*

$$\begin{aligned} \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 & \quad (3.60) \\ & \geq \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (\phi(v_K^{n+1}) - \phi(v_L^{n+1}))^2 = \iint_{\Omega_T} \Lambda \nabla \phi_{\mathcal{T}, \Delta t} \cdot \nabla \phi_{\mathcal{T}, \Delta t} dx dt \end{aligned}$$

Proof. This result can be found in [CG16], we reproduce the proof herein for the sake of completeness.

We first note that by Cauchy's mean value theorem, we have:

$$\frac{\phi(v_K^{n+1}) - \phi(v_L^{n+1})}{p(v_K^{n+1}) - p(v_L^{n+1})} = \sqrt{\eta(b)}, \text{ for some } b \in J_{KL}^{n+1},$$

since for $x \in (0, 1)$, $\phi' = \frac{1}{\sqrt{\eta}}$ and $p' = \frac{1}{\eta}$. Using definition (3.58), we obtain

$$\Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \geq \Lambda_{KL} (\phi(v_K^{n+1}) - \phi(v_L^{n+1}))^2,$$

and estimate (3.60) follows directly. \square

Let $T \in \mathcal{T}$, and let $(K, L) \in \mathcal{V}^2$, we use the notation:

$$\lambda_{KL}^T := - \int_T \Lambda \nabla e_K \cdot \nabla e_L dx = \lambda_{LK}^T, \quad (3.61)$$

so that $\Lambda_{KL} = \sum_{T \in \mathcal{T}} \lambda_{KL}^T$ for all $\sigma_{KL} \in \mathcal{E}$.

Lemma 3.5.3. *Let $\Psi_{\mathcal{T}} = \sum_{K \in \mathcal{V}} \psi_K e_K \in V_{\mathcal{T}}$, then there exists a constant C_0 depending on Λ and $\theta_{\mathcal{T}}$ such that*

$$\sum_{\sigma_{KL} \in \mathcal{E}} \sum_{T \in \mathcal{T}} |\lambda_{KL}^T| (\psi_K - \psi_L)^2 \leq C_0 \int_{\Omega} \Lambda \nabla \Psi_{\mathcal{T}} \cdot \nabla \Psi_{\mathcal{T}} dx. \quad (3.62)$$

Proof. We refer to [[CG16], Lemma 3.2] for the proof of this lemma. \square

Lemma 3.5.4. *There exists a constant C_1 depending on Λ and $\theta_{\mathcal{T}}$ such that*

$$\sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \leq C_1 \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2. \quad (3.63)$$

Proof. We refer to [[CIS17], Lemma 3.3] for the proof of this lemma. \square

Entropy estimate on $v_{\mathcal{M}, \Delta t}$

Lemma 3.5.5. *There exists $C > 0$ depending on $\|v_0\|_{L^2(\Omega)}$, Ω , T such that, for all $n^* \in \{0, \dots, N-1\}$,*

$$\sum_{K \in \mathcal{V}} m_K \Gamma(v_K^{n^*+1}) + \sum_{n=0}^{n^*} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \leq C.$$

Proof. Since the function Γ defined in (3.55) is convex on $(0, 1)$, then by Jensen's inequality there holds

$$\Gamma\left(\frac{1}{m_K} \int_{\omega_K} v_0(x) dx\right) \leq \frac{1}{m_K} \int_{\omega_K} \Gamma(v_0(x)) dx.$$

So

$$\sum_{K \in \mathcal{V}} m_K \Gamma(v_K^0) \leq \int_{\Omega} \Gamma(v_0(x)) dx.$$

Observing that $\Gamma(v) \leq (v-1)^2 + 1$ for $0 \leq v \leq 1$, one gets

$$\sum_{K \in \mathcal{V}} m_K \Gamma(v_K^0) \leq \int_{\Omega} (v_0(x) - 1)^2 + 1 dx \leq C. \quad (3.64)$$

Multiplying equation (3.57) by $p(v_K^{n+1}) \Delta t$ and summing over $K \in \mathcal{V}$ and $n = 0, \dots, n^*$, we reach

$$T_1 + T_2 = T_3, \quad (3.65)$$

where

$$T_1 := \sum_{n=0}^{n^*} \sum_{K \in \mathcal{V}} m_K (v_K^{n+1} - v_K^n) p(v_K^{n+1}),$$

$$T_2 := \sum_{n=0}^{n^*} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2,$$

and

$$T_3 := - \sum_{n=0}^{n^*} \Delta t \sum_{K \in \mathcal{V}} m_K I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) p(v_K^{n+1}).$$

Recalling (3.41) and that $\lim_{v \rightarrow 0^+} p(v) = -\infty$ and $\lim_{v \rightarrow 1^-} p(v) = \infty$, one can show that for $0 \leq v \leq 1$, there exists a positive constants c_2 , such that for all $w_j \in [0, 1]$, $j = 1, \dots, 6$ and $c_m \leq c \leq c_M$, the function $-I_{\text{ion}}(v, \mathbf{w}, c)p(v)$ verifies

$$-\infty < -I_{\text{ion}}(v, \mathbf{w}, c)p(v) \leq c_2.$$

As a result, one obtains

$$T_3 \leq c_2 \sum_{n=0}^{n^*} \Delta t \sum_{K \in \mathcal{V}} m_K \leq c_2 T |\Omega|. \quad (3.66)$$

Since the function p is increasing, a convexity inequality gives

$$(a - b)p(a) \geq \Gamma(a) - \Gamma(b), \quad \forall (a, b) \in \mathbb{R}^+ \times \mathbb{R}^+,$$

providing

$$T_1 \geq \sum_{n=0}^{n^*} \sum_{K \in \mathcal{V}} m_K \left(\Gamma(v_K^{n+1}) - \Gamma(v_K^n) \right) = \sum_{K \in \mathcal{V}} m_K \left(\Gamma(v_K^{n^*+1}) - \Gamma(v_K^0) \right). \quad (3.67)$$

Using estimates (3.67), (3.66) and (3.64) in equation (3.65), the proof of Lemma 3.5.5 is complete. \square

We suggest to derive in the following lemma a classical energy estimate on $v_{\mathcal{T}, \Delta t}$.

Lemma 3.5.6. *There exists C depending on Ω , $\|v_0\|_{L^2(\Omega)}$ and T such that for all $n^* \in \{0, \dots, N-1\}$*

$$\frac{1}{2} \sum_{K \in \mathcal{V}} m_K \left(v_K^{n^*+1} \right)^2 + \sum_{n=0}^{n^*} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (v_K^{n+1} - v_L^{n+1})^2 \leq C.$$

Proof. Let $n \in \{0, \dots, n^*\}$, then multiplying equation (3.57) by $v_K^{n+1} \Delta t$ and summing over $K \in \mathcal{V}$ provides

$$\mathcal{A} + \mathcal{B} = \mathcal{C} \quad (3.68)$$

where

$$\mathcal{A} := \sum_{K \in \mathcal{V}} m_K (v_K^{n+1} - v_K^n) v_K^{n+1},$$

$$\mathcal{B} := \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) (v_K^{n+1} - v_L^{n+1}),$$

and

$$\mathcal{C} := -\Delta t \sum_{K \in \mathcal{V}} m_K \left(I_{\text{Pot}}(v_K^{n+1}) + I_z(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_{Na}(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_s(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right) v_K^{n+1}.$$

The simple inequality $a(a - b) \geq \frac{a^2}{2} - \frac{b^2}{2}$ implies that

$$\mathcal{A} \geq \frac{1}{2} \sum_{K \in \mathcal{V}} m_K (v_K^{n+1})^2 - \frac{1}{2} \sum_{K \in \mathcal{V}} m_K (v_K^n)^2. \quad (3.69)$$

It follows from definitions (3.58) of η_{KL}^{n+1} and (3.54) of p along with the mean value theorem that

$$\Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) (v_K^{n+1} - v_L^{n+1}) \geq \Lambda_{KL} (v_K^{n+1} - v_L^{n+1})^2, \quad \forall \sigma_{KL} \in \mathcal{E}.$$

Hence,

$$\mathcal{B} \geq \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (v_K^{n+1} - v_L^{n+1})^2. \quad (3.70)$$

Considering now the term \mathcal{C} , note that by the maximum principle shown in Lemma 3.5.1 there exists a constant $c_1 > 0$ such that

$$\left| I_{\text{Pot}}(v_K^{n+1}) + I_z(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_{\text{Na}}(v_K^{n+1}, \mathbf{w}_K^{n+1}) + I_s(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right| |v_K^{n+1}| \leq c_1.$$

As a result, one obtains

$$\mathcal{C} \leq \Delta t |\Omega| c_1. \quad (3.71)$$

Using estimates (3.69), (3.70) and (3.71) in equation (3.68) and taking sums over $n \in \{0, \dots, N-1\}$ yields

$$\frac{1}{2} \sum_{K \in \mathcal{V}} m_K (v_K^{n^*+1})^2 + \sum_{n=0}^{n^*} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (v_K^{n+1} - v_L^{n+1})^2 \leq \frac{1}{2} \sum_{K \in \mathcal{V}} m_K (v_K^0)^2 + T |\Omega| c_1.$$

Finally, note that

$$\sum_{K \in \mathcal{V}} m_K (v_K^0)^2 \leq |\Omega|,$$

to conclude the proof of Lemma 3.5.6. \square

Enhanced Estimates on $v_{\mathcal{M}, \Delta t}$

Lemma 3.5.7. *Assume that $\int_{\Omega} v_0(x) dx > 0$, then there exists $\zeta > 0$ depending on the discretization and on the data such that*

$$\int_{\Omega} v_{\mathcal{M}, \Delta t} dx \geq \zeta, \quad \forall t \in [0, T].$$

Proof. Multiplying equation (3.57) by Δt and taking sums over $K \in \mathcal{V}$ one gets

$$\sum_{K \in \mathcal{V}} m_K (v_K^{n+1} - v_K^n) = - \sum_{K \in \mathcal{V}} m_K \Delta t I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n). \quad (3.72)$$

One can use induction over n . Indeed, because of the assumption on the initial datum v_0 , there exists $L^{n_0} \in \mathcal{V}$ such that $v_{L^{n_0}}^0 > 0$. Assume that $v_{L^n}^n > 0$ for some $L^n \in \mathcal{V}$. Suppose

that $\sum_{K \in \mathcal{V}} m_K v_K^{n+1} = 0$. Then by non-negativity of v_K^{n+1} and Equation (3.72), one deduces that $v_K^{n+1} = 0$, for all $K \in \mathcal{V}$ and that (recall (3.41))

$$\sum_{K \in \mathcal{V}} m_K v_K^n = \sum_{K \in \mathcal{V}} m_K \Delta t I_{\text{ion}}(0, \mathbf{w}_K^{n+1}, c_K^n) \leq 0,$$

yielding a contradiction. Hence, there exists $L^{n+1} \in \mathcal{V}$ such that $v_{L^{n+1}}^{n+1}$ is strictly positive and

$$\sum_{K \in \mathcal{V}} m_K v_K^{n+1} := \zeta_{n+1} > 0.$$

Setting $\zeta = \min_{n=1, \dots, N} \zeta_n$, the proof is complete. \square

Lemma 3.5.8. *Assume that $\int_{\Omega} (1 - v_0(x)) dx > 0$, then there exists $\rho > 0$ depending on the discretization and on the data such that*

$$\int_{\Omega} (1 - v_{\mathcal{M}, \Delta t}) dx \geq \rho, \quad \forall t \in [0, T].$$

Proof. Multiplying equation (3.57) by Δt and taking sums over $K \in \mathcal{V}$ one gets

$$\sum_{K \in \mathcal{V}} m_K (v_K^{n+1} - v_K^n) = - \sum_{K \in \mathcal{V}} m_K \Delta t I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n). \quad (3.73)$$

Again, one can use induction over n as in the proof of Lemma 3.5.7. Assume that $v_{L^n}^n > 0$ for some $L^n \in \mathcal{V}$, as this is the case for the initial datum v_0 . Suppose that $\forall K \in \mathcal{V}$, $v_K^{n+1} = 1$. Then by Equation (3.73), one deduces that

$$|\Omega| > \sum_{K \in \mathcal{V}} m_K v_K^n = |\Omega| - \sum_{K \in \mathcal{V}} m_K \Delta t I_{\text{ion}}(1, \mathbf{w}_K^{n+1}, c_K^n) \geq |\Omega|,$$

yielding a contradiction. Hence, there exists $L^{n+1} \in \mathcal{V}$ such that $v_{L^{n+1}}^{n+1} < 1$ and

$$\sum_{K \in \mathcal{V}} m_K v_K^{n+1} := |\Omega| - \rho_{n+1} < |\Omega|.$$

Setting $\rho = \min_{n=1, \dots, N} \rho_n$, the proof is complete. \square

Now we define the notion of *transmissive path* as introduced in [CG16].

Definition 3.5.1. A **transmissive path** \mathfrak{p} joining $K_i \in \mathcal{V}$ to $K_f \in \mathcal{V}$ consists in a list of vertices $(K_q)_{0 \leq q \leq M}$ such that $K_i = K_0$, $K_f = K_M$, with $K_q \neq K_\ell$ if $q \neq \ell$, and such that $\sigma_{K_q K_{q+1}} \in \mathcal{E}$ with $\Lambda_{K_q K_{q+1}} > 0$ for all $q \in \{0, \dots, M-1\}$. We denote by $\mathbb{P}(K_i, K_f)$ the set of all transmissive paths joining $K_i \in \mathcal{V}$ to $K_f \in \mathcal{V}$.

We recall also a result proved in [CG16].

Lemma 3.5.9. *For all $(K_i, K_f) \in \mathcal{V}^2$, there exists a transmissive path $\mathfrak{p} \in \mathbb{P}(K_i, K_f)$.*

Proof. Let $K_i \in \mathcal{V}$, then define $\bar{\mathcal{V}}_{K_i}$ the subset of \mathcal{V} made of the vertices connected to K_i via a transmissive path. Note that $\bar{\mathcal{V}}_{K_i} \neq \emptyset$ since $\sum_{L \neq K} \Lambda_{KL} > 0$ and $\Lambda_{KM} = 0$ for all $M \notin \mathcal{V}_K$ (i.e. $\exists L \in \mathcal{V}_K$ such that $\Lambda_{KL} > 0$). Assume that $\bar{\mathcal{V}}_{K_i} \subsetneq \mathcal{V}$. Introduce the function $\psi_{\mathcal{T}} \in \mathcal{V}_{\mathcal{T}}$ such that

$$\psi_K = \begin{cases} 1 & \text{if } K \in \bar{\mathcal{V}}_{K_i} \\ 0 & \text{otherwise.} \end{cases}$$

The lack of transmissive path between the elements of $\bar{\mathcal{V}}_{K_i}$ and the elements of $\mathcal{V} \setminus \bar{\mathcal{V}}_{K_i}$ leads to

$$\sum_{\sigma_{KL} \in \mathcal{E}} (\Lambda_{KL})^+ (\psi_K - \psi_L)^2 = 0.$$

On the other hand, since $\bar{\mathcal{V}}_{K_i} \neq \emptyset$, the function $\psi_{\mathcal{T}}$ is not constant. Therefore, since Ω is assumed to be connected,

$$\sum_{\sigma_{KL} \in \mathcal{E}} (\Lambda_{KL})^+ (u_K - u_L)^2 \geq \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} (u_K - u_L)^2 = \int_{\Omega} \Lambda \nabla u_{\mathcal{T}} \cdot \nabla u_{\mathcal{T}} dx > 0$$

providing a contradiction. The fact that the path is necessarily of finite length originates from the finite number of possible combinations for designing a path. \square

Lemma 3.5.10. *Assume that $\int_{\Omega} v_0(x) dx > 0$, then there exists $\kappa_h > 0$ depending on the data, the mesh \mathcal{T} and Δt such that*

$$v_K^{n+1} \geq \kappa_h, \quad \forall K \in \mathcal{V}, \forall n \in \{0, \dots, N-1\}. \quad (3.74)$$

Proof. By Lemma 3.5.7, there exists K_i such that $v_{K_i}^{n+1} > 0$. Let $K_f \in \mathcal{V}$, then thanks to Lemma 3.5.9, there exists a transmissive path $\mathfrak{p} = (K_q)_{0 \leq q \leq M} \in \mathbb{P}(K_i, K_f)$, with $K_0 = K_i$ and $K_M = K_f$. Exploiting Lemma 3.5.4 and Lemma 3.5.5, one has the existence of $C > 0$ such that

$$\sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| \eta_{KL}^{n+1} \left(p(v_K^{n+1}) - p(v_L^{n+1}) \right)^2 \leq C.$$

In particular, we get

$$\Lambda_{K_q K_{q+1}} \eta_{K_q K_{q+1}}^{n+1} \left(p(v_{K_q}^{n+1}) - p(v_{K_{q+1}}^{n+1}) \right)^2 \leq \frac{C}{\Delta t}, \quad \forall q \in \{0, \dots, M-1\}.$$

Assuming that $v_{K_q}^{n+1} > 0$, as this holds for $q = 0$, then $\eta_{K_q K_{q+1}}^{n+1} \geq \eta(v_{K_q}^{n+1}) > 0$. Then one has

$$\left(p(v_{K_q}^{n+1}) - p(v_{K_{q+1}}^{n+1}) \right)^2 \leq \frac{C}{\Delta t \Lambda_{K_q K_{q+1}} \eta_{K_q K_{q+1}}^{n+1}} < \infty.$$

Hence, $p(v_{K_{q+1}}^{n+1}) > -\infty$ and $v_{K_{q+1}}^{n+1} > 0$. By a straightforward induction, one can obtain that $v_{K_f}^{n+1} > 0$ and since K_f is arbitrary, one gets that

$$v_K^{n+1} > 0, \quad \forall K \in \mathcal{V}.$$

Keeping in mind that the set $\mathcal{V} \times \{0, \dots, N-1\}$ is finite, one deduces the existence of $\kappa_h > 0$ such that (3.74) holds. \square

Similarly, one can prove the following.

Lemma 3.5.11. *Assume that $\int_{\Omega} (1 - v_0(x)) dx > 0$, then there exists $\rho_h > 0$ depending on the data, the mesh \mathcal{T} and Δt such that*

$$v_K^{n+1} \leq 1 - \rho_h, \quad \forall K \in \mathcal{V}, \forall n \in \{0, \dots, N-1\}. \quad (3.75)$$

Energy estimates on $w_{\mathcal{T}, \Delta t}$ and $c_{\mathcal{T}, \Delta t}$

Definition 3.5.2. For all $(K, L) \in \mathcal{V}^2$, define ξ_{KL} by

$$\xi_{KL} = - \int_{\Omega} \nabla e_K \cdot \nabla e_L dx.$$

Lemma 3.5.12. *Let $(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N\}}$ be a solution of the discrete scheme (3.57), (3.51), (3.52). Assume that $\xi_{KL} \geq 0$ for all $(K, L) \in \mathcal{V}$, then there exist constants C_2 , and $C_3 > 0$ depending on Ω, T, v_0, w_0, c_0 such that*

$$\|\nabla w_{j, \mathcal{T}}\|_{L^2(\Omega_T)}^2 = \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} |w_{j,L}^{n+1} - w_{j,K}^{n+1}|^2 \leq C_2, \quad \forall j = 1, \dots, 6, \quad (3.76)$$

and

$$\|\nabla c_{\mathcal{T}}\|_{L^2(\Omega_T)}^2 = \sum_{n=0}^{N-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} |c_L^{n+1} - c_K^{n+1}|^2 \leq C_3. \quad (3.77)$$

Remark 10. *Note that if all the angles in the primal triangular mesh are acute then the above assumption ($\xi_{KL} \geq 0$ for all $(K, L) \in \mathcal{V}$) is fulfilled.*

Proof. In order to prove estimate (3.76), we proceed as in the proof of Lemma 3.3.8 to obtain for $\Delta t \leq 1/2$,

$$(w_K^n - w_L^n)^2 \leq e^{2T} \left((w_K^0 - w_L^0)^2 + c_4 \Delta t \sum_{j=0}^{n-1} (v_K^j - v_L^j)^2 \right).$$

Multiplying both sides by ξ_{KL} and taking sums, one gets:

$$\sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} (w_K^n - w_L^n)^2 \leq e^{2T} \left(\|\nabla w_{\mathcal{T}}^0\|_{L^2(\Omega)}^2 + c_4 \sum_{j=0}^{n-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} (v_K^j - v_L^j)^2 \right).$$

Now using Lemma 3.5.6, we get:

$$\sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} (w_K^n - w_L^n)^2 \leq e^{2T} \left(\|\nabla w_{\mathcal{T}}^0\|_{L^2(\Omega)}^2 + c_4 C \right),$$

leading to

$$\sum_{n=1}^N \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \xi_{KL} (w_K^n - w_L^n)^2 \leq T e^{2T} \left(\|\nabla w_{\mathcal{T}}^0\|_{L^2(\Omega)}^2 + c_4 C \right).$$

Thus estimate (3.76) is obtained.

To obtain estimate (3.77), the argument of Lemma 3.3.10 modified as in the proof of (3.76) is repeated. \square

Now, we state some estimates obtained on the discrete evolutive terms of the gating and concentration variables analogously to Lemmata 3.3.9 and 3.3.11.

Lemma 3.5.13. *Let $(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^{n+1})_{K \in \mathcal{V}, n \in \{0, \dots, N\}}$ be a solution of the discrete scheme (3.57), (3.51), (3.52). Then there exist constants C_4 , and $C_5 > 0$ depending on Ω, T such that*

$$\sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{V}} m_K \left(\frac{w_{j,K}^{n+1} - w_{j,K}^n}{\Delta t} \right)^2 \leq C_4, \quad \forall j = 1, \dots, 6, \quad (3.78)$$

and

$$\sum_{n=0}^{N-1} \Delta t \sum_{K \in \mathcal{V}} m_K \left(\frac{c_K^{n+1} - c_K^n}{\Delta t} \right)^2 \leq C_5. \quad (3.79)$$

Existence of a discrete solution

Proposition 3.5.14. *Under the assumptions on the model stated in Section 2, there exists at least one solution $(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^{n+1})_{K \in \mathcal{V}}$ of the scheme (3.57), (3.52), (3.51).*

Proof. We show existence of a discrete solution using induction over n . We assume that $(v_K^n, \mathbf{w}_K^n, c_K^n)_{K \in \mathcal{V}}$ exists and we prove the existence of $(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^{n+1})_{K \in \mathcal{V}}$. Using equation (3.51), we get for each $j = 1, \dots, 6$, and for all $K \in \mathcal{V}$ the explicit expression of $w_{j,K}^{n+1}$ as:

$$w_{j,K}^{n+1} = \frac{w_{j,K}^n + \Delta t (\alpha_j(v_K^n))}{1 + \Delta t (\alpha_j(v_K^n) + \beta_j(v_K^n))},$$

and hence $(\mathbf{w}_K^{n+1})_{K \in \mathcal{V}}$ exists since $\alpha_j, \beta_j > 0$. Now, we consider equation (3.57) and we assume that $(v_K^n)_{K \in \mathcal{V}}$ and $(w_K^{n+1})_{K \in \mathcal{V}}$ exist. The existence of a solution $(v_K^{n+1})_{K \in \mathcal{V}}$ can be proved by a slight modification of the proof of Proposition 3.11 in [CG16] or Proposition 3.12 in [CIS17], which rely on a topological degree argument.

Let $\mu \in [0, 1]$, we denote by $(v_{K,\mu}^{n+1})_{K \in \mathcal{V}}$ the solution of the scheme:

$$\begin{aligned} \frac{m_K}{\Delta t} (v_{K,\mu}^{n+1} - v_K^n) + \mu \sum_{\sigma_{KL} \in \mathcal{E}_K} \Lambda_{KL} \eta_{KL,\mu}^{n+1} (p(v_{K,\mu}^{n+1}) - p(v_{L,\mu}^{n+1})) \\ + (1 - \mu) \sum_{\sigma_{KL} \in \mathcal{E}_K} |\Lambda_{KL}| (p(v_{K,\mu}^{n+1}) - p(v_{L,\mu}^{n+1})) = -m_K I_{\text{ion}}(v_{K,\mu}^{n+1}, \mathbf{w}_K^{n+1}, c_K^n), \end{aligned} \quad (3.80)$$

where

$$\eta_{KL,\mu}^{n+1} = \begin{cases} \max_{v \in J_{KL,\mu}^{n+1}} \eta(v) & \text{if } \Lambda_{KL} \geq 0, \\ \min_{v \in J_{KL,\mu}^{n+1}} \eta(v) & \text{if } \Lambda_{KL} < 0, \end{cases}$$

and $J_{KL,\mu}^{n+1} = [\min(v_{K,\mu}^{n+1}, v_{L,\mu}^{n+1}), \max(v_{K,\mu}^{n+1}, v_{L,\mu}^{n+1})]$. Carefully reproducing the analysis carried out in Lemma 3.5.2 and Lemma 3.5.5, one can show that for all $\mu \in [0, 1]$,

$$\sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \left(\phi(v_{K,\mu}^{n+1}) - \phi(v_{L,\mu}^{n+1}) \right)^2 \leq \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL,\mu}^{n+1} \left(p(v_{K,\mu}^{n+1}) - p(v_{L,\mu}^{n+1}) \right)^2 \leq C. \quad (3.81)$$

Furthermore, one can prove as in Lemma 3.5.1 that

$$0 \leq v_{K,\mu}^{n+1} \leq 1,$$

and this last estimate can be enhanced as in § 3.5 that there exists $\epsilon > 0$ such that

$$0 < \epsilon \leq v_{K,\mu}^{n+1} \leq 1 - \epsilon < 1, \quad \forall K \in \mathcal{V}. \quad (3.82)$$

As a result, for all $\mu \in [0, 1]$, the solutions of the numerical scheme (3.80) are kept in the interior of a compact subset \mathcal{B} of $[0, 1]^{\text{Card}(\mathcal{V})}$ such that

$$\text{dist}\left(\mathcal{B}, \{0, 1\}^{\text{Card}(\mathcal{V})}\right) \geq \frac{\epsilon}{2}.$$

Define the function $\Xi : \mathcal{B} \times [0, 1] \rightarrow \mathbb{R}^{\text{Card}(\mathcal{V})}$ by: $\forall K \in \mathcal{V}$,

$$\begin{aligned} \Xi_K((u_K)_K, \mu) := & \frac{m_K}{\Delta t}(u_K - v_K^n) + \mu \sum_{\sigma_{KL} \in \mathcal{E}_K} \Lambda_{KL} \eta_{KL,\mu}^{n+1} \left(p(u_K) - p(u_L) \right) \\ & + (1 - \mu) \sum_{\sigma_{KL} \in \mathcal{E}_K} |\Lambda_{KL}| \left(p(u_K) - p(u_L) \right) + m_K I_{\text{ion}}(u_K, \mathbf{w}_K^{n+1}, c_K^n). \end{aligned}$$

The function Ξ is uniformly continuous on $\mathcal{B} \times [0, 1]$, and it follows from (3.82) that for all $\mu \in [0, 1]$ the solution $(v_{K,\mu}^{n+1})_{K \in \mathcal{V}}$ of the nonlinear system

$$\Xi\left(\left(v_{K,\mu}^{n+1}\right)_{K \in \mathcal{V}}, \mu\right) = 0, \quad (3.83)$$

cannot reach $\partial\mathcal{B}$. Therefore the topological degree $\delta(\Xi, \mathcal{B})(\mu)$ is constant with respect to μ . For $\mu = 0$, the system (3.83) is monotone and it can be proved that its topological degree is equal to 1 (by adapting the existence proof of a discrete solution to the monotone implicit scheme for a hyperbolic equation studied in [EGGH98]). Hence, it admits at least one solution for $\mu = 1$, establishing the existence of $\left(v_K^{n+1}\right)_{K \in \mathcal{V}}$.

Now given v_K^{n+1} and w_K^{n+1} , we can rewrite Equation (3.52) as:

$$(1 + 0.07\Delta t)c_K^{n+1} + 13.0287 \times 10^{-4} g_s f_K^{n+1} r_K^{n+1} \ln(c_K^{n+1}) = c_K^n + 10^{-4} \Delta t \left(0.07 - g_s w_K^{n+1} (v_K^{n+1} - 7.7) \right). \quad (3.84)$$

Since the function $x \mapsto (1 + 0.07\Delta t)x + 13.0287 \times 10^{-4} g_s f_K^{n+1} r_K^{n+1} \ln(x)$, which is defined for $x > 0$ onto \mathbb{R} , is bijective. Thus, Equation (3.84) admits a unique solution c_K^{n+1} . Therefore, the existence of solution of the discrete system is obtained. \square

3.6 Compactness estimates on the family of discrete solutions

The sequences $\left(v_{\mathcal{M}_m, \Delta t_m}\right)_m$, $\left(\mathbf{w}_{\mathcal{M}_m, \Delta t_m}\right)_m$, $\left(c_{\mathcal{M}_m, \Delta t_m}\right)_m$, $\left(v_{\mathcal{T}_m, \Delta t_m}\right)_m$, $\left(\mathbf{w}_{\mathcal{T}_m, \Delta t_m}\right)_m$, and $\left(c_{\mathcal{T}_m, \Delta t_m}\right)_m$ are uniformly bounded w.r.t m in $L^\infty(\Omega_T)$ as implied by Lemma 3.5.1. Moreover, as a consequence of Lemma 3.5.6, equation (3.48) and condition (3.39), the sequence $\left(v_{\mathcal{T}_m, \Delta t_m}\right)_m$ is uniformly bounded in $L^2(0, T; H^1(\Omega))$. Therefore, there exists $v \in L^2(0, T; H^1(\Omega))$ such that, up to a subsequence,

$$v_{\mathcal{T}_m, \Delta t_m} \rightarrow v \text{ weakly in } L^2(0, T; H^1(\Omega)) \text{ as } m \rightarrow \infty.$$

Using the inequality

$$\|u_{\mathcal{T}_m, \Delta t_m} - u_{\mathcal{M}_m, \Delta t_m}\|_{L^2(\Omega)} \leq Ch \|\nabla u_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega)}, \quad \forall u_{\mathcal{T}_m, \Delta t_m} \in \mathcal{H}_{\mathcal{T}_m, \Delta t_m}, \quad (3.85)$$

(see for example [BM13] Lemma 3.4), one deduces that $v_{\mathcal{T}_m, \Delta t_m}$ and $v_{\mathcal{M}_m, \Delta t_m}$ have the same limits, and

$$v_{\mathcal{M}_m, \Delta t_m} \rightarrow v \text{ weak-* in } L^\infty(\Omega_T).$$

On the other hand, making use of Lemma 3.5.12 the sequences $(\mathbf{w}_{\mathcal{T}_m, \Delta t_m})_m$, and $(c_{\mathcal{T}_m, \Delta t_m})_m$ are uniformly bounded in $L^2(0, T; (H^1(\Omega))^6)$ and $L^2(0, T; H^1(\Omega))$ respectively. Hence, there exist $\mathbf{w} \in L^2(0, T; (H^1(\Omega))^6)$ and $c \in L^2(0, T; H^1(\Omega))$ such that, up to a subsequence,

$$\mathbf{w}_{\mathcal{T}_m, \Delta t_m} \rightarrow \mathbf{w} \text{ weakly in } L^2(0, T; (H^1(\Omega))^6) \text{ as } m \rightarrow \infty,$$

$$c_{\mathcal{T}_m, \Delta t_m} \rightarrow c \text{ weakly in } L^2(0, T; H^1(\Omega)) \text{ as } m \rightarrow \infty,$$

$$\mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w} \text{ weak-* in } (L^\infty(\Omega_T))^6,$$

and

$$c_{\mathcal{M}_m, \Delta t_m} \rightarrow c \text{ weak-* in } L^\infty(\Omega_T).$$

In order to establish the convergence of the scheme, it is required to prove that

$$v_{\mathcal{M}_m, \Delta t_m} \rightarrow v, \quad c_{\mathcal{M}_m, \Delta t_m} \rightarrow c \text{ and } \mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w} \text{ a.e. in } \Omega_T.$$

One option is to proceed in estimating the time and space translates of the discrete functions $v_{\mathcal{M}_m, \Delta t_m}$, $\mathbf{w}_{\mathcal{M}_m, \Delta t_m}$ and $c_{\mathcal{M}_m, \Delta t_m}$ as in [AL83] and [EGH00]. The other alternative which we adopt herein is to make use of the technical blackbox proposed in Theorem 3.9 in [ACM17].

First, note that Lemma 3.5.13 provides a discrete $L^2(0, T; L^2(\Omega))$ estimate on the time finite differences of $\mathbf{w}_{\mathcal{M}_m, \Delta t_m}$ and $c_{\mathcal{M}_m, \Delta t_m}$. Second, for a fixed $m \geq 1$, consider a set of nodal values $(\varphi_K^{n+1})_{K \in \mathcal{V}_m, 0 \leq n \leq N_m - 1}$ such that $\varphi_K^{n+1} = 0$ if $x_K \in \partial\Omega$ and the corresponding functions $\varphi_{\mathcal{T}_m, \Delta t_m}$ and $\varphi_{\mathcal{M}_m, \Delta t_m}$. We have the following discrete $L^1(0, T; H^{-1}(\Omega))$ estimate on the finite difference w.r.t time of $v_{\mathcal{M}_m, \Delta t_m}$.

Lemma 3.6.1. *There exists C independent of m such that*

$$\sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} m_K (v_K^{n+1} - v_K^n) \varphi_K^{n+1} \leq C \|\nabla \varphi_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}. \quad (3.86)$$

Proof. Multiply (3.57) by $\Delta t \varphi_K^{n+1}$ and sum over $n \in \{0, \dots, N_m - 1\}$ and $K \in \mathcal{V}_m$ to get

$$\sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} m_K (v_K^{n+1} - v_K^n) \varphi_K^{n+1} \leq T_{1,m} + T_{2,m}, \quad (3.87)$$

where

$$\begin{aligned} T_{1,m} &= - \sum_{n=0}^{N_m-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} \Lambda_{KL} \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) (\varphi_K^{n+1} - \varphi_L^{n+1}), \\ T_{2,m} &= - \sum_{n=0}^{N_m-1} \Delta t \sum_{K \in \mathcal{V}_m} m_K I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \varphi_K^{n+1}. \end{aligned}$$

Applying Cauchy-Schwartz inequality and observing that $0 \leq \eta \leq 1$, there holds

$$|T_{1,m}|^2 \leq \left(\sum_{n=0}^{N_m-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \right) \left(\sum_{n=0}^{N_m-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| (\varphi_K^{n+1} - \varphi_L^{n+1})^2 \right).$$

The combined use of Lemma 3.60 and Lemma 3.5.5 implies

$$\sum_{n=0}^{N_m-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \leq C,$$

whereas Lemma 3.5.3 provides

$$\sum_{n=0}^{N_m-1} \Delta t \sum_{\sigma_{KL} \in \mathcal{E}} |\Lambda_{KL}| (\varphi_K^{n+1} - \varphi_L^{n+1})^2 \leq C \|\nabla \varphi_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}^2.$$

Hence,

$$|T_{1,m}| \leq C \|\nabla \varphi_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}. \quad (3.88)$$

Moreover, applying Cauchy-Schwartz inequality on $T_{2,m}$, one gets

$$|T_{2,m}| \leq \left(\sum_{n=0}^{N_m-1} \Delta t \sum_{K \in \mathcal{V}_m} m_K \left| I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \right| \right)^{1/2} \|\varphi_{\mathcal{M}_m, \Delta t_m}\|_{L^2(\Omega_T)}.$$

Lemma 3.5.1 implies that

$$\left(\sum_{n=0}^{N_m-1} \Delta t \sum_{K \in \mathcal{V}_m} m_K \left| I_{\text{ion}}(v_K^n, \mathbf{w}_K^{n+1}, c_K^n) \right| \right)^{1/2} \leq C,$$

whereas the discrete Poincaré inequality (see for instance Lemma 3.3 in [BM13]) provides

$$\|\varphi_{\mathcal{M}_m, \Delta t_m}\|_{L^2(\Omega_T)} \leq C \|\nabla \varphi_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}.$$

As a result, one gets

$$|T_{2,m}| \leq C \|\nabla \varphi_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}. \quad (3.89)$$

Plugging estimates (3.87) and (3.88) in inequality (3.89) ends the proof of estimate (3.86). \square

We have now all the necessary machinery to use Theorem 3.9 in [ACM17], allowing us to claim that

$$v_{\mathcal{M}_m, \Delta t_m} \rightarrow v \text{ a.e. in } \Omega_T, \quad \mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w} \text{ a.e. in } \Omega_T \text{ and } c_{\mathcal{M}_m, \Delta t_m} \rightarrow c \text{ a.e. in } \Omega_T.$$

3.7 Identification of the limit as a weak solution

It remains to show that the limit (v, \mathbf{w}, c) satisfies the weak formulation (3.43)-(3.45). Consider a test function $\psi \in \mathcal{D}(\bar{\Omega} \times [0, T])$ and denote $\psi(x_K, t_n)$ by ψ_K^n for all $K \in \mathcal{V}_m$ and all $n \in \{0, \dots, N_m\}$. We prove in what follows the convergence of equation (3.57) of the scheme, i.e. we prove that equation (3.43) is satisfied when $m \rightarrow \infty$. The convergence of the other two equations, being standard, is left to the reader.

Multiplying equation (3.57) by $\Delta t_m \psi_K^n$ and summing over $n \in \{0, \dots, N_m - 1\}$ and $K \in \mathcal{V}_m$ yields:

$$A_m + D_{1,m} + D_{2,m} = R_m,$$

where

$$\begin{aligned} A_m &= \sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} m_K (v_K^{n+1} - v_K^n) \psi_K^n \\ D_{1,m} &= \sum_{n=0}^{N_m-1} \Delta t_m \sum_{\sigma_{KL} \in \mathcal{E}_m} \Lambda_{KL} \left(\eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1})) - \sqrt{\eta_{KL}^{n+1}} (\phi(v_K^{n+1}) - \phi(v_L^{n+1})) \right) (\psi_K^n - \psi_L^n) \\ D_{2,m} &= \sum_{n=0}^{N_m-1} \Delta t_m \sum_{\sigma_{KL} \in \mathcal{E}_m} \Lambda_{KL} \sqrt{\eta_{KL}^{n+1}} (\phi(v_K^{n+1}) - \phi(v_L^{n+1})) (\psi_K^n - \psi_L^n) \\ R_m &= - \sum_{n=0}^{N_m-1} \Delta t_m \sum_{K \in \mathcal{V}_m} m_K I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \psi_K^n. \end{aligned}$$

Accumulation term

Using integration by parts in time and keeping in mind that $\psi_K^{N_m} = 0$ for all $K \in \mathcal{V}_m$, notice that A_m can be written as:

$$\begin{aligned} A_m &= \sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} m_K (v_K^{n+1} - v_K^n) \psi_K^n \\ &= - \sum_{n=0}^{N_m-1} \Delta t_m \sum_{K \in \mathcal{V}_m} m_K v_K^{n+1} \frac{\psi_K^{n+1} - \psi_K^n}{\Delta t_m} - \sum_{K \in \mathcal{V}_m} m_K v_K^0 \psi_K^0 \\ &= - \iint_{\Omega_T} v_{\mathcal{M}_m, \Delta t_m}(t, x) \partial_t \psi_{\mathcal{M}_m, \Delta t_m}(t, x) dx dt - \int_{\Omega} v_{\mathcal{M}_m, \Delta t_m}(0, x) \psi_{\mathcal{M}_m, \Delta t_m}(0, x) dx. \end{aligned}$$

By regularity of ψ , and the convergence in $L^1(\Omega_T)$ of the sequence $(v_{\mathcal{M}_m, \Delta t_m})_m$ towards v , one obtains:

$$A_m \rightarrow - \iint_{\Omega_T} v(t, x) \partial_t \psi(t, x) dx dt - \int_{\Omega} v(0, x) \psi(0, x) dx, \text{ as } m \rightarrow \infty.$$

Diffusion term

It is required to prove that $\lim_{m \rightarrow \infty} D_{1,m} = 0$, and $\lim_{m \rightarrow \infty} D_{2,m} = \iint_{\Omega_T} \Lambda \nabla v \cdot \nabla \psi dx dt$.

Let us prove first that $\lim_{m \rightarrow \infty} D_{1,m} = 0$.

For all $\sigma_{KL} \in \mathcal{E}_m$ and all $n \in \{0, \dots, N_m - 1\}$, denote by $\bar{\eta}_{KL}^{n+1}$ the following quantity:

$$\bar{\eta}_{KL}^{n+1} = \begin{cases} \left(\frac{\phi(v_K^{n+1}) - \phi(v_L^{n+1})}{p(v_K^{n+1}) - p(v_L^{n+1})} \right)^2 & \text{if } v_K^{n+1} \neq v_L^{n+1} \\ \eta(v_K^{n+1}) & \text{if } v_K^{n+1} = v_L^{n+1} \end{cases}$$

Then the term $D_{1,m}$ is rewritten as:

$$D_{1,m} = \sum_{n=0}^{N_m-1} \Delta t_m \sum_{\sigma_{KL} \in \mathcal{E}_m} \Lambda_{KL} \sqrt{\eta_{KL}^{n+1}} \left(\sqrt{\eta_{KL}^{n+1}} - \sqrt{\bar{\eta}_{KL}^{n+1}} \right) \left(p(v_K^{n+1}) - p(v_L^{n+1}) \right) (\psi_K^n - \psi_L^n).$$

An application of Cauchy-Schwartz' inequality yields

$$|D_{1,m}| \leq \left(\sum_{n=0}^{N_m-1} \Delta t_m \sum_{\sigma_{KL} \in \mathcal{E}_m} |\Lambda_{KL}| \eta_{KL}^{n+1} (p(v_K^{n+1}) - p(v_L^{n+1}))^2 \right)^{1/2} \times P_m^{1/2},$$

where P_m is given by:

$$P_m = \sum_{n=0}^{N_m-1} \Delta t_m \sum_{\sigma_{KL} \in \mathcal{E}_m} |\Lambda_{KL}| \left(\sqrt{\eta_{KL}^{n+1}} - \sqrt{\bar{\eta}_{KL}^{n+1}} \right)^2 (\psi_K^n - \psi_L^n)^2.$$

Exploiting Lemma 3.5.4 and Lemma 3.5.5, one has $D_{1,m} \leq CP_m^{1/2}$. So, it is enough to show that $\lim_{m \rightarrow \infty} P_m = 0$ in order to obtain $\lim_{m \rightarrow \infty} D_{1,m} = 0$. For all $T \in \mathcal{T}_m$, we introduce the notations:

$$\bar{\phi}_T^{n+1} = \max_{x \in T} \left(\phi_{\mathcal{T}_m, \Delta t_m}(v)(t_{n+1}, x) \right), \quad \underline{\phi}_T^{n+1} = \min_{x \in T} \left(\phi_{\mathcal{T}_m, \Delta t_m}(v)(t_{n+1}, x) \right),$$

and for all $(t, x) \in (t_n, t_{n+1}) \times T$

$$\bar{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) = \bar{\phi}_T^{n+1}, \quad \underline{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) = \underline{\phi}_T^{n+1}.$$

Now for all $\sigma_{KL} \in \mathcal{E}_T$, there holds

$$\left| \sqrt{\eta_{KL}^{n+1}} - \sqrt{\bar{\eta}_{KL}^{n+1}} \right| \leq \mu \left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1} \right), \quad (3.90)$$

where μ is the continuity modulus of $\sqrt{\eta \circ \phi^{-1}}$. Indeed, the continuity and boundedness of $\sqrt{\eta \circ \phi^{-1}}$ on the interval $[\phi(0), \phi(1)]$ ensure the existence and boundedness of the continuity modulus μ . Therefore,

$$0 \leq P_m \leq \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \mu \left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1} \right)^2 \sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| (\psi_K^n - \psi_L^n)^2, \quad (3.91)$$

where λ_{KL}^T is defined by (3.61).

Using the proof of Lemma 3.5.3, there exists a constant C such that

$$\sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| (\psi_K^n - \psi_L^n)^2 \leq Cm_T,$$

where m_T denotes the measure of the triangle T . Therefore, (3.91) implies that

$$\begin{aligned} 0 \leq P_m &\leq C \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} m_T \mu \left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1} \right)^2 \\ &\leq C \iint_{\Omega_T} \mu \left(\bar{\phi}_{\mathcal{T}_m, \Delta t_m} - \underline{\phi}_{\mathcal{T}_m, \Delta t_m} \right)^2 dx dt. \end{aligned}$$

Since μ is bounded, continuous with $\mu(0) = 0$, it is enough to show that up to an unlabeled subsequence $\bar{\phi}_{\mathcal{T}_m, \Delta t_m} - \underline{\phi}_{\mathcal{T}_m, \Delta t_m} \rightarrow 0$ a.e. in Ω_T in order to conclude the proof of $\lim_{m \rightarrow \infty} P_m = 0$. By a generalization of Lemma A.1 in [CG16], there holds

$$\iint_{\Omega_T} \left| \bar{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) - \underline{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) \right|^2 dx dt \leq Ch_m^2 \|\nabla \phi(v)_{\mathcal{T}_m, \Delta t_m}\|_{L^2(\Omega_T)}^2.$$

Consequently, by Lemma 3.5.2, ellipticity of Λ and Lemma 3.5.5, one obtains

$$\iint_{\Omega_T} \left| \bar{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) - \underline{\phi}_{\mathcal{T}_m, \Delta t_m}(t, x) \right|^2 dx dt \leq Ch_m^2.$$

Hence, up to a subsequence,

$$\lim_{m \rightarrow \infty} D_{1,m} = \lim_{m \rightarrow \infty} P_m = 0.$$

Now, we prove that

$$\lim_{m \rightarrow \infty} D_{2,m} = \iint_{\Omega_T} \Lambda \nabla v \cdot \nabla \psi dx dt.$$

For this sake, we introduce the term $D_{2,m}^*$ defined by:

$$D_{2,m}^* := \iint_{\Omega_T} \Theta_{\mathcal{T}_m, \Delta t_m} \Lambda(x) \nabla \phi(v)_{\mathcal{T}_m, \Delta t_m} \cdot \nabla \psi_{\mathcal{T}_m, \Delta t_m}(\cdot, t - \Delta t_m) dx dt,$$

where $\Theta_{\mathcal{T}_m, \Delta t_m}$ is a piecewise constant (per triangle) function given by

$$\Theta_{\mathcal{T}_m, \Delta t_m}(t, x) = \sqrt{\eta \circ \phi^{-1}} \left(\Phi_{\mathcal{T}_m, \Delta t_m}(t, x) \right), \quad \forall x \in T, t \in (t_n, t_{n+1}], \forall T \in \mathcal{T}_m,$$

and

$$\Phi_{\mathcal{T}_m, \Delta t_m}(t, x) = \phi(v)_{\mathcal{T}_m, \Delta t_m}(t, x_T), \quad \forall x \in T, t \in (t_n, t_{n+1}], \forall T \in \mathcal{T}_m,$$

where x_T is the center of mass of T . Adapting a slightly modified version of the proof of Lemma A.1 in [CG16], it is simple to check that

$$\Phi_{\mathcal{T}_m, \Delta t_m} \rightarrow \phi(v) \text{ in } L^2(\Omega_T) \text{ as } m \rightarrow \infty.$$

Moreover, the function $\sqrt{\eta \circ \phi^{-1}}$ being continuous and bounded, one gets

$$\Theta_{\mathcal{T}_m, \Delta t_m} \rightarrow \sqrt{\eta(v)} \text{ in } L^2(\Omega_T) \text{ as } m \rightarrow \infty.$$

Furthermore, $\nabla \phi(v)_{\mathcal{T}_m, \Delta t_m}$ converges weakly in $L^2(\Omega_T)$ to $\nabla \phi(v)$ and $\nabla \psi_{\mathcal{T}_m, \Delta t_m}$ converges uniformly to $\nabla \psi$. Hence,

$$\begin{aligned} \lim_{m \rightarrow \infty} D_{2,m}^* &= \iint_{\Omega_T} \sqrt{\eta(v)} \Lambda(x) \nabla \phi(v) \cdot \nabla \psi dx dt \\ &= \iint_{\Omega_T} \Lambda(x) \nabla v \cdot \nabla \psi dx dt, \end{aligned}$$

where the last equality follows from the observation that

$$\nabla\phi(v) = \frac{1}{\sqrt{\eta(v)}}\nabla v.$$

Therefore, it is only required to verify that

$$|D_{2,m} - D_{2,m}^*| \rightarrow 0 \text{ as } m \rightarrow \infty.$$

Introducing the notation

$$\eta_T^{n+1} := \left(\Theta_{\mathcal{T}_m, \Delta t_m}(t_{n+1}, x_T)\right)^2, \quad \forall T \in \mathcal{T}_m, \forall n \in \{0, \dots, N_m - 1\},$$

then the discrete form of $D_{2,m}^*$ becomes

$$D_{2,m}^* = \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \sqrt{\eta_T^{n+1}} \sum_{\sigma_{KL} \in \mathcal{E}_T} \lambda_{KL}^T \left(\phi(v_K^{n+1}) - \phi(v_L^{n+1})\right) (\psi_K^n - \psi_L^n).$$

By a similar argument to the one used in getting inequality (3.90), there holds

$$\left|\sqrt{\eta_{KL}^{n+1}} - \sqrt{\eta_T^{n+1}}\right| \leq \mu\left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1}\right), \quad \forall \sigma_{KL} \in \mathcal{E}_T.$$

Therefore,

$$|D_{2,m} - D_{2,m}^*|^2 \leq \left(\sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \mu\left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1}\right) \sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| |\phi(v_K^{n+1}) - \phi(v_L^{n+1})| |\psi_K^n - \psi_L^n|\right)^2.$$

Using Cauchy-Schwartz' inequality, we get

$$\begin{aligned} |D_{2,m} - D_{2,m}^*|^2 &\leq \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \mu\left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1}\right)^2 \sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| (\psi_K^n - \psi_L^n)^2 \\ &\quad \times \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| |\phi(v_K^{n+1}) - \phi(v_L^{n+1})|^2, \end{aligned}$$

Using Lemmata 3.5.2, 3.5.3 and 3.5.5, there exists C independent of h_m such that

$$|D_{2,m} - D_{2,m}^*|^2 \leq C \sum_{n=0}^{N_m-1} \Delta t_m \sum_{T \in \mathcal{T}_m} \mu\left(\bar{\phi}_T^{n+1} - \underline{\phi}_T^{n+1}\right)^2 \sum_{\sigma_{KL} \in \mathcal{E}_T} |\lambda_{KL}^T| (\psi_K^n - \psi_L^n)^2 := Q_m,$$

and the same argument as in the proof of $\lim_{m \rightarrow \infty} P_m = 0$, implies that $\lim_{m \rightarrow \infty} Q_m = 0$. Hence,

$$\lim_{m \rightarrow \infty} |D_{2,m} - D_{2,m}^*| = 0.$$

Reaction term

It is required to prove now that

$$\lim_{m \rightarrow \infty} R_m = - \iint_{\Omega_T} I_{\text{ion}}(v(t, x), \mathbf{w}(t, x), c(t, x)) \psi(t, x) dx dt := R.$$

First rewrite R_m and R as:

$$R_m = - \sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} \int_{t_n}^{t_{n+1}} \int_{\omega_K} I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \psi(t_n, x_K),$$

and

$$R = \sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} \int_{t_n}^{t_{n+1}} \int_{\omega_K} -I_{\text{ion}}(v, \mathbf{w}, c) \psi(t, x) dx dt.$$

Then note that $|R_m - R|$ can be written as:

$$\begin{aligned} |R_m - R| &= \left| \sum_{n=0}^{N_m-1} \sum_{K \in \mathcal{V}_m} \left[I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \int_{t_n}^{t_{n+1}} \int_{\omega_K} (\psi(t_n, x_K) - \psi(t, x)) \right. \right. \\ &\quad \left. \left. + \int_{t_n}^{t_{n+1}} \int_{\omega_K} (I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n) \psi(t, x) - I_{\text{ion}}(v, \mathbf{w}, c) \psi(t, x)) \right] \right|. \end{aligned}$$

For all $x \in \omega_K$ and $t \in [t_n, t_{n+1}]$, there holds

$$|\psi(t_n, x_K) - \psi(t, x)| \leq C_1(\Delta t_m + h_m),$$

for some $C_1 > 0$. Moreover, $|\psi(t, x)| \leq C_2$ for some $C_2 > 0$. Therefore,

$$\begin{aligned} |R_m - R| &\leq C_1(\Delta t_m + h_m) \sum_{n=0}^{N_m-1} \Delta t_m \sum_{K \in \mathcal{V}_m} m_K |I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)| \\ &\quad + C_2 \iint_{\Omega_T} |I_{\text{ion}}(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m}) - I_{\text{ion}}(v, \mathbf{w}, c)| dx dt. \end{aligned}$$

Since $|I_{\text{ion}}(v_K^{n+1}, \mathbf{w}_K^{n+1}, c_K^n)|$ is bounded, we get

$$|R_m - R| \leq C_3(\Delta t_m + h_m) T |\Omega| + C_2 \iint_{\Omega_T} |I_{\text{ion}}(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m}) - I_{\text{ion}}(v, \mathbf{w}, c)| dx dt.$$

On the other hand, since $v_{\mathcal{M}_m, \Delta t_m} \rightarrow v$, $\mathbf{w}_{\mathcal{M}_m, \Delta t_m} \rightarrow \mathbf{w}$, and $c_{\mathcal{M}_m, \Delta t_m} \rightarrow c$ a.e. in Ω_T and I_{ion} is continuous, then $I_{\text{ion}}(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m}) \rightarrow I_{\text{ion}}(v, \mathbf{w}, c)$ a.e. in Ω_T . Moreover, since $I_{\text{ion}}(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m}) \in L^\infty(\Omega_T)$, then by Lebesgue's dominated convergence we get the convergence of $I_{\text{ion}}(v_{\mathcal{M}_m, \Delta t_m}, \mathbf{w}_{\mathcal{M}_m, \Delta t_m}, c_{\mathcal{M}_m, \Delta t_m})$ to $I_{\text{ion}}(v, \mathbf{w}, c)$ in $L^1(\Omega_T)$. As a result, we conclude that $R_m \rightarrow R$.

This ends the proof of convergence of discrete solutions to the weak solution.

3.8 Numerical Results

In this section, we illustrate the efficiency of the nonlinear CVFE scheme (3.57), (3.51), (3.52) and we compare it to the CVFE scheme (3.50), (3.51), (3.52). Newton's algorithm is used to implement both schemes.

Numerical Tests

In this paragraph, we provide some academic examples to estimate the error between the computed solution and the analytical solution to some model problems. We test and compare the efficiency and convergence of various numerical schemes: the classical CVFE scheme, the nonlinear positive CVFE scheme with different choices of p and η . The first one, which is labeled as the nonlinear CVFE scheme with $\ln(\cdot)$, corresponds to the choice of the functions p and η as in [CG16, CIS17] given by

$$\eta(v) = \max(0, \min(v, 1)) = \begin{cases} 0, & \text{if } v \leq 0, \\ v, & \text{if } 0 \leq v \leq 1, \\ 1, & \text{if } v \geq 1, \end{cases}$$

$$p(v) = \int_1^v \frac{1}{\eta(s)} ds = \begin{cases} \ln(v), & \text{if } 0 < v \leq 1, \\ v - 1, & \text{if } v \geq 1, \end{cases}$$

with the convention $\eta(v)p(v) = 0$ if $v \leq 0$. The second choice is the one considered in the present work and given in (3.53) and (3.54). The third choice, labeled as nonlinear CVFE scheme with $\sqrt{\cdot}$, corresponds to the following definition of η and p :

$$\eta(v) = \begin{cases} 0 & \text{if } v \leq 0 \\ 2\sqrt{v}, & \text{if } v > 0. \end{cases}$$

$$p(v) = \begin{cases} 0 & \text{if } v \leq 0 \\ \sqrt{v}, & \text{if } v > 0. \end{cases}$$

In the following examples, we consider the diffusion problem:

$$\begin{aligned} \frac{\partial u}{\partial t} - \nabla \cdot (\Lambda \nabla u) &= f(x, y, t), & \text{for a.e. } (x, y, t) \in (0, 1) \times (0, 1) \times (0, T), \\ u(x, y, 0) &= u_0(x, y), & \text{for a.e. } (x, y) \in (0, 1) \times (0, 1), \\ \Lambda \nabla u \cdot n &= 0 & \text{a.e. on } \partial \left((0, 1) \times (0, 1) \right) \times (0, T), \end{aligned} \quad (3.92)$$

with different choices of the functions f and u_0 and the diffusion tensor Λ .

Example 1. In this example, we let

$$\Lambda := \begin{pmatrix} 1 & 0.5 \\ 0.5 & 1 \end{pmatrix}, \text{ and } u_0(x, y) := \frac{1}{4}(1 - \cos(2\pi x))(1 - \cos(2\pi y)).$$

The exact solution is given by:

$$u(x, y, t) = \frac{1}{4}(1 - \sin^2(t))(1 - \cos(2\pi x))(1 - \cos(2\pi y)).$$

Figures 3.2 and 3.3 show the log-log scale of the relative error at the final time instant $T = 0.5$ for the classical CVFE scheme and the three nonlinear CVFE schemes using a structured mesh with mesh size $h\sqrt{2}$ for the following values of $h = 1/20, 1/30, 1/40, 1/50, 1/60$ and the corresponding values of time step Δt obtained by $\Delta t = \frac{25h^2}{2}$.

Tables 3.1, 3.2, 3.3 and 3.4 contain the minimum and maximum values of the numerical solution $u_{h,\Delta t}$ and the relative L^2 and L^∞ errors obtained for a structured mesh with mesh size

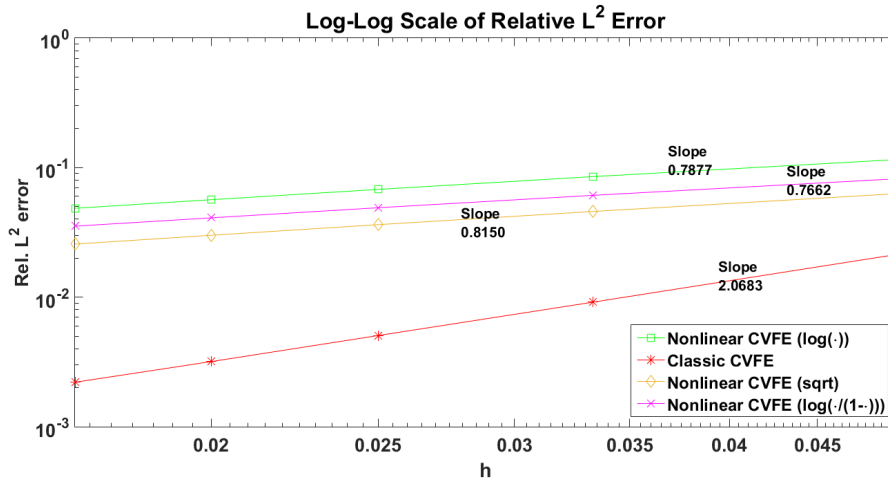


Figure 3.2 – Relative L²-error in a log-log scale for Example 1.

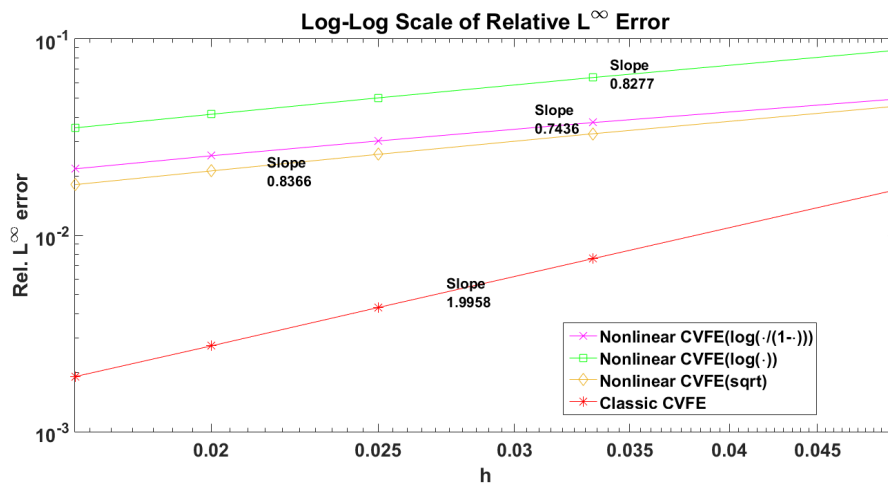


Figure 3.3 – Relative L[∞]-error in a log-log scale for Example 1.

$h\sqrt{2}$ and time step Δt for $T = 0.5$ with the classical CVFE scheme, and the nonlinear CVFE schemes with the choice $\ln(\cdot)$, $\ln(\cdot/(1 - \cdot))$ and $\sqrt{\cdot}$ for p respectively.

As observed in Tables 3.1, 3.2, 3.3 and 3.4, the three nonlinear CVFE schemes assure the discrete maximum principle property as opposed to the classical CVFE scheme where under- and overshoots are observed. However, the rate of convergence which is almost 2 for the classical CVFE scheme decreases to values slightly less than 1 in the case of the nonlinear CVFE schemes (see Figures 3.2 and 3.3).

Table 3.1 – Classical CVFE: Results for Example 1.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	-0.0131	0.7750	0.0213	0.0171
0.0333	0.0139	-0.0059	0.7723	0.0092	0.0076
0.0250	0.0078	-0.0033	0.7714	0.0051	0.0043
0.0200	0.0050	-0.0021	0.7751	0.0032	0.0027
0.0167	0.0035	-0.0015	0.7707	0.0022	0.0019

Table 3.2 – Nonlinear CVFE with $\ln(\cdot)$: Results for Example 1.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	0.0183	0.7028	0.1154	0.0875
0.0333	0.0139	0.0163	0.7212	0.0852	0.0636
0.0250	0.0078	0.0141	0.7316	0.0679	0.0501
0.0200	0.0050	0.0124	0.7424	0.0566	0.0413
0.0167	0.0035	0.0109	0.7430	0.0486	0.0353

Table 3.3 – Nonlinear CVFE with $\ln(\cdot/(1-\cdot))$: Results for Example 1.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	0.0129	0.7321	0.0820	0.0494
0.0333	0.0139	0.0122	0.7413	0.0611	0.0375
0.0250	0.0078	0.0108	0.7469	0.0490	0.0302
0.0200	0.0050	0.0096	0.7547	0.0410	0.0254
0.0167	0.0035	0.0086	0.7534	0.0353	0.0218

Table 3.4 – Nonlinear CVFE with $\sqrt{\cdot}$: Results for Example 1.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	0.0060	0.7355	0.0629	0.0454
0.0333	0.0139	0.0071	0.7449	0.0459	0.0329
0.0250	0.0078	0.0041	0.7563	0.0308	0.0233
0.0200	0.0050	0.0060	0.7579	0.0300	0.0213
0.0167	0.0035	0.0054	0.7562	0.0257	0.0181

Example 2. In this example, we consider

$$\Lambda := \begin{pmatrix} 1 & 0.5 \\ 0.5 & 1 \end{pmatrix}, \text{ and } u_0(x, y) := 256x^2(x-1)^2y^2(y-1)^2 \frac{1 + \cos(\pi(y - \frac{1}{2}))}{2}.$$

The exact solution is given by:

$$u(x, y, t) = v(x, y, t)g(y),$$

where $g(y) = \frac{(1 + \cos(\pi(y - \frac{1}{2})))}{2}$ and $v(x, y, t) = 256(1 - \sin^2(t))x^2(x - 1)^2y^2(y - 1)^2$.

As for the previous example, Figures 3.4 and 3.5 show the log-log scale of the relative error at the final time instant $T = 0.5$ for the classical CVFE scheme and the three nonlinear CVFE schemes using a structured mesh.

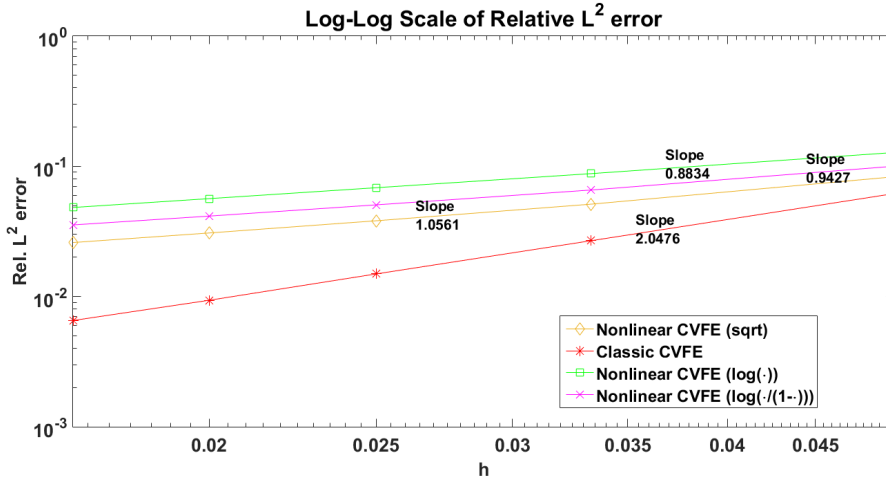


Figure 3.4 – Relative L²-error in a log-log scale for Example 2.

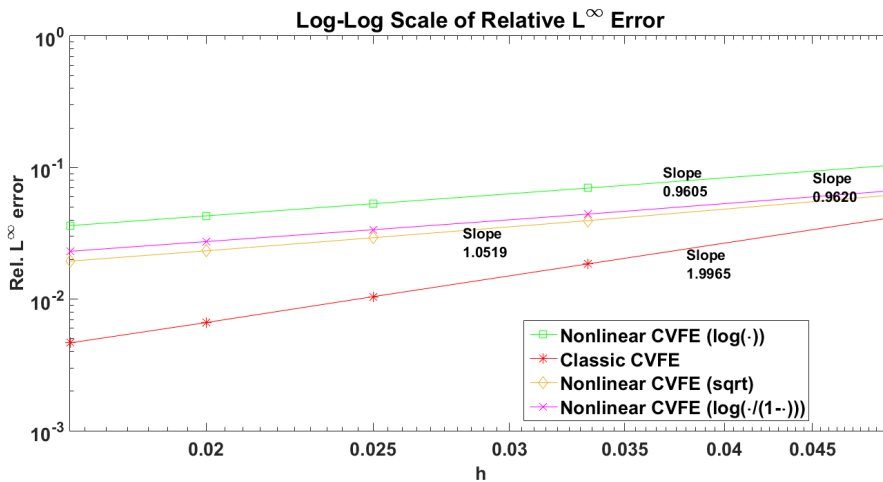


Figure 3.5 – Relative L[∞]-error in a log-log scale for Example 2.

Also, Tables 3.5, 3.6, 3.7 and 3.8 contain the minimum and maximum values of the numerical solution $u_{h,\Delta t}$ and the relative L² and L[∞] errors obtained for a structured mesh with mesh size h and time step Δt for the final time instant $T = 0.5$.

Clearly, the classical CVFE scheme violates the discrete maximum principle property as shown in Table 3.5. Both nonlinear CVFE schemes with $\ln(\cdot)$ and $\ln(\cdot)/(1 - \cdot)$ guarantee this property irrespective of the mesh and the anisotropy while the nonlinear CVFE scheme with $\sqrt{\cdot}$ does not verify it for the coarsest mesh (see Tables 3.6, 3.7 and 3.8). Again, this property is ensured at the expense of the rate of convergence which decreases from almost 2 for the classical CVFE scheme to values almost 1 in the case of the nonlinear CVFE schemes (see Figures 3.4 and 3.5).

Indeed, the slower convergence rate may be attributed to the numerical diffusion introduced by the upwind scheme.

Table 3.5 – Classical CVFE: Results for Example 2.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	-0.0320	0.7637	0.0618	0.0416
0.0333	0.0139	-0.0143	0.7673	0.0268	0.0185
0.0250	0.0078	-0.0080	0.7685	0.0149	0.0104
0.0200	0.0050	-0.0051	0.7733	0.0094	0.0066
0.0167	0.0035	-0.0036	0.7694	0.0065	0.0046

Table 3.6 – Nonlinear CVFE with $\ln(\cdot)$: Results for Example 2.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	0.0079	0.6900	0.1277	0.1040
0.0333	0.0139	0.0114	0.7164	0.0879	0.0699
0.0250	0.0078	0.0114	0.7293	0.0685	0.0531
0.0200	0.0050	0.0108	0.7411	0.0565	0.0429
0.0167	0.0035	0.0099	0.7423	0.0483	0.0362

Table 3.7 – Nonlinear CVFE with $\ln(\cdot/(1 - \cdot))$: Results for Example 2.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	0.0036	0.7189	0.1002	0.0666
0.0333	0.0139	0.0075	0.7360	0.0658	0.0443
0.0250	0.0078	0.0082	0.7442	0.0506	0.0337
0.0200	0.0050	0.0080	0.7531	0.0415	0.0274
0.0167	0.0035	0.0075	0.7524	0.0355	0.0231

Table 3.8 – Nonlinear CVFE with $\sqrt{\cdot}$: Results for Example 2.

h	Δt	min $u_{h,\Delta t}$	max $u_{h,\Delta t}$	rel. L² error	rel. L[∞] error
0.05	0.0313	-0.0247	0.7228	0.0831	0.0618
0.0333	0.0139	0.0019	0.7398	0.0512	0.0395
0.0250	0.0078	0.0036	0.7476	0.0382	0.0293
0.0200	0.0050	0.0041	0.7563	0.0308	0.0233
0.0167	0.0035	0.0041	0.7552	0.0260	0.0195

Numerical Tests on the Monodomain Model

For our test, we first consider a rectangular domain permitting to visualize all the phases of the action potential (fast depolarization, short repolarization period, plateau, repolarization) . We fix: $\Delta t = 0.5$, $\chi = 1000$ and $C_m = 1$.

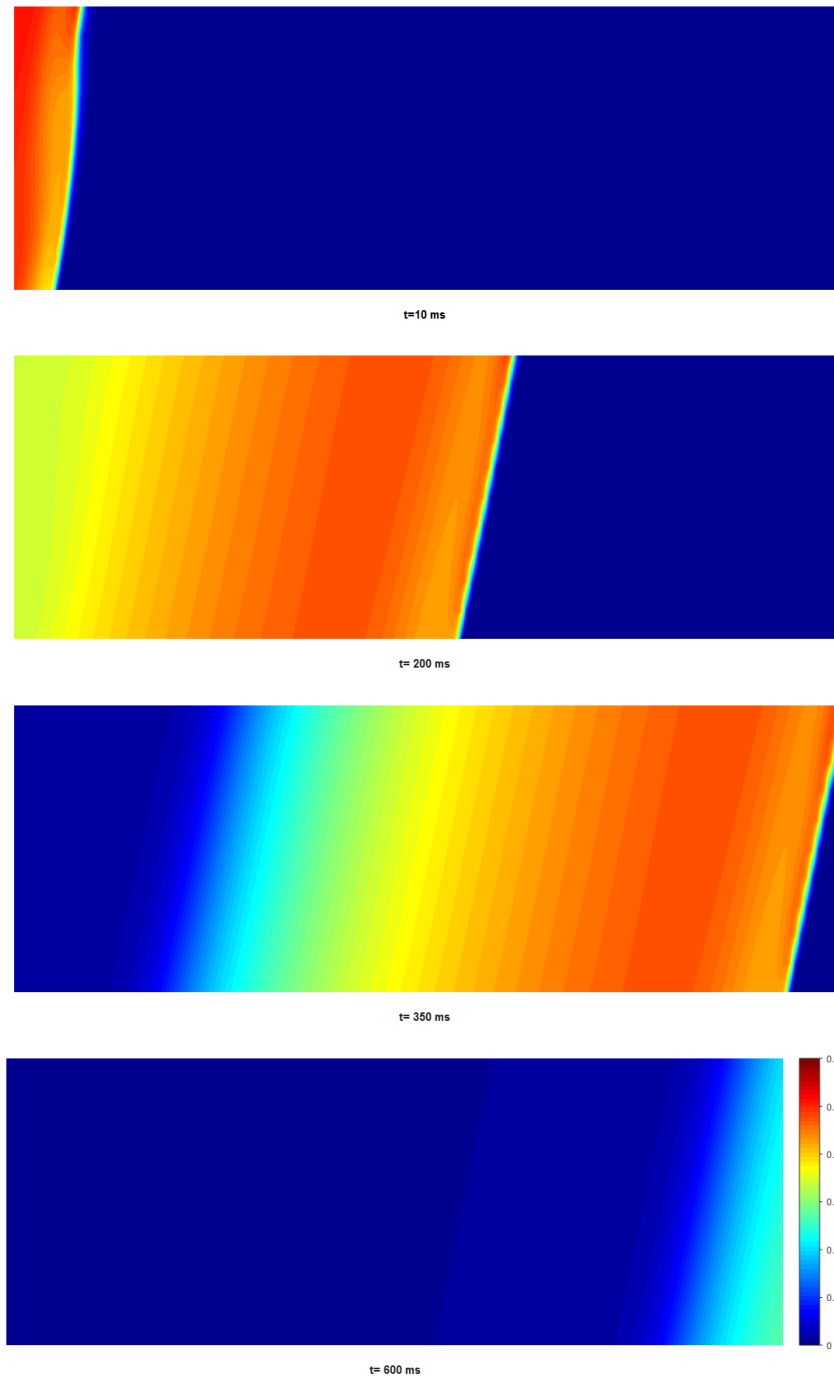


Figure 3.6 – From top to bottom consecutively: The propagation of the action potential for $t = 10, 200, 350, 600$ ms respectively using CVFE scheme.

We assume that the conductivity tensor is anisotropic and is given by:

$$\Lambda = \begin{pmatrix} 1.2042 & 0.4500 \\ 0.4500 & 0.1843 \end{pmatrix},$$

which eigenvalues are $\lambda_1 = 0.0141$ and $\lambda_2 = 1.3744$.

Due to the anisotropy condition, a vertical stimulus at the initial time $t = 0$ ms at the left side of

the domain ($v_0(x, y) = 0.6$ mV for $x < 0.1$ cm and for all $0 \leq y \leq 1$ cm and $v_0(x, y) = 0$ mV otherwise) propagates in a slanted way towards the right side of the domain with both schemes, see Figures 3.6 and 3.7. The number of vertices in the mesh is 3311 vertices, and the number of triangles is 6000.

As expected from the previous analysis, the maximum principle is verified in the case of the positive nonlinear CVFE scheme (3.57), (3.51), (3.52). In particular, the values of the rescaled potential difference v are between 0 and 1. However, in the CVFE scheme (3.50), (3.51), (3.52), it takes negative values which are not physiological. However, due to the numerical diffusion of the nonlinear scheme, the wave reaches the left side of the rectangle faster than the wave in the classical CVFE scheme as shown at the time instant $t = 350$ ms in Figures 3.6 and 3.7.

Moreover, the violation of the discrete maximum principle by the classical CVFE scheme is clearly seen in Figure 3.8 where the values of the transmembrane potential fluctuate below -85 mV. In the same figure, the results of a finite element simulation (implemented with freefem++, with P_2 elements, 4411 vertices and 8000 triangles) using the same initial conditions and the same parameters (domain, Δt , χ , C_m) is shown. One can easily observe the oscillations in the wave (drawn in 3D) obtained by both the FE scheme and the CVFE scheme. Such oscillations are absent when the positive CVFE scheme is used and the discrete maximum principle is also ensured. However, the wavefront, drawn at the same time instant for the three methods in Figure 3.8, seems to have a faster propagation. Again, this is attributed to the numerical diffusion in the upwind schemes.

Furthermore, we have tested the positive CVFE scheme on a 2D-domain imitating a cross section of the heart with the left and right ventricles. The mesh is shown in Figure 3.9 and the time step Δt is 0.5 ms. We initiated a stimulus in the interventricular septal wall, and we recorded the propagation of the action potential using two different conductivities:

$$\Lambda_1 = \begin{pmatrix} 1.2042 & 0 \\ 0 & 0.1843 \end{pmatrix} \text{ and } \Lambda_2 = \begin{pmatrix} 1.2042 & 0.4500 \\ 0.4500 & 0.1843 \end{pmatrix}.$$

Figures 3.10 and 3.12 show the propagation of the electrical wave in the 2D section for the diagonal and the full conductivity matrices Λ_1 and Λ_2 respectively. The propagation of the wave is clearly different showing the effect of the different conductivities. On the other hand, the recorded action potential at the points A, B, C, D and E indicated in Figure 3.9 are very close to the physiological Action Potential of Beeler-Reuter model especially at points D and E as shown in Figures 3.11 and 3.13. Although the conductivity matrix Λ_2 produces a non-monotone rigidity matrix (negative transmissibility coefficients), the recorded values of the transmembrane potential do not drop below or exceed the values in the physiological range. This is particularly observed in Figure 3.13 where the action potential is drawn at the points A, B, C, D and E.

3.9 Conclusion

In conclusion, we have studied, in this chapter, a finite volume scheme and a positive nonlinear CVFE scheme for the monodomain model coupled with Beeler-Reuter ionic model. The aim was to approximate the fluxes properly keeping in mind that the solutions must satisfy some natural bounds in addition to some estimates on the discrete gradients. The numerical tests exhibited the ability of the nonlinear CVFE scheme to efficiently simulate the propagation

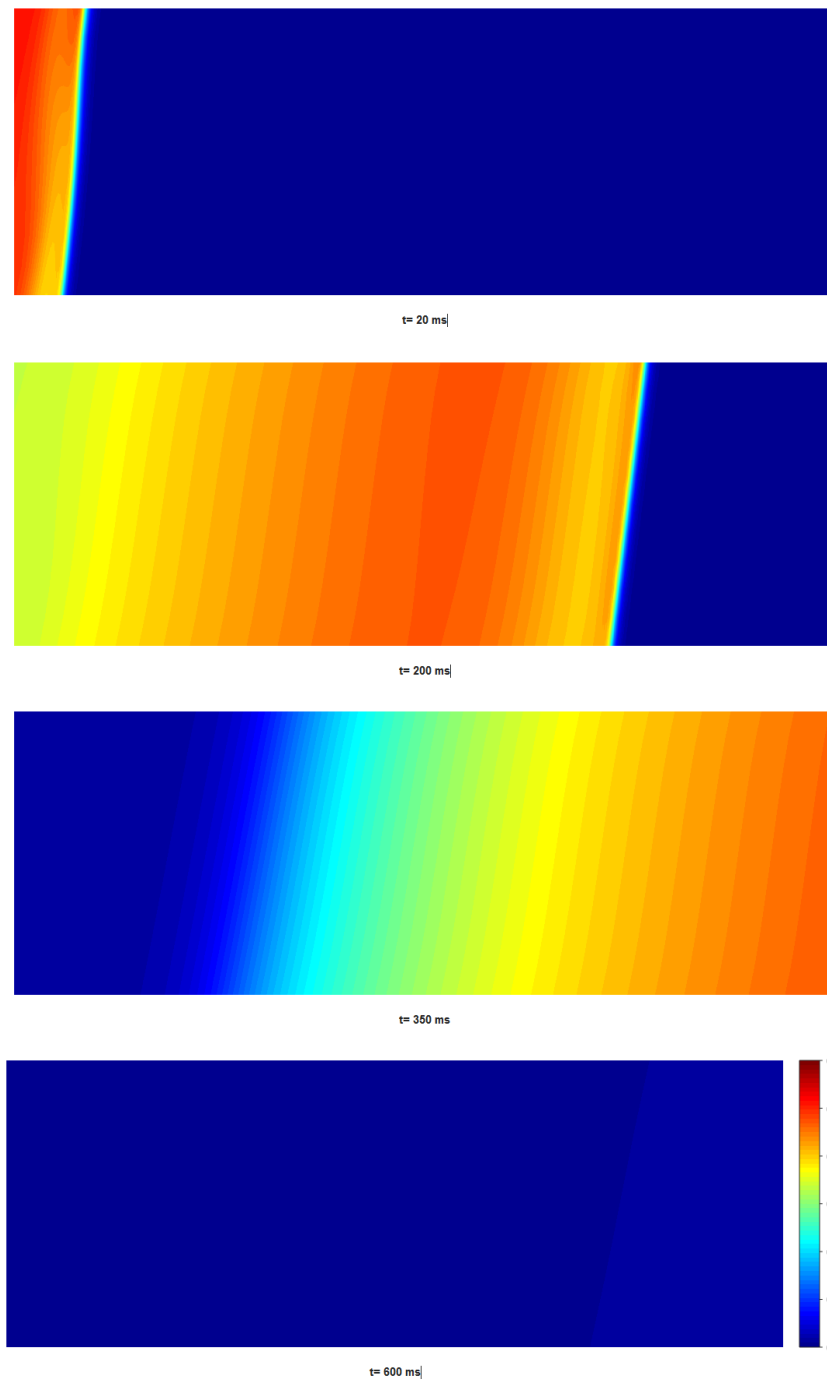


Figure 3.7 – From top to bottom consecutively: The propagation of the action potential for $t = 10, 200, 350, 600$ ms respectively using the positive nonlinear CVFE scheme with $\ln(\cdot/(1 - \cdot))$.

of the action potential without any over- and undershoots. However, some numerical diffusion is observed during the simulations mainly due to the upwind technique.

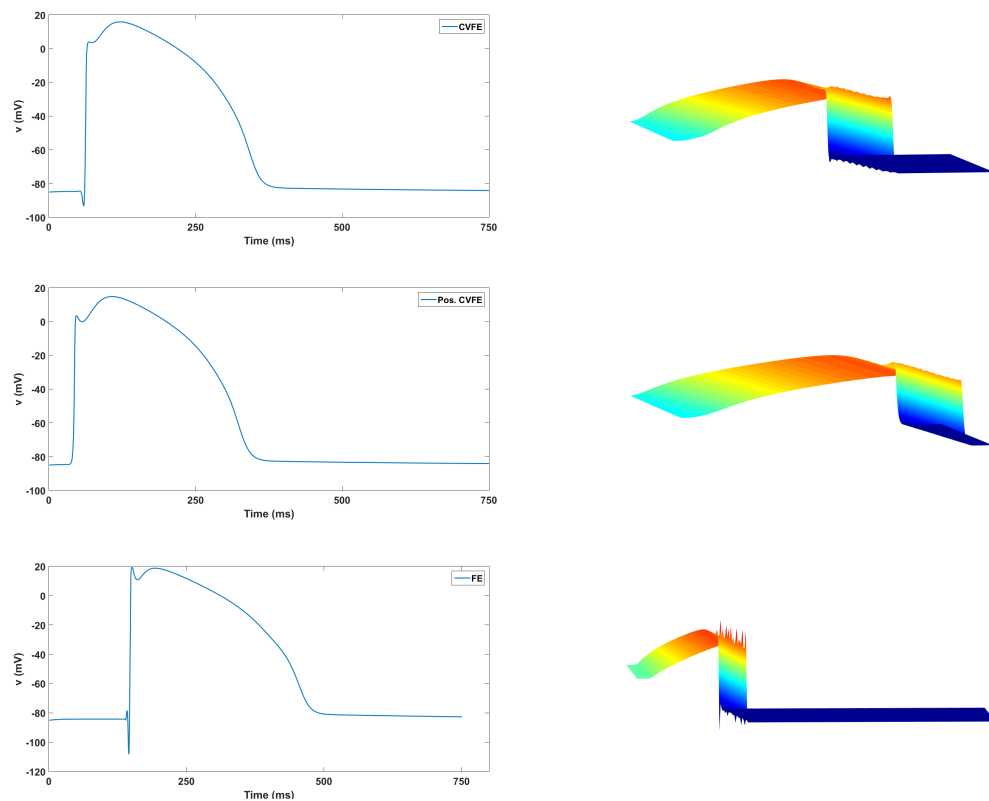


Figure 3.8 – First Column: Action potentials obtained from the CVFE scheme (top), the positive nonlinear CVFE scheme (center) and the finite elements method (bottom) at the same point. Second column: the respective wave propagation at time $t = 250$ ms.

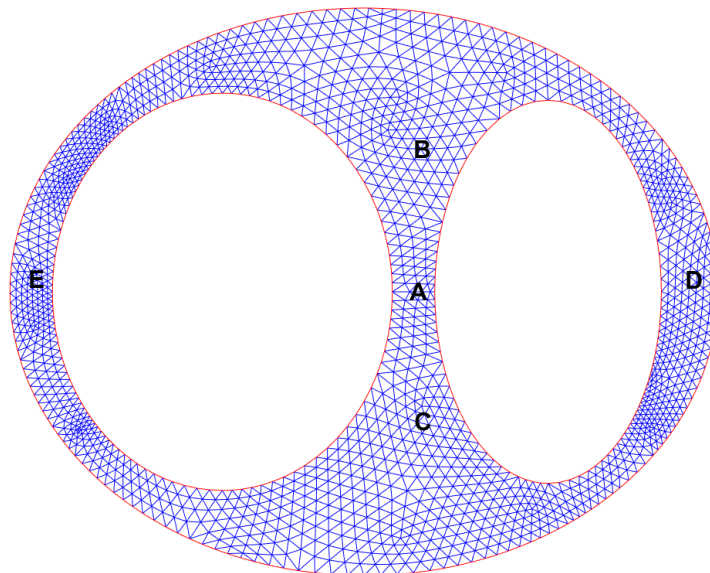


Figure 3.9 – The mesh of the cross section using 1701 vertices and 2992 triangles, along with the points at which the action potential is drawn.

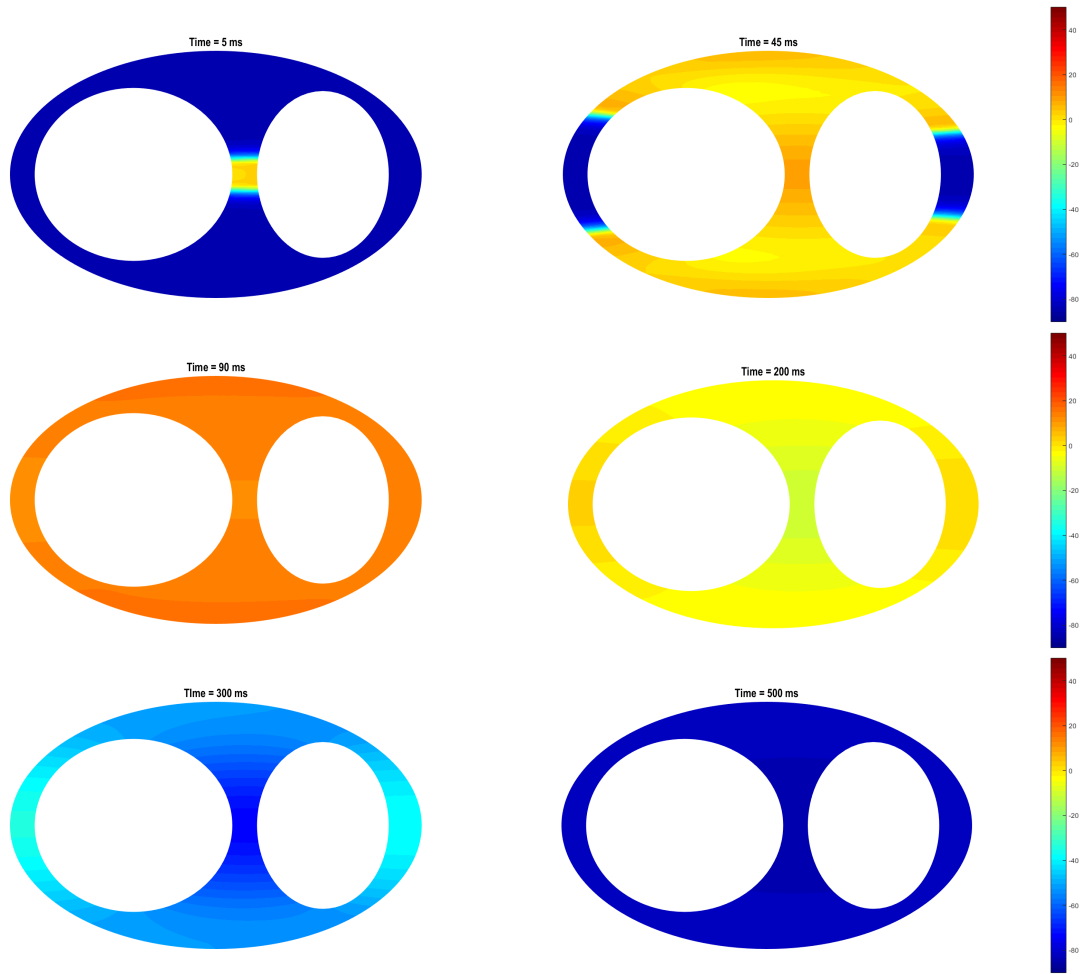


Figure 3.10 – The propagation of the action potential using the conductivity Λ_1 at $t = 10, 45, 90, 200, 300$ and 500 ms from top left to bottom right respectively.

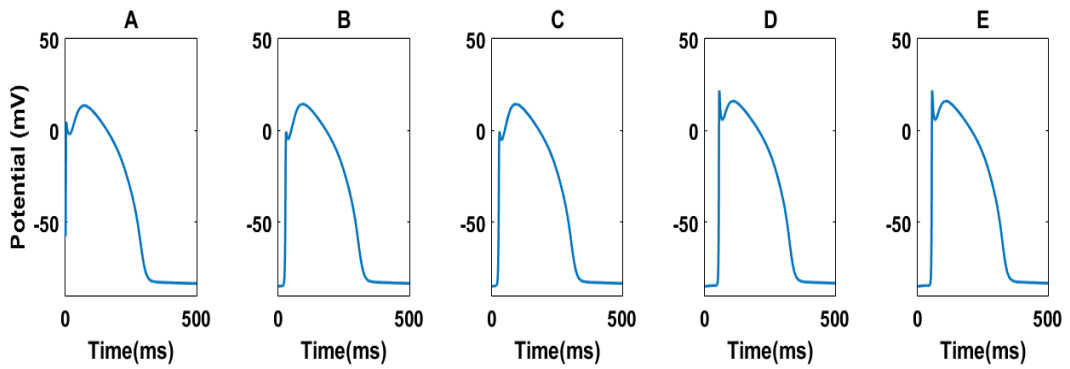


Figure 3.11 – Action potentials recorded at the points A, B, C, D and E using conductivity Λ_1 .

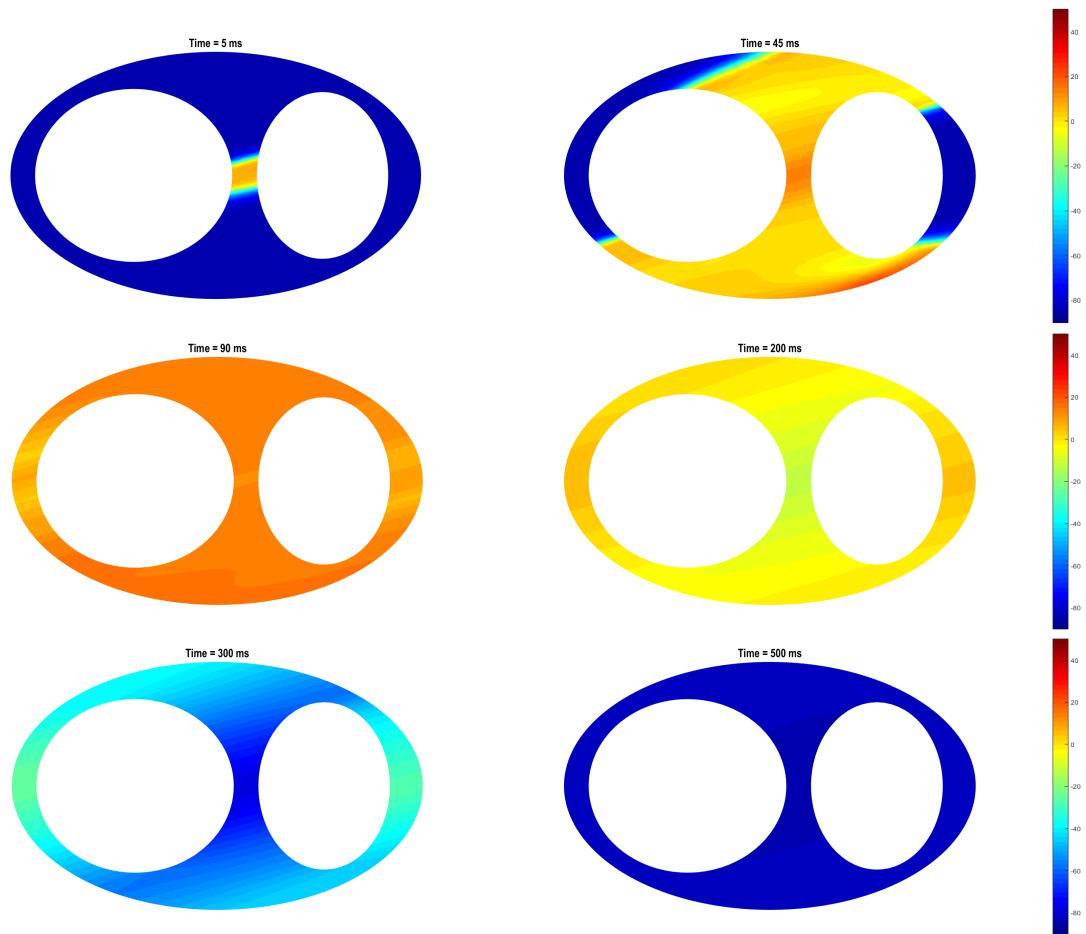


Figure 3.12 – The propagation of the action potential using the conductivity Λ_2 at $t = 10, 45, 90, 200, 300$ and 500 ms from top left to bottom right respectively.

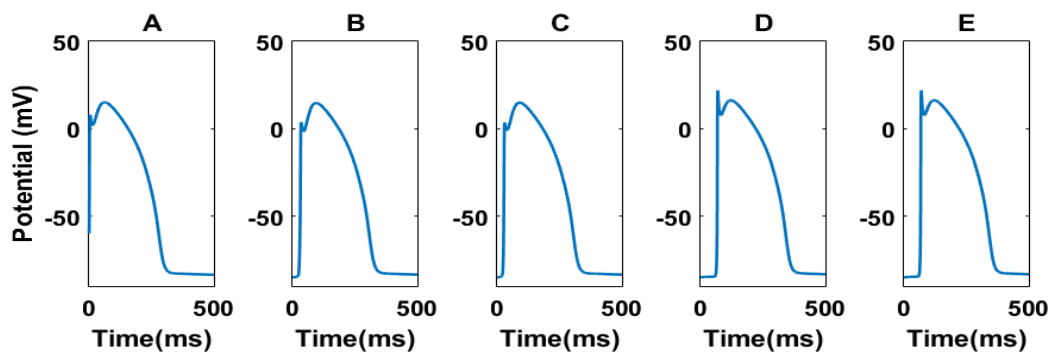


Figure 3.13 – Action potentials recorded at the points A, B, C, D and E using conductivity Λ_2 .

Mathematical analysis of cardiac electromechanics

4.1 Introduction

This chapter 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 the 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 [NT07, CFNT08]. 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 chapter, is proved by means of a non-degenerate approximation system, the Faedo-Galerkin method, and the compactness method.

The equations of the bidomain model may be coupled with phenomenological or physiological ionic models. Although it was proposed forty years ago [Tun78], the bidomain system was extensively studied from a well-posedness point of view in the last two decades. A variational approach was first introduced by Savaré and Franzone [FS02a]. Later analyses took different directions: Bendahmane and Karlsen used nondegenerate approximation systems to which they applied the Faedo-Galerkin scheme [BK06], Bourgault et al. introduced a “Bidomain” operator and used a semigroup approach [BCP09], Matano and Mori derived global classical solutions [MM11] 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 [Ven09].

Mathematical analysis of general nonlinear elasticity can be found in [Cia87, Bal77], whereas applications of those theories to the particular case of hyperelastic materials and cardiac mechanics are available in [NH00, KSMSU06, HO09, RRBQ12, SWO⁺14, BQRB13]. Despite the large availability of references related to numerical methods and models for cardiac electromechanics (e.g. [GK10, LAVH12, NP04, NNN⁺11, Tra11]), there are open questions in their mathematical validity. To our knowledge, some existence results have been established by Pathmanatan *et al.* [PCGW10, POK13] and Andreianov *et al.* [ABQRB15]. 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 this chapter, but we use a general physiological ionic model whose kinetics overlaps with Beeler-Reuter model [BR77] or Luo-Rudy model [LR94]. 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.

Comparing to the work [Ven09] (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 [ABQRB15], 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. The existence of weak solutions to the coupled electromechanical problem is proved by introducing non-degenerate approximation systems including an “artificial compressibility” condition. We prove existence of solutions to those approximation systems (for each fixed $\varepsilon > 0$) by applying the Faedo-Galerkin method, deriving a priori estimates, and then passing to the limit in the approximate solutions using compactness arguments. Having proved existence for the approximation systems, the goal is to send the regularization parameter ε to zero in sequences of such solutions to fabricate weak solutions of the original systems. Again convergence is achieved by a priori estimates and compactness arguments. On the technical side, we point out that the passage to the limit in the pressure term is not straightforward due to the artificial compressibility assumption along with the use of “Navier-type” boundary conditions.

The contents of this chapter are organized as follows. Section 4.2 presents the linearization of the elasticity equations and the resulting problem, lists the basic assumptions of the model and provides a definition of weak solution. In Section 4.3 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 4.4 by using (one more time) a priori estimates and compactness arguments.

4.2 Governing equations for the electromechanical coupling

The active strain formulation for the electromechanical activity in the heart is written as follows [NQRB12]:

$$\begin{aligned}
-\nabla \cdot (a(\mathbf{x}, \gamma, \mathbf{F}, p)) &= \mathbf{g} && \text{in } \Omega_R, \\
\det(\mathbf{F}) &= 1 && \text{in } \Omega_R \text{ for a.e. } t \in (0, T), \\
\partial_t v + \nabla \cdot (\mathbf{M}_e(\mathbf{x}, \mathbf{F}) \nabla v_e) + I_{\text{ion}} &= I_s^e && \text{in } Q_T, \\
\partial_t v - \nabla \cdot (\mathbf{M}_i(\mathbf{x}, \mathbf{F}) \nabla v_i) + I_{\text{ion}} &= I_s^i && \text{in } Q_T, \\
v_i - v_e &= v && \text{in } Q_T, \\
\partial_t \mathbf{w} - \mathbf{R}(v, \mathbf{w}) &= 0 && \text{in } Q_T, \\
\partial_t z - G(v, \mathbf{w}, z) &= 0 && \text{in } Q_T, \\
\partial_t \gamma - S(\gamma, \mathbf{w}) &= 0 && \text{in } Q_T,
\end{aligned} \tag{4.1}$$

where $Q_T := (0, T) \times \Omega_R$. Here, according to the discussion in Chapter 1, we should take

$$a(\mathbf{x}, \gamma, \mathbf{F}, p) := \mu \mathbf{F} \mathbf{C}_a^{-1}(\mathbf{x}, \gamma) - p \text{Cof}(\mathbf{F}), \tag{4.2}$$

and

$$\mathbf{M}_k(\mathbf{x}, \mathbf{F}) := (\mathbf{F})^{-1} \mathbf{K}_k(\mathbf{x}) (\mathbf{F})^{-T}, \quad k \in \{i, e\} \tag{4.3}$$

The system of equations (4.1) has to be completed with suitable initial conditions for v , \mathbf{w} , γ , z and with boundary conditions on $v_{i,e}$ and on the elastic flux $a(\cdot, \cdot, \cdot, \cdot)$. Indeed, for the elastic flux, we chose the Robin boundary condition:

$$\mathbf{P} \mathbf{n} = -\alpha \phi, \text{ on } \partial\Omega. \tag{4.4}$$

Such a choice of boundary conditions is due to the fact that they can be tuned to mimic the global motion of the cardiac muscle [RLRB⁺14]. Typically in the literature, other choices have been used such as excessively rigid boundary conditions, or fixing the atrioventricular plane, or leaving the tissue completely free to move.

4.2.1 Linearizing the elasticity equations

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

$$\begin{aligned}
\det(\mathbf{F}) &= \det(\mathbf{I}) + \frac{\partial(\det)}{\partial \mathbf{F}}(\mathbf{I})(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I}) \\
&= 1 + \text{tr}(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I}).
\end{aligned}$$

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

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

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

Now, when \mathbf{u} denotes the displacement i.e. $\mathbf{u} = \phi(X) - X$, the above condition becomes $\nabla \cdot \mathbf{u} = 0$, which is the linearized incompressibility condition. We also linearize the flux in (4.2) with respect to \mathbf{F} using Taylor series' expansion of $\text{Cof}(\mathbf{F})$ about \mathbf{I} , given by:

$$\begin{aligned} \text{Cof}(\mathbf{F}) &= \text{Cof}(\mathbf{I}) + \frac{\partial \text{Cof}}{\partial \mathbf{F}}(\mathbf{I})(\mathbf{F} - \mathbf{I}) + o(\mathbf{F} - \mathbf{I}) \\ &= \mathbf{I} + \text{tr}(\mathbf{F} - \mathbf{I})\mathbf{I} - (\mathbf{F} - \mathbf{I})^T + o(\mathbf{F} - \mathbf{I}). \end{aligned}$$

and we obtain

$$a(\mathbf{x}, \gamma, \mathbf{F}, p) := \mu \mathbf{F} \mathbf{C}_a^{-1}(\mathbf{x}, \gamma) - p \mathbf{I}. \quad (4.5)$$

Introducing the notation $\sigma(\mathbf{x}, \gamma)$ for $\mu \mathbf{C}_a^{-1}(\mathbf{x}, \gamma)$, and using the displacement gradient $\nabla \mathbf{u}$ we rewrite the first equation of (4.1) as

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

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

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

where

$$\mathbf{f}(t, \mathbf{x}, \gamma) = \nabla \cdot (\sigma(\mathbf{x}, \gamma)) + \mathbf{g}. \quad (4.6)$$

4.2.2 The problem to be solved and its weak formulation

For simplicity of notation, we will use Ω and Ω_T to denote Ω_R and Q_T respectively in all what follows, unless otherwise specified.

Let us consider the following class of problems:

$$-\nabla \cdot (\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma)) + \nabla p = \mathbf{f}(t, \mathbf{x}, \gamma), \quad \text{in } \Omega, \text{ for a.e. } t \in (0, T), \quad (4.7)$$

$$\nabla \cdot \mathbf{u} = 0 \quad \text{in } \Omega, \text{ for a.e. } t \in (0, T), \quad (4.8)$$

$$\partial_t v - \nabla \cdot (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}) \nabla v_i) + I_{\text{ion}}(v, \mathbf{w}, z) = I_s^i(t, \mathbf{x}) \quad \text{in } \Omega_T, \quad (4.9)$$

$$\partial_t v + \nabla \cdot (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}) \nabla v_e) + I_{\text{ion}}(v, \mathbf{w}, z) = I_s^e(t, \mathbf{x}) \quad \text{in } \Omega_T, \quad (4.10)$$

$$v = v_i - v_e \quad \text{in } \Omega_T, \quad (4.11)$$

$$\partial_t \mathbf{w} = \mathbf{R}(v, \mathbf{w}, z) \quad \text{in } \Omega_T, \quad (4.12)$$

$$\partial_t z = G(v, \mathbf{w}, z) \quad \text{in } \Omega_T, \quad (4.13)$$

$$\partial_t \gamma = S(\gamma, \mathbf{w}) \quad \text{in } \Omega_T. \quad (4.14)$$

Equations (4.7),(4.9),(4.10) are complemented with the boundary data (including the linearization of (4.4)):

$$\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma) \mathbf{n} - p \mathbf{n} = -\alpha \mathbf{u} \quad \text{on } \partial \Omega, \text{ for a.e. } t \in (0, T) \quad (4.15)$$

for some $\alpha > 0$ and

$$(\mathbf{M}_k(\mathbf{x}, \nabla \mathbf{u}) \nabla v_k) \cdot \mathbf{n} = 0 \quad \text{on } (0, T) \times \partial \Omega, \quad k = i, e \quad (4.16)$$

(different boundary conditions can be imposed on $v_{i,e}$; the choice of Neumann conditions (4.16) results in the compatibility constraint (4.28) below). The initial data are:

$$v(0, \cdot) = v_0, \quad \mathbf{w}(0, \cdot) = \mathbf{w}_0, \quad z(0, \cdot) = z_0, \quad \gamma(0, \cdot) = \gamma_0 \quad \text{in } \Omega. \quad (4.17)$$

For simplicity we take $m = 1$ in the concentration variable z . The following properties of the model (4.7)–(4.14) and (4.15)–(4.17) are instrumental for the subsequent analysis:

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

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

(A.2) the function $\sigma(\cdot, \cdot)$ is in $C^1(\bar{\Omega} \times \mathbb{R})$;

(A.3) $\left(\mathbf{M}_{i,e}(\mathbf{x}, \mathbf{M})\right)_{x \in \Omega, \mathbf{M} \in \mathbb{M}_{3 \times 3}}$ is a family of symmetric matrices, uniformly bounded and positive definite:

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

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

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

(A.6) the functions \mathbf{R}, G and I_{ion} are given by the kinetics of a general physiological ionic model and it can be verified that the assumptions, stated below, are satisfied by the gating and ionic concentration variables in Beeler-Reuter or Luo-Rudy ionic models [Ven09, BR77, LR94]. We assume that the function $\mathbf{R}(v, \mathbf{w}) := (R_1(v, w_1), \dots, R_k(v, w_k))$ where $R_j : \mathbb{R}^2 \rightarrow \mathbb{R}$ are locally Lipschitz continuous functions defined by

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

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

$$\begin{aligned} 0 < \alpha_j(v), \beta_j(v) &\leq C_{\alpha, \beta}(1 + |v|), \\ \frac{d\alpha_j}{dv} \text{ and } \frac{d\beta_j}{dv} &\text{ are uniformly bounded,} \end{aligned} \tag{4.18}$$

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:

$$I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{j=1}^k I_{\text{ion}}^j(v, w_j) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \tag{4.19}$$

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

$$|I_{\text{ion}}^j(v, w_j)| \leq C_{1,I}(1 + |w_j| + |v|), \tag{4.20}$$

and I_{ion}^z is such that:

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

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \leq C_{2,I}(1 + |v| + |\mathbf{w}| + |z| + \ln z), \quad (4.21)$$

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3,I} \sum_{j=1}^k (|v| + w_j + w_j \ln z), \quad (4.22)$$

$$0 < \underline{\Theta}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(\mathbf{w}), \quad (4.23)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \right| \leq L(\mathbf{w}), \quad (4.24)$$

$$\frac{\partial}{\partial w_j} I_{\text{ion}}^z \leq C_{4,I}(1 + |v| + |\ln z|), \quad \forall j = 1, \dots, k, \quad (4.25)$$

$$0 \leq \frac{\partial}{\partial z} I_{\text{ion}}^z \leq C_{5,I}, \quad (4.26)$$

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

$$G(v, \mathbf{w}, z) = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z), \quad (4.27)$$

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

$$\int_{\Omega} I_s^i = \int_{\Omega} I_s^e \text{ and } \int_{\Omega} v_e(\mathbf{x}, t) d\mathbf{x} = 0 \text{ for a.e. } t \in (0, T). \quad (4.28)$$

(A.8) The data v_0, w_0, γ_0, z_0 lie in $H^1(\Omega)$ with $z_0 \geq c_0 > 0$ (c_0 is a positive constant) whereas $\mathbf{g} \in L^2(\Omega_T)^3$ (recall definition (4.6)), and $I_s^{i,e} \in L^2(\Omega_T)$.

Note that, in practice, one starts with an undeformed configuration, i.e., with $\gamma \equiv 0$. Thanks to properties (A.1)–(A.8), the following weak formulation makes sense.

Definition 4.2.1. A weak solution of problem (4.7)–(4.17) is $U = (\mathbf{u}, p, v_i, v_e, v, \mathbf{w}, \gamma, z)$ such that:

- (i) $\mathbf{u} \in L^2(0, T; H^1(\Omega)^3)$, $p \in L^2(\Omega_T)$, $v_i \in L^2(0, T; H^1(\Omega))$;
 $v_e \in L^2(0, T; H^{1,0}(\Omega))$ where $H^{1,0}(\Omega) := \{v_e \in H^1(\Omega); \int_{\Omega} v_e d\mathbf{x} = 0\}$;
 $v \in E := L^2(0, T; H^1(\Omega))$ with $\partial_t v \in E' := L^2(0, T; (H^1(\Omega))')$;
 $\gamma, z \in C([0, T]; L^2(\Omega))$ and $\mathbf{w} \in C([0, T]; L^2(\Omega)^k)$;
 $z(t, x) > 0$ and $0 \leq w_j(t, x) \leq 1$ for a.e. $(t, x) \in \Omega_T$ and for $j = 1, \dots, k$;

(ii) For a.e. $t \in (0, T)$, for all $\mathbf{v} \in H^1(\Omega)^3$ there holds:

$$\int_{\Omega} (\nabla \mathbf{u} \sigma(\mathbf{x}, \gamma) : \nabla \mathbf{v} - p \nabla \cdot \mathbf{v}) d\mathbf{x} = \int_{\Omega} \mathbf{f} \cdot \mathbf{v} d\mathbf{x} - \int_{\partial\Omega} \alpha \mathbf{u} \cdot \mathbf{v} ds \quad (4.29)$$

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

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

$$\int_{\Omega} q(\nabla \cdot \mathbf{u}) d\mathbf{x} = 0. \quad (4.30)$$

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

$$\langle \partial_t v, \xi \rangle + \int_{\Omega} \left(\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}) \nabla v_i \cdot \nabla \xi + I_{\text{ion}}(v, \mathbf{w}, z) \xi \right) = \int_{\Omega} I_s^i \xi, \quad (4.31)$$

$$\langle \partial_t v, \mu \rangle - \int_{\Omega} \left(\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}) \nabla v_e \cdot \nabla \mu + I_{\text{ion}}(v, \mathbf{w}, z) \mu \right) = \int_{\Omega} I_s^e \mu, \quad (4.32)$$

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

(iv) For a.e. $t \in (0, T)$ the equations (4.12), (4.14), (4.13) are fulfilled in $L^2(\Omega)$, and $\mathbf{w}(0, \cdot) = \mathbf{w}_0$, $\gamma(0, \cdot) = \gamma_0$, $z(0, \cdot) = z_0$ a.e. in Ω .

Our main result in this chapter is the following theorem:

Theorem 4.2.2. *Assume that conditions (A.1)–(A.8) hold. If $v_0 \in L^2(\Omega)$, $\mathbf{w}_0 \in H^1(\Omega)^k$, $\gamma_0, z_0 \in H^1(\Omega)$, with $z_0 \geq c_0 > 0$, $\mathbf{g} \in L^2(\Omega_T)^3$, $I_s^{i,e} \in L^2(\Omega_T)$ then there exists a weak solution $U = (\mathbf{u}, p, v_i, v_e, v, \mathbf{w}, \gamma, z)$ to (4.7)–(4.14) with the boundary and initial data specified as in (4.15)–(4.17).*

Remark 11. *In definition 4.2.1, the integrals are well defined since the tensors σ and $\mathbf{M}_{i,e}$ are uniformly bounded and the functions $\mathbf{u}(t, \cdot)$, $v_{i,e}(t, \cdot)$ are in $H^1(\Omega)^3$ and $H^1(\Omega)$ respectively.*

4.3 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 [BK06] 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.

4.3.1 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 $\text{span}(\psi_l)_{l \in \mathbb{N}}$ 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 [RTCL98]). In order to impose the compatibility condition (4.28), we let

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

We observe that $\text{span}\{\mu_l\}_{l \in \mathbb{N}}$ is dense in the space $H^{1,0}(\Omega)$, given as in Definition 4.2.1. Furthermore, we orthonormalize the basis $(\mu_l)_{l \in \mathbb{N}}$ by the Gram-Schmidt process, and we denote by $(\mu_l)_{l \in \mathbb{N}}$ the new basis that is orthonormal in $L^2(\Omega)$. For $m \geq 0$, we introduce the finite dimensional spaces $\mathbf{H}_m = \text{span}\{\psi_0, \dots, \psi_m\} \subset H^1(\Omega)^3$, $L_m = \text{span}(\mu_0, \dots, \mu_m) \subset H^{1,0}(\Omega)$ and $W_m = \text{span}(\omega_0, \dots, \omega_m) \subset H^1(\Omega)$.

We are looking for a discrete solution

$$\mathbf{u}_m = (\mathbf{u}_{\varepsilon,m}, p_{\varepsilon,m}, v_m, v_{i,\varepsilon,m}, v_{e,\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}, \gamma_{\varepsilon,m})$$

(for fixed $\varepsilon > 0$) of the system (4.34) below with

$$\begin{aligned}
\mathbf{u}_m &= \sum_{l=0}^m \mathbf{u}_{l,m} \psi_l, & p_m &= \sum_{l=0}^m p_{l,m} \omega_l & v_{i,m} &= \sum_{l=0}^m v_{i,l,m} \omega_l, \\
v_{e,m} &= \sum_{l=0}^m v_{e,l,m} \mu_l, & v_m &= v_{i,m} - v_{e,m}, & \gamma_m &= \sum_{l=0}^m \gamma_{l,m} \omega_l, \\
w_{j,m} &= \sum_{l=0}^m w_{j,l,m} \omega_l, & \forall j &= 1, \dots, k, & z_m &= \sum_{l=0}^m z_{l,m} \omega_l.
\end{aligned} \tag{4.33}$$

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 [BK06]. We obtain the following regularized system

$$\begin{aligned}
\varepsilon \frac{d}{dt} \int_{\Omega} \mathbf{u}_{\varepsilon,m} \cdot \psi_l + \int_{\Omega} (\nabla \mathbf{u}_{\varepsilon,m}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) : \nabla \psi_l - p_{\varepsilon,m} \nabla \cdot \psi_l \, d\mathbf{x} \\
+ \int_{\partial\Omega} \alpha \mathbf{u}_{\varepsilon,m} \cdot \psi_l \, ds = \int_{\Omega} \mathbf{f} \cdot \psi_l \, d\mathbf{x}, \\
\varepsilon \frac{d}{dt} \int_{\Omega} p_{\varepsilon,m} \cdot \omega_l + \int_{\Omega} \omega_l \nabla \cdot \mathbf{u}_{\varepsilon,m} = 0, \\
\frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \omega_l + \varepsilon \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_l + \int_{\Omega} (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_l) \, d\mathbf{x} = \int_{\Omega} I_s^i \omega_l \, d\mathbf{x}, \\
\frac{d}{dt} \int_{\Omega} v_{\varepsilon,m} \mu_l - \varepsilon \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_l - \int_{\Omega} (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_l) \, d\mathbf{x} = \int_{\Omega} I_s^e \mu_l \, d\mathbf{x}, \\
\frac{d}{dt} \int_{\Omega} w_{j,\varepsilon,m} \omega_l = \int_{\Omega} R_j(v_{\varepsilon,m}, w_{j,\varepsilon,m}) \omega_l, \\
\frac{d}{dt} \int_{\Omega} z_{\varepsilon,m} \omega_l = \int_{\Omega} G(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_l, \\
\frac{d}{dt} \int_{\Omega} \gamma_{\varepsilon,m} \omega_l = \int_{\Omega} S(\gamma_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}) \omega_l,
\end{aligned} \tag{4.34}$$

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

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

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

$$\begin{aligned}
\mathbf{u}_{\varepsilon,m}(0) &= 0, \quad p_{\varepsilon,m}(0) = \sum_{l=0}^m p_{0,l,m} \omega_l, & \text{where } p_{0,l,m} &= \langle p_0, \omega_l \rangle_{L^2}, \\
v_{i,\varepsilon,m}(0) &= \sum_{l=0}^m v_{i,0,l,m} \omega_l, & \text{where } v_{i,0,l,m} &= \langle v_{i,0}, \omega_l \rangle_{L^2}, \\
v_{e,\varepsilon,m}(0) &= \sum_{l=0}^m v_{e,0,l,m} \mu_l, & \text{where } v_{e,0,l,m} &= \langle v_{e,0}, \mu_l \rangle_{L^2}, \\
w_{j,\varepsilon,m}(0) &= \sum_{l=0}^m w_{j,0,l,m} \omega_l, & \text{where } w_{j,0,l,m} &= \langle w_{j,0}, \omega_l \rangle_{L^2} \\
z_{\varepsilon,m}(0) &= \sum_{l=1}^m z_{0,l,m} \omega_l & \text{where } z_{0,l,m} &= \langle z_0, \omega_l \rangle_{L^2} \\
\gamma_{\varepsilon,m}(0) &= \sum_{l=0}^m \gamma_{0,l,m} \omega_l & \text{where } \gamma_{0,l,m} &= \langle \gamma_0, \omega_l \rangle_{L^2},
\end{aligned} \tag{4.35}$$

for $j = 1, \dots, k$. Using the orthonormality of the bases, we can write (4.34) as a system of ordinary differential equations in the coefficients:

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

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:

$$\begin{aligned}
\frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_l - \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \omega_l + \varepsilon \frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \omega_l + \int_{\Omega} (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_l) d\mathbf{x} = \int_{\Omega} I_s^i \omega_l d\mathbf{x}, \\
\frac{d}{dt} \int_{\Omega} v_{i,\varepsilon,m} \mu_l - \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_l - \varepsilon \frac{d}{dt} \int_{\Omega} v_{e,\varepsilon,m} \mu_l - \int_{\Omega} (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_l) d\mathbf{x} = \int_{\Omega} I_s^e \mu_l d\mathbf{x},
\end{aligned}$$

Replacing $v_{i,\varepsilon,m}$ and $v_{e,\varepsilon,m}$ by their expressions as in (4.33), we obtain for $l = 0, \dots, m$:

$$\begin{aligned}
(1 + \varepsilon) \sum_{r=0}^m v'_{i,r,m} \int_{\Omega} \omega_r \omega_l - \sum_{r=0}^m v'_{e,r,m} \int_{\Omega} \mu_r \omega_l + \int_{\Omega} (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \omega_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_l) d\mathbf{x} = \int_{\Omega} I_s^i \omega_l d\mathbf{x}, \\
\sum_{r=0}^m v'_{i,r,m} \int_{\Omega} \omega_r \mu_l - (1 + \varepsilon) \sum_{r=0}^m v'_{e,r,m} \int_{\Omega} \mu_r \mu_l - \int_{\Omega} (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_l \\
+ I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_l) d\mathbf{x} = \int_{\Omega} I_s^e \mu_l d\mathbf{x},
\end{aligned}$$

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

$$\begin{aligned} (1 + \varepsilon)v'_{i,r,m} - \sum_{r=0}^m \left(\int_{\Omega} \mu_r \omega_l \right) v'_{e,r,m} \\ = F_i \left(\{\mathbf{u}_{l,m}\}_{r=0}^m, \{v_{i,r,m}\}_{r=0}^m, \{v_{e,r,m}\}_{r=0}^m, \{\mathbf{w}_{r,m}\}_{r=0}^m, \{z_{r,m}\}_{r=0}^m \right), \\ - \sum_{r=0}^m v'_{i,r,m} \int_{\Omega} \omega_r \mu_l + (1 + \varepsilon)v'_{e,l,m} \\ = F_e \left(\{\mathbf{u}_{l,m}\}_{r=0}^m, \{v_{i,r,m}\}_{r=0}^m, \{v_{e,r,m}\}_{r=0}^m, \{\mathbf{w}_{r,m}\}_{r=0}^m, \{z_{r,m}\}_{r=0}^m \right), \end{aligned}$$

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

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

where

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

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

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

It is enough to prove that the matrix $\mathbf{N} := \begin{bmatrix} \mathbf{I}_{m+1} & -\mathbf{A} \\ -\mathbf{A}^T & \mathbf{I}_{m+1} \end{bmatrix}$ is positive.

Let $\xi = \begin{pmatrix} \xi_i \\ \xi_e \end{pmatrix}$, where $\xi_i = (\xi_{i,0}, \dots, \xi_{i,m})^T \in \mathbb{R}^{m+1}$ and $\xi_e = (\xi_{e,0}, \dots, \xi_{e,m})^T \in \mathbb{R}^{m+1}$. Then

$$\xi^T \mathbf{N} \xi = \xi_i^T \xi_i - \xi_i^T \mathbf{A} \xi_e + \xi_e^T \xi_e - \xi_e^T \mathbf{A}^T \xi_i.$$

So we have

$$\begin{aligned} \xi^T \mathbf{N} \xi &= \sum_{k,l} \left[\xi_{i,k} \xi_{i,l} \int_{\Omega} \omega_k \omega_l - 2\xi_{i,k} a_{kl} \xi_{e,l} + \xi_{e,k} \xi_{e,l} \int_{\Omega} \mu_k \mu_l \right] \\ &= \int_{\Omega} \sum_{k,l} [\xi_{i,k} \xi_{i,l} \omega_k \omega_l - 2\xi_{i,k} \xi_{e,l} \omega_l \mu_k + \xi_{e,k} \xi_{e,l} \mu_k \mu_l] \\ &= \int_{\Omega} \left(\sum_l \xi_{i,l} \omega_l \right)^2 - 2 \sum_{k,l} \xi_{i,k} \xi_{e,l} \omega_l \mu_k + \left(\sum_l \xi_{e,l} \mu_l \right)^2 \\ &= \int_{\Omega} \left[\sum_l \xi_{i,l} \omega_l - \sum_l \xi_{e,l} \mu_l \right]^2 \geq 0. \end{aligned}$$

Thus the matrix \mathbf{M} is positive definite, hence invertible. Consequently, the whole system (4.34) can be written as a system of ordinary differential equations in the form $y'(t) = f(t, y(t))$.

To prove existence of a local solution to the obtained ODE system, we note that by virtue of assumptions (A.1)-(A.8), the functions on the right hand side of the system are Carathéodory functions bounded by L^1 functions. According to classical ODE theory, the system admits a local in time unique solution and the functions defined by (4.33) are well-defined and constitute approximate solutions to the regularized system (4.34). The global existence of the Faedo-Galerkin solutions is a consequence of the m -independent a priori estimates on $\mathbf{u}_{\varepsilon,m}$, $p_{\varepsilon,m}$, $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $\mathbf{w}_{\varepsilon,m}$, $\gamma_{\varepsilon,m}$ and $z_{\varepsilon,m}$ that are derived in the next section. For more details, consult [BK06].

4.3.2 A priori estimates

To prove global existence of the Faedo-Galerkin solutions we derive m -independent a priori estimates bounding $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $\mathbf{u}_{\varepsilon,m}$, $p_{\varepsilon,m}$, $\mathbf{w}_{j,\varepsilon,m}$, $z_{\varepsilon,m}$ and $\gamma_{\varepsilon,m}$ in various Banach spaces. Given some (absolutely continuous) coefficients $a_{l,m}(t)$, $c_{l,m}(t)$, $b_{k,l,m}(t)$, $k = i, e$, and $d_{l,m}^\kappa(t)$ we form the functions $\psi_m(t, \mathbf{x}) := \sum_{l=1}^m a_{l,m}(t) \psi_l(\mathbf{x})$, $\rho_m(t, \mathbf{x}) := \sum_{l=1}^m c_{l,m}(t) \omega_l(\mathbf{x})$, $\xi_m(t, \mathbf{x}) := \sum_{l=1}^m b_{i,l,m}(t) \omega_l(\mathbf{x})$, $\mu_m(t, \mathbf{x}) := \sum_{l=1}^m b_{e,l,m}(t) \omega_l(\mathbf{x})$, and $\omega_m^\kappa(t, \mathbf{x}) := \sum_{l=1}^m d_{l,m}^\kappa(t) \omega_l(\mathbf{x})$ for $\kappa := w, z, \gamma$. 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:

$$\begin{aligned}
& \varepsilon \int_{\Omega} \partial_t \mathbf{u}_{\varepsilon,m} \cdot \psi_m + \int_{\Omega} \left((\nabla \mathbf{u}_{\varepsilon,m}) \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) : \nabla \psi_m - p_{\varepsilon,m} \nabla \cdot \psi_m \right) d\mathbf{x} \\
& \quad + \int_{\partial\Omega} \alpha \mathbf{u}_{\varepsilon,m} \cdot \psi_m ds = \int_{\Omega} \mathbf{f} \cdot \psi_m d\mathbf{x}, \\
& \varepsilon \int_{\Omega} \partial_t p_{\varepsilon,m} \rho_m + \int_{\Omega} \rho_m \nabla \cdot \mathbf{u}_{\varepsilon,m} = 0, \\
& \int_{\Omega} \partial_t v_{\varepsilon,m} \xi_m + \varepsilon \int_{\Omega} \partial_t v_{i,\varepsilon,m} \xi_m + \int_{\Omega} \left(\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla \xi_m \right. \\
& \quad \left. + I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \xi_m \right) d\mathbf{x} = \int_{\Omega} I_s^i \xi_m d\mathbf{x}, \\
& \int_{\Omega} \partial_t v_{e,\varepsilon,m} \mu_m - \varepsilon \int_{\Omega} \partial_t v_{e,\varepsilon,m} \mu_m - \int_{\Omega} \left(\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla \mu_m \right. \\
& \quad \left. + I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \mu_m \right) d\mathbf{x} = \int_{\Omega} I_s^e \mu_m d\mathbf{x}, \\
& \int_{\Omega} \partial_t w_{j,\varepsilon,m} \omega_m^w = \int_{\Omega} R_j(v_{\varepsilon,m}, w_{j,\varepsilon,m}) \omega_m^w, \\
& \int_{\Omega} \partial_t z_{\varepsilon,m} \omega_m^z = \int_{\Omega} G(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_m^z, \\
& \int_{\Omega} \partial_t \gamma_{\varepsilon,m} \omega_m^\gamma = \int_{\Omega} S(\gamma_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}) \omega_m^\gamma,
\end{aligned} \tag{4.36}$$

for $j = 1, \dots, k$. To simplify the notation, we perform the derivations in the following three Lemmata while omitting the subscript ε, m . We start first by obtaining estimates on the gating and concentration variables ($\mathbf{w}_{\varepsilon,m}$ and $z_{\varepsilon,m}$) that are needed to prove the uniform bounds. In the following Lemma, we show that the gating variables w_j , $j = 1, \dots, k$ satisfy the universal bounds $0 \leq w_j \leq 1$.

Lemma 4.3.1. *Let $w_j \in C([0, T], L^2(\Omega))$ and $v \in H^1(0, T, L^2(\Omega))$ such that for all $\omega_m^w \in H^1(\Omega)$:*

$$\int_{\Omega} \partial_t w_j \omega_m^w = \int_{\Omega} R_j(v, w_j) \omega_m^w, \quad (4.37)$$

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

$$0 \leq w_j \leq 1, \quad \text{a.e. in } \Omega_T. \quad (4.38)$$

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

$$R_j(v, w_j) = \begin{cases} -\beta_j w_j & \text{if } w_j > 1, \\ \alpha_j(1 - w_j) - \beta_j w_j & \text{if } w_j \leq 1 \end{cases} \quad (4.39)$$

We substitute $\omega_m^w = -w_j^-$ in (4.37) and we use (4.39) to deduce

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

Using Gronwall's inequality, we get $w_j^- = 0$ and $w_j \geq 0$, for $j = 1, \dots, k$. Similarly, substituting $\omega_m^w = (w_j - 1)^+$ in (4.37) and using (4.39), we obtain by using Gronwall's inequality that $w_j \leq 1$, for a.e. $(t, \mathbf{x}) \in \Omega_T$ and for $j = 1, \dots, k$. \square

Now we establish some estimates on the concentration variable z that will help us in getting the uniform bound on $v_{\varepsilon, m}$. The difficulty arises from the presence of a logarithmic term in the definition of the function G (4.27) and the ionic current I_{ion} (4.19). 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 4.3.2. *Let $z \in C([0, T], L^2(\Omega))$, $v \in H^1(0, T, L^2(\Omega))$ and $\mathbf{w} \in C([0, T], L^2(\Omega)^k)$ such that:*

$$\partial_t z = G(v, \mathbf{w}, z), \quad (4.40)$$

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

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

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

Proof. For a.e. $\mathbf{x} \in \Omega$ fixed, we have $z(0, \mathbf{x}) = z_0 > 0$ and the map: $t \mapsto z(t, \mathbf{x})$ is in $C[0, T]$. Assume that at some time t , $z(t, \mathbf{x}) = 0$ and let $t_1 = \inf\{t \in (0, T) : z(t, \mathbf{x}) = 0\}$. Using (4.21) and (4.27), we see that $G(v, \mathbf{w}, z) \rightarrow +\infty$ as $t \rightarrow t_1$. So, for a given $A > 0$ there exists $\delta > 0$ such that $G(v, \mathbf{w}, z) > A$ for all $t_1 - \delta < t < t_1$. Then using equation (4.40), one obtains $\partial_t z > 0$. Hence, z is strictly increasing over $[t_1 - \delta, t_1]$. Therefore $z(t_1, \mathbf{x}) > z(t_1 - \delta, \mathbf{x}) > 0$ which is a contradiction.

Consequently by diagonalisation and compactness of $[0, T]$, $z > 0$. \square

Remark 12. *Having an ordinary differential equation, the strong formulation (4.40) is equivalent to its corresponding weak formulation given in System (4.36).*

Lemma 4.3.3. *Under the same assumptions as Lemma 4.3.2, the concentration variable z satisfies the following estimates for a.e. $\mathbf{x} \in \Omega$, $t \in (0, T)$:*

$$|z(t, \mathbf{x})| \leq C(1 + |z_0(\mathbf{x})| + \|v(\mathbf{x})\|_{L^2(0,t)}), \quad \forall t \in [0, T], \quad (4.41)$$

$$|\ln z(t, \mathbf{x})| \leq C(1 + |z_0(\mathbf{x})| + |v(t, \mathbf{x})| + \|v(\mathbf{x})\|_{L^2(0,t)}) \quad (4.42)$$

$$\int_0^t |\partial_s z|^2 \leq C \left(1 + |z_0 \ln z_0| + |z_0|^2 + \|v\|_{L^2(0,t)}^2 \right), \quad (4.43)$$

$$\int_0^t |\ln z|^2 \leq C \left(1 + |z_0 \ln z_0| + |z_0|^2 + \|v\|_{L^2(0,t)}^2 \right), \quad (4.44)$$

Proof. In our proof, we follow the idea in [Ven09].

Proof of (4.41): Fixing $\mathbf{x} \in \Omega$ and multiplying equation (4.40) by z , we get

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

Next, we use (4.22) 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 Ω_T , we find

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

By Young's inequality, we have

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

which can be rewritten as

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

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

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

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 (4.42): In order to prove this estimate, we fix $\mathbf{x} \in \Omega$ and we use definition (4.27) of the function G in equation (4.40) to get

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

Exploiting (4.21) and the uniform boundedness of \mathbf{w} in Lemma 4.3.1, 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 (4.41), we have

$$\frac{dz}{dt} \geq c_6 - c_9(1 + |z_0(\cdot)| + \|v\|_{L^2(0,t)}) - c_8|v| - c_8 \ln z, \quad (4.45)$$

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

$$c_8 \ln z \geq c_6 - c_9(1 + |z_0(\cdot)| + \|v\|_{L^2(0,t)}) - c_8|v| - \frac{dz}{dt}. \quad (4.46)$$

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

$$\ln z \geq c_{10}(1 + |z_0(\cdot)| + |v(t, \cdot)| + \|v\|_{L^2(0,t)}) \quad (4.47)$$

On the other hand, knowing that $\ln z < z$, one has by (4.41):

$$\ln z < C(1 + |z_0(\cdot)| + \|v\|_{L^2(0,t)}) \leq C(1 + |z_0(\cdot)| + |v(t, \cdot)| + \|v\|_{L^2(0,t)}). \quad (4.48)$$

Estimate (4.42) follows easily from (4.47) and (4.48).

Proof of (4.43): We fix $\mathbf{x} \in \Omega$, we multiply equation (4.40) by $\frac{dz}{dt}$ and we use (4.27) to get

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

Letting

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

and observing that

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

The above equation simplifies to

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

Therefore

$$\int_0^t \frac{1}{\Theta(s)} \left(\frac{dz}{ds}\right)^2 ds = \int_0^t \left[\frac{a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, 0)}{\Theta(s)} \right] \frac{dz}{ds} ds - a_3(z \ln z - z - z_0 \ln z_0 + z_0).$$

Note that by (4.23), the mean value theorem and Lemma 4.3.1, there exist $\theta_1, \theta_2 > 0$ such that

$$\theta_2 \leq \Theta(t) \leq \theta_1. \quad (4.49)$$

Using $z \ln z - z \geq -1$, (4.49) and (4.21), we get:

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

By (4.49), 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 (4.41) with C denoted by C' , one gets

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

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

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

Consequently,

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

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

$$\int_0^t \left(\frac{dz}{ds} \right)^2 ds \leq c_{11} \left(1 + |z_0 \ln z_0 - z_0| + |z_0|^2 + \|v(\mathbf{x})\|_{L^2(0,t)}^2 \right), \quad \forall t \in (0, T), \quad (4.50)$$

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

Proof of (4.44): We have by (4.13) and (4.27)

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

We rewrite it as:

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

After squaring both sides, we obtain:

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

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

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

Therefore, by (4.41), (4.50) and (4.21) 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 $c_{12} > 0$. □

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

Lemma 4.3.4. *Under the same conditions of Lemma 4.3.3, there exists a constant $C > 0$ (dependent on T) such that*

$$\|I_{\text{ion}}(v, \mathbf{w}, z, \ln(z))\|_{L^2(\Omega_T)}^2 \leq C(1 + \|v\|_{L^2(\Omega_T)}^2). \quad (4.51)$$

Proof. By definition (4.19) of I_{ion} , by properties (4.20) and (4.21), and by the uniform bound obtained on w_j (4.38), there holds:

$$|I_{\text{ion}}(v, \mathbf{w}, z, \ln(z))|^2 \leq C \left(\sum_{j=1}^k (1 + |v|^2) + 1 + |v|^2 + |z|^2 + |\ln z|^2 \right),$$

where C is a generic constant.

Using (4.41) and (4.42), one obtains

$$|I_{\text{ion}}(v, \mathbf{w}, z, \ln(z))|^2 \leq C(1 + |z_0|^2 + |v|^2 + \|v\|_{L^2(0,t)}^2) \quad (4.52)$$

Finally, integrate (4.52) over $(0, t) \times \Omega$ and use (4.44) along with the condition that z_0 is in $L^2(\Omega)$, to get (4.51). □

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

Lemma 4.3.5. *There exist constants $\mathcal{C}_1, \mathcal{C}_2$ and $\mathcal{C}_3 > 0$ independent of ε and m such that*

$$\max_{t \in [0, T]} \left(\|v_{\varepsilon, m}(t)\|_{L^2(\Omega)} + \sum_{j=i, e} \|\sqrt{\varepsilon} v_{j, \varepsilon, m}(t)\|_{L^2(\Omega)} \right) \leq \mathcal{C}_1, \quad (4.53)$$

$$\left(\sum_{j=i, e} \|v_{j, \varepsilon, m}\|_{L^2(0, T; H^1(\Omega))} + \|v_{\varepsilon, m}\|_{L^2(0, T; H^1(\Omega))} \right) \leq \mathcal{C}_2, \quad (4.54)$$

$$\|\partial_t(v_{\varepsilon, m} + \varepsilon v_{i, \varepsilon, m})\|_{L^2(0, T; (H^1(\Omega))')} + \|\partial_t(v_{\varepsilon, m} - \varepsilon v_{e, \varepsilon, m})\|_{L^2(0, T; (H^1(\Omega))')} \leq \mathcal{C}_3, \quad (4.55)$$

Proof. Proofs of (4.53) and (4.54): First, we make use of the relation $v_{\varepsilon,m} = v_{i,\varepsilon,m} - v_{e,\varepsilon,m}$. We take $\xi_m := v_{i,\varepsilon,m}$ and $\mu_m := -v_{e,\varepsilon,m}$ as test functions in (4.36) to get

$$\begin{aligned} \int_{\Omega} v_{i,\varepsilon,m} \partial_t v_{\varepsilon,m} + \varepsilon \int_{\Omega} v_{i,\varepsilon,m} \partial_t v_{i,\varepsilon,m} + \int_{\Omega} \left(\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{i,\varepsilon,m} \cdot \nabla v_{i,\varepsilon,m} \right. \\ \left. + I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{i,\varepsilon,m} \right) d\mathbf{x} = \int_{\Omega} I_s^i v_{i,\varepsilon,m} d\mathbf{x}, \end{aligned} \quad (4.56)$$

$$\begin{aligned} - \int_{\Omega} v_{e,\varepsilon,m} \partial_t v_{\varepsilon,m} + \varepsilon \int_{\Omega} v_{e,\varepsilon,m} \partial_t v_{e,\varepsilon,m} + \int_{\Omega} \left(\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{e,\varepsilon,m} \cdot \nabla v_{e,\varepsilon,m} \right. \\ \left. - I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{e,\varepsilon,m} \right) d\mathbf{x} = - \int_{\Omega} I_s^e v_{e,\varepsilon,m} d\mathbf{x}. \end{aligned} \quad (4.57)$$

Secondly, we add equations (4.56) and (4.57) to obtain

$$\begin{aligned} \int_{\Omega} \left(I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{\varepsilon,m} + \sum_{j=i,e} \mathbf{M}_j(x, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{j,\varepsilon,m} \cdot \nabla v_{j,\varepsilon,m} \right) \\ + \frac{1}{2} \int_{\Omega} |\partial_t v_{\varepsilon,m}|^2 + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} \partial_t v_{k,\varepsilon,m}|^2 = \int_{\Omega} (I_s^i v_{i,\varepsilon,m} - I_s^e v_{e,\varepsilon,m}). \end{aligned} \quad (4.58)$$

Then we integrate equation (4.58) on $(0, s)$ for every $s \leq T$, to get:

$$\begin{aligned} \int_0^s \int_{\Omega} \left(I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) v_{\varepsilon,m} + \sum_{j=i,e} \mathbf{M}_j(x, \nabla \mathbf{u}_{\varepsilon,m}) \nabla v_{j,\varepsilon,m} \cdot \nabla v_{j,\varepsilon,m} \right) \\ + \frac{1}{2} \int_{\Omega} |v_{\varepsilon,m}(s, \cdot)|^2 + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,\varepsilon,m}(s, \cdot)|^2 \\ = \frac{1}{2} \int_{\Omega} |v_{0,\varepsilon,m}|^2 + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,0,\varepsilon,m}|^2 + \int_0^s \int_{\Omega} (I_s^i v_{i,\varepsilon,m} - I_s^e v_{e,\varepsilon,m}) \\ = \frac{1}{2} \int_{\Omega} |v_{0,\varepsilon,m}|^2 + \frac{1}{2} \sum_{k=i,e} \int_{\Omega} |\sqrt{\varepsilon} v_{k,0,\varepsilon,m}|^2 + \int_0^s \int_{\Omega} \left(I_s^i v_{\varepsilon,m} + (I_s^i - I_s^e) v_{e,\varepsilon,m} \right). \end{aligned} \quad (4.59)$$

Note that, by construction, $|v_{j,0,\varepsilon,m}| \leq \frac{|v_{0,\varepsilon,m}|}{2} + \frac{1}{|\Omega|} \left| \int_{\Omega} \frac{v_{0,\varepsilon,m}}{2} \right|$, $j = i, e$. Using this, the ellipticity condition **(A.3)**, Young's and Hölder's inequalities, and in addition estimate (4.51) on

I_{ion} in Lemma 4.3.4 and Poincaré's inequality with compatibility condition (4.28), we get

$$\begin{aligned}
 & \frac{1}{c} \sum_{j=i,e} \|\nabla v_{j,\varepsilon,m}\|_{L^2(\Omega_s)}^2 + \frac{1}{2} \|v_{\varepsilon,m}(s)\|_{L^2(\Omega)}^2 + \frac{1}{2} \sum_{j=i,e} \|\sqrt{\varepsilon} v_{j,\varepsilon,m}\|_{L^2(\Omega)}^2 \\
 & \leq \left(\varepsilon + \frac{1}{2}\right) \|v_{0,\varepsilon,m}\|_{L^2(\Omega)}^2 + \|I_i^s\|_{L^2(\Omega_s)} \|v_{\varepsilon,m}\|_{L^2(\Omega_s)} \\
 & \quad + \sum_{j=i,e} \|I_j^s\|_{L^2(\Omega_s)} \|v_{e,\varepsilon,m}\|_{L^2(\Omega_s)} \\
 & \quad + \frac{1}{2} \|I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m})\|_{L^2(\Omega_s)}^2 + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2 \\
 & \leq \left(\varepsilon + \frac{1}{2}\right) \|v_{0,\varepsilon,m}\|_{L^2(\Omega)}^2 + \frac{1}{2} \|I_i^s\|^2 + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2 + \frac{c}{2} \sum_{j=i,e} \|I_j^s\|_{L^2(\Omega_s)}^2 \\
 & \quad + \frac{1}{2c} \|\nabla v_{e,\varepsilon,m}\|_{L^2(\Omega_s)}^2 + \frac{C}{2} \left(1 + \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2\right) + \frac{1}{2} \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2 \\
 & \leq \left(\varepsilon + \frac{1}{2}\right) \|v_0\|_{L^2(\Omega)}^2 + \frac{1}{2} \left((1+c)\|I_i^s\|^2 + \|I_e^s\|^2\right) + \frac{1}{2c} \|\nabla v_{e,\varepsilon,m}\|_{L^2(\Omega_s)}^2 \\
 & \quad + \left(\frac{C}{2} + 1\right) \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2 + \frac{C}{2},
 \end{aligned}$$

where $C > 0$ is the constant of estimate (4.51). Or equivalently:

$$\begin{aligned}
 \|v_{\varepsilon,m}(s)\|_{L^2(\Omega)}^2 + \sum_{j=i,e} \|\sqrt{\varepsilon} v_{j,\varepsilon,m}(t)\|_{L^2(\Omega)}^2 - c_{13} \|v_{\varepsilon,m}\|_{L^2(\Omega_s)}^2 \\
 + \frac{2}{c} \|\nabla v_{i,\varepsilon,m}\|_{L^2(\Omega_s)}^2 + \frac{1}{c} \|\nabla v_{e,\varepsilon,m}\|_{L^2(\Omega_s)}^2 \leq c_{14},
 \end{aligned} \tag{4.60}$$

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

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

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

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

Hence, one obtains

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

for some constant $c_{17} > 0$. Using this and (4.60), (4.53) is proved. Again using (4.60), we have for all $t \in (0, T)$

$$c_{18} \sum_{j=i,e} \|\nabla v_{j,\varepsilon,m}\|_{L^2(\Omega)}^2 + \|v_{\varepsilon,m}(t)\|_{L^2(\Omega)}^2 \leq c_{14} + c_{13} \|v_{\varepsilon,m}\|_{L^2(\Omega_t)}^2 := c_{19}, \tag{4.61}$$

for some constants $c_{18}, c_{19} > 0$. The last inequality implies the bound on $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$ and $v_{\varepsilon,m}$ in $L^2(0, T; H^1(\Omega))$ (recall that $v_{\varepsilon,m} = v_{i,\varepsilon,m} - v_{e,\varepsilon,m}$). The proof of estimate (4.54) is thus achieved.

Proof of (4.55): In order to prove (4.55), we introduce the sequences $U_{i,\varepsilon,m} = v_{\varepsilon,m} + \varepsilon v_{i,\varepsilon,m}$ and $U_{e,\varepsilon,m} = v_{\varepsilon,m} - \varepsilon v_{e,\varepsilon,m}$. Indeed, $\partial_t U_{i,\varepsilon,m}$ and $\partial_t U_{e,\varepsilon,m}$ are bounded (independent of ε) in $L^2(0, T; (H^1(\Omega))')$; this is easily seen by the following argument:

We let $\varphi \in L^2(0, T; H^1(\Omega))$, we take $\xi_m := \varphi$ in (4.36) and we exploit assumption (A.3) to get from (4.53) and (4.54)

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

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

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

Lemma 4.3.6. *There exist constants \mathcal{C}_4 and $\mathcal{C}_5 > 0$ independent of ε and m such that:*

$$\|\mathbf{w}_{\varepsilon,m}\|_{L^2(0,T;H^1(\Omega)^k)} + \|z_{\varepsilon,m}\|_{L^2(0,T;H^1(\Omega))} + \|\gamma_{\varepsilon,m}\|_{L^2(0,T;H^1(\Omega))} \leq \mathcal{C}_4, \quad (4.62)$$

$$\|\partial_t \mathbf{w}_{\varepsilon,m}\|_{L^2(\Omega_T)^k} + \|\partial_t z_{\varepsilon,m}\|_{L^2(\Omega_T)} + \|\partial_t \gamma_{\varepsilon,m}\|_{L^2(\Omega_T)} \leq \mathcal{C}_5. \quad (4.63)$$

Proof. Proof of (4.62): We turn now to the gating variables $w_{j,\varepsilon,m}$ (recall that $0 \leq w_{j,\varepsilon,m} \leq 1$). Observe that by differentiation of equation (4.12) with respect to \mathbf{x} and by the chain rule, one has

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

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

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

for some positive constant c_{22} . An application of Gronwall's inequality and (4.54) yield

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

for all $t \in (0, T)$. Estimate (4.62) for $w_{j,\varepsilon,m}$ follows easily. Now to obtain the uniform bound on the concentration variable $z_{\varepsilon,m}$, we integrate (4.41) to get

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

Using (4.53) for $v_{\varepsilon,m}$, this implies the uniform bound of $z_{\varepsilon,m}$ in $L^\infty(0, T; L^2(\Omega))$. Now we differentiate both sides of equation (4.13) with respect to \mathbf{x} and then use (4.27) to obtain

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

Multiplying this equation by $\nabla z_{\varepsilon,m}$, using (4.23) and (4.26), we get

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

By assumptions (4.24) and (4.25), we deduce

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

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

$$\begin{aligned} |\nabla z_{\varepsilon,m}(t)|^2 &\leq e^{c_{24}t} \left(|\nabla z_0|^2 + c_{24} \int_0^t (|\nabla v_{\varepsilon,m}|^2 + |v_{\varepsilon,m}|^2 + |\ln z_{\varepsilon,m}|^2 \right. \\ &\quad \left. + \sum_{j=1}^k |\nabla w_{j,\varepsilon,m}|^2 + 1) ds \right), \end{aligned}$$

for all $t \in (0, T)$. Estimate (4.62) for $z_{\varepsilon,m}$ is a consequence of (4.44), (4.54) and the uniform bound of $w_{j,\varepsilon,m}$ in $L^2(H^1)$ for $j = 1, \dots, k$.

Now, we substitute $\omega_m^\gamma := \gamma_{\varepsilon,m}$ into the equation satisfied by γ in (4.36) to deduce after an integration in time t and an application of Young's inequality (recall the definition of the function S in (A.5))

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

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

$$\begin{aligned} \|\gamma_{\varepsilon, m}(s)\|_{L^2(\Omega)}^2 &\leq (k\beta\eta - 2\beta\eta_0) \int_0^s \|\gamma_{\varepsilon, m}(t)\|_{L^2(\Omega)}^2 dt + \|\gamma_{\varepsilon, m}(0)\|_{L^2(\Omega)}^2 \\ &\quad + \beta\eta \sum_{j=1}^k \|w_{j, \varepsilon, m}\|_{L^2(\Omega_T)}^2 \\ &\leq c_{25} \int_0^s \|\gamma_{\varepsilon, m}(t)\|_{L^2(\Omega)}^2 dt + \|\gamma(0)\|_{L^2(\Omega)}^2 + \beta\eta k c_{26}, \end{aligned}$$

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

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

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 (4.14) with respect to \boldsymbol{x} and multiplying by $\nabla\gamma_{\varepsilon, m}$, we get

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

An application of Gronwall's inequality, we deduce

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

Upon integration of this inequality over Ω_T , we get the uniform bound of $\nabla\gamma_{\varepsilon, m}$ in L^2 . This concludes the proof of (4.62)

Proof of (4.63): To prove the L^2 uniform bound of $\partial_t w_{j, \varepsilon, m}$ we exploit $0 \leq w_{j, \varepsilon, m} \leq 1$ and $\beta_j(v) > 0$ in the following equation

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

where the last inequality follows from (4.18). Squaring both sides, integrating over Ω_T and using the uniform estimate on $\|v_{\varepsilon, m}\|_{L^2(\Omega_T)}^2$, we obtain (for a positive constant c_{28} dependent on T)

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

Now the $L^2(\Omega_T)$ uniform estimate on $\partial_t z_{\varepsilon, m}$ is a direct consequence of the structure of the governing equation along with (4.27), (4.21) and Lemmata 4.3.1 and 4.3.3. Actually, squaring both sides of (4.13), and using the inequality $(a - b)^2 \leq 2a^2 + 2b^2$ twice, we have

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

and by (4.21) and Lemma 4.3.1, we can find a positive constant C such that

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

Integrating the above inequality over Ω_T and exploiting the estimates of Lemma 4.3.3 along with estimate (4.53), we obtain (4.63) for $z_{\varepsilon,m}$. Similarly, we get the $L^2(\Omega_T)$ uniform bound of $\partial_t \gamma_{\varepsilon,m}$. \square

Lemma 4.3.7. *There exist constants \mathcal{C}_6 and $\mathcal{C}_7 > 0$ independent of ε and m such that:*

$$\max_{t \in [0, T]} (\|\sqrt{\varepsilon} \mathbf{u}_{\varepsilon,m}\|_{L^2(\Omega)^3}^2 + \|\sqrt{\varepsilon} p_{\varepsilon,m}\|_{L^2(\Omega)}^2) + \|\mathbf{u}_{\varepsilon,m}\|_{L^2(0, T; H^1(\Omega)^3)} \leq \mathcal{C}_6, \quad (4.64)$$

$$\|\varepsilon \partial_t p_{\varepsilon,m}\|_{L^2(0, T; (H^1(\Omega))')} + \|\varepsilon \partial_t \mathbf{u}_{\varepsilon,m}\|_{L^2(0, T; (H^1(\Omega)^3)')} \leq \mathcal{C}_7. \quad (4.65)$$

Proof. *Proof of (4.64):* In this proof, we first substitute $\psi_m := \mathbf{u}_{\varepsilon,m}$ and $\rho_m := p_{\varepsilon,m}$ in the first two equations of system (4.36) and we add them to obtain

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

Next, we define the continuous bilinear form

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

Furthermore, we claim and we prove the following statement:

Claim. *The bilinear form a is coercive on $(H^1(\Omega))^3$.*

Proof of Claim. By the uniform ellipticity of $\boldsymbol{\sigma}$ (A.1), we have:

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

We want to show that there exists $c > 0$ such that

$$c(\|\nabla \mathbf{u}\|_{(L^2(\Omega))^{3 \times 3}}^2 + \alpha \|\mathbf{u}\|_{L^2(\partial\Omega)}^2) \geq \|\mathbf{u}\|_{(H^1(\Omega))^3}, \quad \forall \mathbf{u} \in (H^1(\Omega))^3.$$

We proceed by contradiction.

Assume that for all $n > 0$,

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

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

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

which implies that

$$\nabla \mathbf{v}_n \rightarrow 0 \quad \text{in } (L^2(\Omega))^{3 \times 3}, \quad (4.66)$$

and

$$\mathbf{v}_n \rightarrow 0 \quad \text{in } (L^2(\partial\Omega))^3. \quad (4.67)$$

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

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

and

$$\nabla \mathbf{v}_{n_k} \rightarrow \nabla \mathbf{v} \quad \text{in } \mathbf{D}'(\Omega).$$

Now using (4.66), we deduce that $\nabla \mathbf{v} = 0$, hence $\mathbf{v} = C$, since Ω is connected. Also, using (4.66) and the convergence of \mathbf{v}_{n_k} to C in $(L^2(\Omega))^3$, we obtain

$$\mathbf{v}_{n_k} \rightarrow C \quad \text{in } (H^1(\Omega))^3$$

which implies by the continuity of the trace map γ_0 that

$$\gamma_0 \mathbf{v}_{n_k} \rightarrow C \quad \text{in } (L^2(\partial\Omega))^3.$$

On the other hand, by (4.67), we have $\mathbf{v}_{n_k} \rightarrow 0$ in $(L^2(\partial\Omega))^3$. So $C = 0$, hence we obtain a contradiction since $\|\mathbf{v}_n\|_{(H^1(\Omega))^3} = 1$. \square

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

$$\frac{1}{2} \frac{d}{dt} \left(\|\sqrt{\varepsilon} \mathbf{u}_{\varepsilon,m}\|_{L^2(\Omega)^3}^2 + \|\sqrt{\varepsilon} p_{\varepsilon,m}\|_{L^2(\Omega)}^2 \right) + \frac{c}{2} \|\mathbf{u}_{\varepsilon,m}\|_{H^1(\Omega)^3}^2 \leq \frac{1}{2c} \|\mathbf{f}\|_{L^2(\Omega)}^2. \quad (4.68)$$

Integrating (4.68) over $(0, t)$ with $0 < t \leq T$, noting that $\mathbf{u}_{\varepsilon,m}(0) = 0$ and $\|p_{0,\varepsilon,m}\|_{L^2(\Omega)} \leq \|p_0\|_{L^2(\Omega)}$, we obtain

$$\|\sqrt{\varepsilon} \mathbf{u}_{\varepsilon,m}(t)\|_{L^2(\Omega)^3}^2 + \|\sqrt{\varepsilon} p_{\varepsilon,m}(t)\|_{L^2(\Omega)}^2 \leq c_{28} (\|\mathbf{f}\|_{L^2(\Omega_t)}^2 + \varepsilon \|p_0\|_{L^2(\Omega)}^2).$$

Hence,

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

We also have upon integration of (4.68)

$$c \int_0^T \|\mathbf{u}_{\varepsilon,m}(t)\|_{H^1(\Omega)^3}^2 dt \leq c_{30}(T) (\|\mathbf{f}\|_{L^2(\Omega_T)}^2 + \varepsilon \|p_0\|_{L^2(\Omega_T)}^2). \quad (4.69)$$

As a result, estimate (4.64) follows.

In order to obtain estimate (4.65), we let $\psi \in L^2(0, T; H^1(\Omega))$ and we take $\rho_m = \psi$ in (4.36) to get

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

Similarly, we get

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

for some constant $C'_6 > 0$. Therefore, estimate (4.65) follows directly. \square

Remark 13. *We note that one can exploit the structure of the equations to obtain upper bounds on $\|\varepsilon \partial_t \mathbf{u}_{\varepsilon,m}\|_{L^1(0,T;(H^1(\Omega))')}$ 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 $\varepsilon \partial_t \mathbf{u}_{\varepsilon,m}$.*

4.3.3 Compactness properties and Convergence

Having proved that the Faedo-Galerkin solutions (4.33) are well defined, we are ready to prove existence of solutions to the regularized system.

Theorem 4.3.8. *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 4.3.8.

In view of Lemma 4.3.5, we can construct subsequences of $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $\mathbf{w}_{\varepsilon,m}$, $\gamma_{\varepsilon,m}$, $z_{\varepsilon,m}$, $\mathbf{u}_{\varepsilon,m}$, $p_{\varepsilon,m}$ which we do not bother to relabel, such that:

- $v_{\varepsilon,m} \rightharpoonup v_\varepsilon$, weakly in $L^2(0,T;H^1(\Omega))$,
- $\mathbf{w}_{\varepsilon,m} \rightharpoonup \mathbf{w}_\varepsilon$ weakly in $L^2(0,T;H^1(\Omega)^k)$ and $\partial_t \mathbf{w}_{\varepsilon,m} \rightharpoonup \partial_t \mathbf{w}_\varepsilon$ weakly in $(L^2(\Omega_T))^k$,
- $\gamma_{\varepsilon,m} \rightharpoonup \gamma_\varepsilon$ weakly in $L^2(0,T;H^1(\Omega))$ and $\partial_t \gamma_{\varepsilon,m} \rightharpoonup \partial_t \gamma_\varepsilon$ weakly in $L^2(\Omega_T)$,
- $z_{\varepsilon,m} \rightharpoonup z_\varepsilon$ weakly in $L^2(0,T;H^1(\Omega))$ and $\partial_t z_{\varepsilon,m} \rightharpoonup \partial_t z_\varepsilon$ weakly in $L^2(\Omega_T)$,
- $v_{i,\varepsilon,m} \rightharpoonup v_{i,\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\nabla v_{i,\varepsilon,m} \rightharpoonup \nabla v_{i,\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $v_{e,\varepsilon,m} \rightharpoonup v_{e,\varepsilon}$ weakly in $L^2(0,T;H^1(\Omega))$ and $\nabla v_{e,\varepsilon,m} \rightharpoonup \nabla v_{e,\varepsilon}$ weakly in $L^2(\Omega_T)$,
- $\mathbf{u}_{\varepsilon,m} \rightharpoonup \mathbf{u}_\varepsilon$ weakly in $L^2(0,T;H^1(\Omega)^3)$ and $\nabla \mathbf{u}_{\varepsilon,m} \rightharpoonup \nabla \mathbf{u}_\varepsilon$ weakly in $L^2(\Omega_T)^{3 \times 3}$,
- and $p_{\varepsilon,m} \rightharpoonup p_\varepsilon$ weak star in $L^\infty(0,T;L^2(\Omega))$ and weakly in $L^2(\Omega_T)$.

We also observe that from the sequences $U_{i,\varepsilon,m}$ and $U_{e,\varepsilon,m}$ introduced in the proof of Lemma 4.3.5, we can extract subsequences such that:

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

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

$$\begin{aligned} U_{i,\varepsilon,m} &\rightarrow U_{i,\varepsilon} = v_\varepsilon + \varepsilon v_{i,\varepsilon} \text{ in } L^2(\Omega_T) \text{ and a.e. in } \Omega_T, \\ U_{e,\varepsilon,m} &\rightarrow U_{e,\varepsilon} := v_\varepsilon - \varepsilon v_{e,\varepsilon} \text{ in } L^2(\Omega_T) \text{ and a.e. in } \Omega_T. \end{aligned}$$

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

Also from classical compactness results, (see [Lio69] Theorem 5.1 p58), we have

- $\mathbf{w}_{\varepsilon,m} \rightarrow \mathbf{w}_\varepsilon$ strongly in $L^2(\Omega_T)^k$ and a.e. in Ω_T ,

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

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

$$\begin{aligned} \varepsilon \int_0^T \int_\Omega \partial_t \mathbf{u}_{\varepsilon,m} \psi_l \phi &= -\varepsilon \int_0^T \int_\Omega \mathbf{u}_{\varepsilon,m} \psi_l \phi' \rightarrow -\varepsilon \int_0^T \int_\Omega \mathbf{u}_\varepsilon \psi_l \phi', \\ \varepsilon \int_0^T \int_\Omega \partial_t p_{\varepsilon,m} \psi_l \phi &= -\varepsilon \int_0^T \int_\Omega p_{\varepsilon,m} \omega_l \phi' \rightarrow -\varepsilon \int_0^T \int_\Omega p_\varepsilon \omega_l \phi'. \end{aligned}$$

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

$$\varepsilon \int_\Omega \partial_t \mathbf{u}_{\varepsilon,m} \psi_l \rightarrow \varepsilon \int_\Omega \partial_t \mathbf{u}_\varepsilon \psi_l \text{ and } \varepsilon \int_\Omega \partial_t p_{\varepsilon,m} \omega_l \rightarrow \varepsilon \int_\Omega \partial_t p_\varepsilon \omega_l.$$

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

We have $\mathbf{w}_{\varepsilon,m} \rightarrow \mathbf{w}_\varepsilon$ and $\gamma_{\varepsilon,m} \rightarrow \gamma_\varepsilon$ a.e. in Ω_T and S is continuous, so that $S(\gamma_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}) \rightarrow S(\gamma_\varepsilon, \mathbf{w}_\varepsilon)$ a.e. in Ω_T ; and $S(\gamma_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}) \rightharpoonup S(\gamma_\varepsilon, \mathbf{w}_\varepsilon)$ 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 [Lio69] Lemma 1.3 p 12, the continuity of $\mathbf{R}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m})$ and its bound in $L^2(\Omega_T)$ (which is a consequence of assumption **(A.6)**, (4.18) and assertion (4.53)), yield the weak convergence $\mathbf{R}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}) \rightharpoonup \mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon)$ in $L^2(\Omega_T)^k$.

Similarly, by continuity of $G(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m})$ and its boundedness in $L^2(\Omega_T)$ (as a result of (4.44), and (4.53)), we obtain the weak convergence $G(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \rightharpoonup G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)$ in $L^2(\Omega_T)$.

The strong $L^2(\Omega_T)$ and a.e. Ω_T convergence of $\gamma_{\varepsilon,m}$ implies the strong and a.e. convergence of the uniformly bounded family of tensors $\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m})$, due to assumptions **(A.1)** and **(A.2)**.

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

$$\begin{aligned} & \int_0^T \langle \nabla \mathbf{u}_{\varepsilon,m} \boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}), \nabla \psi_l \rangle_{L^2(\Omega), L^2(\Omega)} \varphi dt \\ &= \int_0^T \langle \nabla \mathbf{u}_{\varepsilon,m} (\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)), \nabla \psi_l \rangle \varphi dt \\ & \quad + \int_0^T \langle \nabla \mathbf{u}_{\varepsilon,m} \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon), \nabla \psi_l \rangle \varphi dt \\ &= \int_0^T \langle \nabla \mathbf{u}_{\varepsilon,m} (\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)), \nabla \psi_l \rangle \varphi dt \\ & \quad + \int_0^T \langle \nabla \mathbf{u}_{\varepsilon,m}, \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon) \nabla \psi_l \rangle \varphi dt. \end{aligned}$$

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

the first term converges to 0; we write

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

Knowing that

$$(\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)) \nabla \boldsymbol{\psi}_l \rightarrow 0 \text{ a.e. in } \Omega \text{ and a.e. in } (0, T)$$

and that $|(\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)) \nabla \boldsymbol{\psi}_l|$ is (due to assumption **(A.1)**) bounded by a constant multiple of $|\nabla \boldsymbol{\psi}_l| \in L^2(\Omega)$ for a.e. $t \in (0, T)$, we can apply Lebesgue's dominated convergence theorem to obtain

$$\|[\boldsymbol{\sigma}(\cdot, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\cdot, \gamma_\varepsilon)] \nabla \boldsymbol{\psi}_l\|_{L^2(\Omega)} \rightarrow 0 \text{ for a.e. } t \in (0, T).$$

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 $\mathbf{f}(t, \mathbf{x}, \gamma_{\varepsilon,m})$, by (4.6) and assumption **(A.2)** we obtain the a.e. convergence of $\mathbf{f}(t, \mathbf{x}, \gamma_{\varepsilon,m})$ from the a.e. convergence of $\gamma_{\varepsilon,m}$ in Ω_T . Furthermore, by assumption **(A.8)** and estimate (4.62) we get:

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

In order to pass to the limit in the electrical part of the system, the strong L^2 convergence of the gradients $\nabla \mathbf{u}_{\varepsilon,m}$ is needed. Indeed, since the limit \mathbf{u} solves the limit equation of (4.34), using the Minty-Browder trick (see, e.g. [AL83, Lio69, Eva98]), we are able to assert that $\nabla \mathbf{u}_{\varepsilon,m} \rightarrow \nabla \mathbf{u}_\varepsilon$ strongly in $(L^2(\Omega_T))^{3 \times 3}$. Indeed, one can also exploit the structure of the elasticity equations and the coercivity of the bilinear form a to obtain

$$\begin{aligned} & \frac{1}{\mathcal{C}} \|\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon\|_{L^2(0,T;H^1(\Omega)^3)}^2 \\ & \leq \int_0^T a(\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon, \mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon) dt \\ & = - \int_0^T \langle \varepsilon \partial_t (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon), \mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon \rangle dt - \varepsilon \|p_{\varepsilon,m}(T) - p_\varepsilon(T)\|_{L^2(\Omega_T)}^2 \\ & \quad + \varepsilon \|p_{\varepsilon,m}(0) - p_0\|_{L^2(\Omega_T)}^2 \\ & \quad - \int_{\Omega_T} \nabla \mathbf{u}_\varepsilon [\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)] : \nabla (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon) d\mathbf{x} dt \\ & \quad - \int_{\Omega_T} [f(\mathbf{x}, \gamma_{\varepsilon,m}) - f(\mathbf{x}, \gamma_\varepsilon)] \cdot (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon) d\mathbf{x} dt \\ & \leq - \int_0^T \langle \varepsilon \partial_t (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon), \mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon \rangle dt + \varepsilon \|p_{\varepsilon,m}(0) - p_0\|_{L^2(\Omega_T)}^2 \\ & \quad - \int_{\Omega_T} \nabla \mathbf{u}_\varepsilon [\boldsymbol{\sigma}(\mathbf{x}, \gamma_{\varepsilon,m}) - \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon)] : \nabla (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon) d\mathbf{x} dt \\ & \quad - \int_{\Omega_T} [f(\mathbf{x}, \gamma_{\varepsilon,m}) - f(\mathbf{x}, \gamma_\varepsilon)] \cdot (\mathbf{u}_{\varepsilon,m} - \mathbf{u}_\varepsilon) d\mathbf{x} dt. \end{aligned}$$

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

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

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

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

$$\int_0^T \int_\Omega I_{\text{ion}}(v_{\varepsilon,m}, \mathbf{w}_{\varepsilon,m}, z_{\varepsilon,m}) \omega_l \phi(t) \rightarrow \int_0^T \int_\Omega I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \omega_l \phi(t), \quad \forall \phi \in \mathcal{D}(0, T).$$

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

$$\begin{aligned} \langle \varepsilon \partial_t \mathbf{u}_\varepsilon, \psi \rangle + \int_\Omega (\nabla \mathbf{u}_\varepsilon) \boldsymbol{\sigma}(\mathbf{x}, \gamma_\varepsilon) : \nabla \psi - p_\varepsilon \nabla \cdot \psi \, dx + \int_{\partial\Omega} \alpha \mathbf{u}_\varepsilon \cdot \psi \, ds &= \int_\Omega \mathbf{f} \cdot \psi \, dx \\ \langle \varepsilon p'_\varepsilon, \rho \rangle + \int_\Omega \rho \nabla \cdot \mathbf{u}_\varepsilon &= 0 \\ \langle \partial_t v_\varepsilon + \varepsilon \partial_t v_{i,\varepsilon}, \omega \rangle + \int_\Omega (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_\varepsilon) \nabla v_{i,\varepsilon} \cdot \nabla \omega + I_{\text{ion}}(v, \mathbf{w}_\varepsilon, z_\varepsilon) \omega) \, dx &= \int_\Omega I_i^s \omega \, dx \\ \langle \partial_t v_\varepsilon - \varepsilon \partial_t v_{e,\varepsilon}, \mu \rangle - \int_\Omega (\mathbf{M}_e(\mathbf{x}, \mathbf{u}_\varepsilon) \nabla v_{e,\varepsilon} \cdot \nabla \mu + I_{\text{ion}}(v, \mathbf{w}_\varepsilon, z_{\varepsilon,m}) \mu) \, dx &= \int_\Omega I_e^s \mu \, dx \\ \forall j = 1, \dots, k, \quad \int_\Omega \partial_t w_{j,\varepsilon} \omega &= \int_\Omega R_j(v_\varepsilon, \mathbf{w}_\varepsilon) \omega \\ \int_\Omega \partial_t z_\varepsilon \omega &= \int_\Omega G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \omega \\ \int_\Omega \partial_t \gamma_\varepsilon \omega &= \int_\Omega S(\gamma_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \omega. \end{aligned} \tag{4.70}$$

Finally, having \mathbf{u}_ε in $L^2(0, T; H^1(\Omega)^3)$, $U_{i,e,\varepsilon}, \gamma_\varepsilon, z_\varepsilon$ in $L^2(0, T; H^1(\Omega))$, \mathbf{w}_ε in $L^2(0, T; H^1(\Omega)^k)$ and p_ε in $L^\infty(0, T; L^2(\Omega))$, and their weak derivatives $\partial_t \mathbf{u}_\varepsilon$ in $L^2(0, T; (H^1(\Omega)')^3)$, $\partial_t U_{i,e,\varepsilon}$, $\partial_t p_\varepsilon$ in $L^2(0, T; (H^1(\Omega))')$, $\partial_t \mathbf{w}_\varepsilon$ in $L^2(\Omega_T)^k$ and $\partial_t \gamma_\varepsilon, \partial_t z_\varepsilon$ in $L^2(\Omega_T)$, it is deduced from a classical result, that the functions $\mathbf{u}_\varepsilon : t \in [0, T] \mapsto \mathbf{u}_\varepsilon(t) \in H^1(\Omega)^3$, $U_{i,e,\varepsilon} : t \in [0, T] \mapsto U_{i,e,\varepsilon}(t) \in H^1(\Omega)$, $\mathbf{w}_\varepsilon : t \in [0, T] \mapsto \mathbf{w}_\varepsilon(t) \in L^2(\Omega)^k$, $\gamma_\varepsilon : t \in [0, T] \mapsto \gamma_\varepsilon(t) \in L^2(\Omega)$, and $z_\varepsilon : t \in [0, T] \mapsto z_\varepsilon(t) \in L^2(\Omega)$ are continuous. For p_ε , it only proves that they are weakly continuous in $H^1(\Omega)$.

Furthermore, since $\mathbf{u}_{\varepsilon,m}(0) \rightarrow \mathbf{u}_0, p_{\varepsilon,m}(0) \rightarrow p_0, v_{\varepsilon,m}(0) \rightarrow v_0, v_{k,\varepsilon,m}(0) \rightarrow v_{k,0}, k = i, e, \mathbf{w}_{\varepsilon,m}(0) \rightarrow \mathbf{w}_0, \gamma_{\varepsilon,m}(0) \rightarrow \gamma_0$ and $z_{\varepsilon,m}(0) \rightarrow z_0$ in $L^2(\Omega)$, we easily prove that $\mathbf{u}_\varepsilon(0) = \mathbf{u}_0, p_\varepsilon(0) = p_0, v_\varepsilon(0) = v_0, v_{k,\varepsilon}(0) = v_{k,0}, k = i, e, \mathbf{w}_\varepsilon(0) = \mathbf{w}_0, \gamma_\varepsilon(0) = \gamma_0$ and $z_\varepsilon(0) = z_0$. The proof is by a standard argument given in [Eva98] and one can refer to [BK06] for further details.

4.4 Existence of solution to the original problem

From the previous section, we know there exist sequences $\{\mathbf{u}_\varepsilon\}_{\varepsilon>0}$, $\{p_\varepsilon\}_{\varepsilon>0}$, $\{v_\varepsilon\}_{\varepsilon>0}$, $\{v_{i,\varepsilon}\}_{\varepsilon>0}$, $\{v_{e,\varepsilon}\}_{\varepsilon>0}$, $\{\mathbf{w}_\varepsilon\}_{\varepsilon>0}$, $\{\gamma_\varepsilon\}_{\varepsilon>0}$, and $\{z_\varepsilon\}_{\varepsilon>0}$ of solutions of (4.70). Moreover, by the lower semi-continuity of norms, the following a priori estimates are immediately obtained as in Lemma 4.3.5 with $\mathbf{u}_{\varepsilon,m}$, $p_{\varepsilon,m}$, $v_{\varepsilon,m}$, $v_{i,\varepsilon,m}$, $v_{e,\varepsilon,m}$, $\mathbf{w}_{\varepsilon,m}$, $\gamma_{\varepsilon,m}$, $z_{\varepsilon,m}$ replaced by \mathbf{u}_ε , p_ε , v_ε , $v_{i,\varepsilon}$, $v_{e,\varepsilon}$, \mathbf{w}_ε , γ_ε , z_ε , respectively.

Lemma 4.4.1. *There exist constants $\mathcal{C}_1, \dots, \mathcal{C}_6$ independent of ε such that*

$$\max_{t \in [0, T]} \left(\|v_\varepsilon(t)\|_{L^2(\Omega)}^2 + \sum_{j=i,e} \|\sqrt{\varepsilon} v_{j,\varepsilon}\|_{L^2(\Omega)}^2 \right) \leq \mathcal{C}_1, \quad \forall t \in [0, T], \quad (4.71)$$

$$\left(\sum_{j=i,e} \|v_{i,\varepsilon}\|_{L^2(0, T; H^1(\Omega))} + \|v_\varepsilon\|_{L^2(0, T; H^1(\Omega))} \right) \leq \mathcal{C}_2, \quad (4.72)$$

$$\|\partial_t(v_\varepsilon + \varepsilon v_{i,\varepsilon})\|_{L^2(0, T; (H^1)')(\Omega)} + \|\partial_t(v_\varepsilon - \varepsilon v_{e,\varepsilon})\|_{L^2(0, T; (H^1)')(\Omega)} \leq \mathcal{C}_3, \quad (4.73)$$

$$\|\mathbf{w}_\varepsilon\|_{L^2(0, T; H^1(\Omega)^k)} + \|z_\varepsilon\|_{L^2(0, T; H^1(\Omega))} + \|\gamma_\varepsilon\|_{L^2(0, T; H^1(\Omega))} \leq \mathcal{C}_4, \quad (4.74)$$

$$\|\partial_t \mathbf{w}_\varepsilon\|_{L^2(\Omega_T)^k} + \|\partial_t z_\varepsilon\|_{L^2(\Omega_T)} + \|\partial_t \gamma_\varepsilon\|_{L^2(\Omega_T)} \leq \mathcal{C}_5, \quad (4.75)$$

$$\max_{t \in [0, T]} \left(\|\sqrt{\varepsilon} \mathbf{u}_\varepsilon\|_{L^2(\Omega)^3}^2 + \|\sqrt{\varepsilon} p_\varepsilon\|_{L^2(\Omega)}^2 \right) + \|\mathbf{u}_\varepsilon\|_{L^2(0, T; H^1(\Omega)^3)} \leq \mathcal{C}_6. \quad (4.76)$$

In view of Lemma 4.4.1, we can assume there exist limit functions \mathbf{u} , p , v , v_i , v_e , with $v = v_i - v_e$, \mathbf{w} , γ and z such that as $\varepsilon \rightarrow 0$, we can extract subsequences (which we do not bother to relabel) with the following convergence properties:

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

We briefly note that in the distribution sense

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

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

$$\varepsilon \langle \partial_t p_\varepsilon, \psi \rangle \rightarrow 0,$$

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

Remark 14. 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 ε except in $L^1(0, T; L^2(\Omega))$, (see remark 13), 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 (4.15) 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 [BF12], see also [BB03, ASV88]).

Lemma 4.4.2. $\forall q \in L_0^2(\Omega) := \{q \in L^2(\Omega) : \int_{\Omega} q \, d\mathbf{x} = 0\}$, there exists $\mathbf{v} \in (H_0^1(\Omega))^3$ such that $\nabla \cdot \mathbf{v} = q$.

This lemma will be used to prove the following result.

Lemma 4.4.3. There exists $p \in L^2(\Omega_T)$ such that for a.e. $t \in (0, T)$ and for all $\mathbf{v} \in (H^1(\Omega))^3$

$$\int_{\Omega} p_{\varepsilon} \nabla \cdot \mathbf{v} \, d\mathbf{x} \rightarrow \int_{\Omega} p \nabla \cdot \mathbf{v} \, d\mathbf{x}.$$

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

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

Passing to the limit in ε we get

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

Therefore, by de Rham's Lemma (see Theorem IV.2.5 in [BF12], see also [dR84, Wan93, Sim93, Tem01]), there exists, up to an additive constant, $p \in \mathcal{D}'(\Omega)$ such that

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

in the distribution sense. Moreover, by Nevcas inequality (see Theorem IV.1.1 in [BF12], see also [Nc66, Nc11, Tem01]), for a.e. $t \in (0, T)$, $p \in L^2(\Omega)$ since $\mathbf{u} \in (H^1(\Omega))^3$. Hence, $p \in L^2(\Omega_T)$.

Now we have, for all $\mathbf{v} \in (H_0^1(\Omega))^3$,

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

and

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

Subtracting these two equations, we obtain

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

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

$$\lim_{\varepsilon \rightarrow 0} \int_{\Omega} (p_{\varepsilon} - p) \nabla \cdot \mathbf{v} \, d\mathbf{x} = 0. \quad (4.77)$$

Thus, $\nabla p_{\varepsilon} \rightarrow \nabla p$ 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:

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

Let $q \in L^2(\Omega)$, set $\tilde{q} = q - C$ where $C = \frac{1}{|\Omega|} \int_{\Omega} q \, d\mathbf{x}$, so $\tilde{q} \in L_0^2(\Omega)$. By Lemma 4.4.2, there exists $\tilde{\mathbf{v}} \in (H_0^1(\Omega))^3$ such that $\nabla \cdot \tilde{\mathbf{v}} = \tilde{q}$.

By Equation (4.77), we have

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

In other words,

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

So in order to obtain $\int_{\Omega} (p_{\varepsilon} - p) q \, d\mathbf{x} \rightarrow 0$, it is sufficient to show $\int_{\Omega} (p_{\varepsilon} - p) \, d\mathbf{x} \rightarrow 0$. In fact, by the first equation of (4.70) we have for all $\mathbf{v} \in (H^1(\Omega))^3$,

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

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

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

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

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

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

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

□

Therefore, according to all of the preceding convergence results, and repeating some of the arguments of the previous section, we have for all $\boldsymbol{\psi} \in H^1(\Omega)^3$, ρ in $L^2(\Omega)$, $\mu \in H^{1,0}(\Omega)$

(given as in Definition 4.2.1) and ω in $H^1(\Omega)$:

$$\begin{aligned}
\int_{\Omega} (\nabla \mathbf{u}) \boldsymbol{\sigma}(\mathbf{x}, \gamma) : \nabla \boldsymbol{\psi} - p \nabla \cdot \boldsymbol{\psi} \, d\mathbf{x} + \int_{\partial\Omega} \alpha \mathbf{u} \cdot \boldsymbol{\psi} \, ds &= \int_{\Omega} \mathbf{f} \cdot \boldsymbol{\psi} \, d\mathbf{x} \\
\int_{\Omega} \rho \nabla \cdot \mathbf{u} &= 0 \\
\langle \partial_t v, \omega \rangle + \int_{\Omega} (\mathbf{M}_i(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon, m}) \nabla v_i \cdot \nabla \omega + I_{\text{ion}}(v, \mathbf{w}, z) \omega) \, d\mathbf{x} &= \int_{\Omega} I_i^s \omega \, d\mathbf{x} \\
\langle \partial_t v, \mu \rangle - \int_{\Omega} (\mathbf{M}_e(\mathbf{x}, \nabla \mathbf{u}_{\varepsilon, m}) \nabla v_e \cdot \nabla \mu + I_{\text{ion}}(v, \mathbf{w}, z) \mu) \, d\mathbf{x} &= \int_{\Omega} I_e^s \mu \, d\mathbf{x} \\
\forall j = 1, \dots, k, \quad \int_{\Omega} \partial_t w_j \omega &= \int_{\Omega} R_j(v, \mathbf{w}) \omega \\
\int_{\Omega} \partial_t z \omega &= \int_{\Omega} G(v, \mathbf{w}, z) \omega \\
\int_{\Omega} \partial_t \gamma \omega &= \int_{\Omega} S(\gamma, \mathbf{w}, z) \omega.
\end{aligned} \tag{4.78}$$

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

4.5 Conclusion

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 [ABQRB15]) 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 reductions 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.

Bibliography

- [AANQ11] 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. 50
- [ABKP11] B. Andreianov, M. Bendahmane, K. Karlsen, and C. Pierre. Convergence of discrete duality finite volume schemes for the cardiac bidomain model. *Networks and Heterogeneous Media*, 6(2):195–240, 2011. 102
- [ABQRB15] B. Andreianov, M. Bendahmane, A. Quarteroni, and R. Ruiz-Baier. Solvability analysis and numerical approximation of linearized cardiac electromechanics. *Mathematical Models and Methods in Applied Sciences*, 25(05):959–993, 2015. 12, 164, 193
- [ACM17] B. Andreianov, C. Cancès, and A. Moussa. A nonlinear time compactness result and applications to discretization of degenerate parabolic–elliptic pdes. *Journal of Functional Analysis*, 273(12):3633–3670, 2017. 144, 145
- [ADH90] T. Arbogast, J. Douglas, Jr, and U. Hornung. Derivation of the double porosity model of single phase flow via homogenization theory. *SIAM Journal on Mathematical Analysis*, 21(4):823–836, 1990. 55
- [ADH95] G. Allaire, A. Damlamian, and U. Hornung. Two-scale convergence on periodic surfaces and applications. *Proceedings of the International Conference on Mathematical Modelling of Flow through Porous Media*, 1995. 72, 87
- [AGG⁺16] H. Ammari, J. Garnier, L. Giovangigli, W. Jing, and J.-K. Seo. Spectroscopic imaging of a dilute cell suspension. *Journal de Mathématiques Pures et Appliquées*, 105(5):603–661, 2016. 56, 72
- [AL83] H.W. Alt and S. Luckhaus. Quasilinear elliptic-parabolic differential equations. *Mathematische Zeitschrift*, 183(3):311–341, 1983. 144, 188
- [All92] G. Allaire. Homogenization and two-scale convergence. *SIAM Journal on Mathematical Analysis*, 23(6):1482–1518, 1992. 55, 96
- [Ama00] H. Amann. Compact embeddings of vector valued Sobolev and Besov spaces. *Glasnik Matematički*, 35(1):161–177, 2000. 56
- [AP96] R.R. Aliev and A.V. Panfilov. A simple two-variable model of cardiac excitation. *Chaos, Solitons & Fractals*, 7(3):293–301, 1996. 43
- [ASV88] D.N. Arnold, L.R. Scott, and M. Vogelius. Regular inversion of the divergence operator with Dirichlet boundary conditions on a polygon. *Annali della Scuola Normale Superiore di Pisa - Classe di Scienze*, Ser. 4, 15(2):169–192, 1988. 191

- [AWZ16] H. Ammari, T. Widlak, and W. Zhang. Towards monitoring critical microscopic parameters for electropermeabilization. *arXiv preprint arXiv:1603.00764*, 2016. 56
- [Bal77] J.M. Ball. Convexity conditions and existence theorems in nonlinear elasticity. *Arch. Rational Mech. Anal.*, 63(4):337–403, 1976/77. 164
- [BB03] J. Bourgain and H. Brezis. On the equation $\operatorname{div} Y = f$ and application to control of phases. *Journal of the American Mathematical Society*, 16(2):393–426, 2003. 191
- [BBRB10] M. Bendahmane, R. Bürger, and R. Ruiz-Baier. A finite volume scheme for cardiac propagation in media with isotropic conductivities. *Mathematics and Computers in Simulation*, 80(9):1821–1840, 2010. 102
- [BCP09] Y. Bourgault, Y. Coudière, and C. Pierre. Existence and uniqueness of the solution for the bidomain model used in cardiac electrophysiology. *Nonlinear Analysis: Real World Applications*, 10(1):458–482, 2009. 40, 56, 90, 163
- [BDMHB16] J.G. Bensley, R. De Matteo, R. Harding, and M.J. Black. Three-dimensional direct measurement of cardiomyocyte volume, nuclearity, and ploidy in thick histological sections. *Scientific reports*, 6:23756, 2016. 37, 207
- [Ber02] D.M. Bers. Cardiac excitation-contraction coupling. *Nature*, 415(6868):198–205, 2002. 50
- [BF12] F. Boyer and P. Fabrie. *Mathematical tools for the study of the incompressible Navier-Stokes equations and related models*, volume 183. Springer Science & Business Media, 2012. 104, 191
- [BK06] M. Bendahmane and K.H. Karlsen. Analysis of a class of degenerate reaction-diffusion systems and the bidomain model of cardiac tissue. *Networks and Heterogeneous Media*, 1(1):185–218, 2006. 69, 73, 90, 163, 169, 170, 173, 189
- [BK09] M. Bendahmane and K. H. Karlsen. Convergence of a finite volume scheme for the bidomain model of cardiac tissue. *Applied Numerical Mathematics*, 59(9):2266–2284, 2009. 101, 102, 111, 122
- [BLM96] A. Bourgeat, S. Luckhaus, and A. Mikelić. Convergence of the homogenization process for a double-porosity model of immiscible two-phase flow. *SIAM Journal on Mathematical Analysis*, 27(6):1520–1543, 1996. 55
- [BLP11] A. Bensoussan, J.-L. Lions, and G. Papanicolaou. *Asymptotic analysis for periodic structures*, volume 374. American Mathematical Society, 2011. 55, 60, 61, 90
- [BM13] K. Brenner and R. Masson. Convergence of a vertex centred discretization of two-phase darcy flows on general meshes. *International Journal on Finite Volumes*, 10:1–37, 2013. 144, 145
- [BMST19] M. Bendahmane, F. Mroue, M. Saad, and R. Talhouk. Mathematical analysis of cardiac electromechanics with physiological ionic model. *DCDS-B*, 22:1–35, 2019. 94
- [BP80] B.R. Baliga and S.V. Patankar. A new finite-element formulation for convection-diffusion problems. *Numerical Heat Transfer*, 3(4):393–409, 1980. 102

- [BP10] Y. Bourgault and C. Pierre. Comparing the bidomain and monodomain models in electro-cardiology through convergence analysis. <hal-00545888v2>, 2010. 101
- [BQRB13] 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. 164
- [BR77] G.W. Beeler and H. Reuter. Reconstruction of the action potential of ventricular myocardial fibres. *The Journal of Physiology*, 268(1):177–210, 1977. 11, 19, 41, 42, 91, 164, 167
- [Cai98] H. Cai. *Loi de comportement en grandes déformations du muscle à fibres actives: application à la mécanique du cœur humain et à sa croissance*. PhD thesis, Chambéry, 1998. 48
- [CD99] D. Cioranescu and P. Donato. *An introduction to homogenization, volume 17 of Oxford Lecture Series in Mathematics and its Applications*, volume 4. 1999. 55
- [CDD⁺12] D. Cioranescu, A. Damlamian, P. Donato, G. Griso, and R. Zaki. The periodic unfolding method in domains with holes. *SIAM Journal on Mathematical Analysis*, 44(2):718–760, 2012. 55, 63, 72, 76, 78, 81, 90
- [CDG08] D. Cioranescu, A. Damlamian, and G. Griso. The periodic unfolding method in homogenization. *SIAM Journal on Mathematical Analysis*, 40(4):1585–1620, 2008. 55, 56, 81
- [CDZ06] D. Cioranescu, P. Donato, and R. Zaki. The periodic unfolding method in perforated domains. *Portugaliae Mathematica*, 63(4):467, 2006. 55, 56, 78, 81
- [CFNT08] 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(2–3):562 – 573, 2008. 49, 50, 163
- [CG16] C. Cancès and C. Guichard. Convergence of a nonlinear entropy diminishing control volume finite element scheme for solving anisotropic degenerate parabolic equations. *Mathematics of Computation*, 85(298):549–580, 2016. 127, 129, 132, 135, 136, 139, 142, 148, 151
- [CGM15] C. Corrado, J.-F. Gerbeau, and P. Moireau. Identification of weakly coupled multiphysics problems. application to the inverse problem of electrocardiography. *Journal of Computational Physics*, 283:271–298, 2015. 58
- [Cha82] R.S. Chadwick. Mechanics of the left ventricle. *Biophysical journal*, 39(3):279–288, 1982. 48
- [CI18] A. Collin and S. Imperiale. Mathematical analysis and 2-scale convergence of a heterogeneous microscopic bidomain model. *Mathematical Models and Methods in Applied Sciences*, 28(05):979–1035, 2018. 56, 96
- [Cia87] P.G. Ciarlet. *Mathematical elasticity Vol. 1: Threedimensional elasticity*. Amsterdam, 1987. 43, 44, 164
- [CIS17] C. Cancès, M. Ibrahim, and M. Saad. Positive nonlinear CVFE scheme for degenerate anisotropic Keller-Segel system. *SMAI Journal of Computational Mathematics*, 3:1–28, 2017. 127, 129, 136, 142, 151

- [CMM91] Z. Cai, J. Mandel, and S. McCormick. The finite volume element method for diffusion equations on general triangulations. *SIAM Journal on Numerical Analysis*, 28(2):392–402, 1991. 102
- [CP06] Y. Coudière and C. Pierre. Stability and convergence of a finite volume method for two systems of reaction-diffusion equations in electro-cardiology. *Nonlinear Analysis: Real World Applications*, 7(4):916–935, 2006. 101
- [CP08] R.H. Clayton and A.V. Panfilov. A guide to modelling cardiac electrical activity in anatomically detailed ventricles. *Progress in Biophysics and Molecular Biology*, 96(1-3):19–43, 2008. 37, 38, 41, 101
- [Dob15] S. Dobberschütz. Homogenization of a diffusion-reaction system with surface exchange and evolving hypersurface. *Mathematical Methods in the Applied Sciences*, 38(3):559–579, 2015. 88
- [dR84] G. de Rham. Differentiable manifolds, volume 266 of Grundlehren der mathematischen Wissenschaften. *Berlin: Springer*, 1(9):84, 1984. 191
- [EG93] R. Eymard and T. Gallouët. Convergence d’un schéma de type éléments finis-volumes finis pour un système formé d’une équation elliptique et d’une équation hyperbolique. *ESAIM: Mathematical Modelling and Numerical Analysis*, 27(7):843–861, 1993. 102
- [EGGH98] R. Eymard, T. Gallouët, M. Ghilani, and R. Herbin. Error estimates for the approximate solutions of a nonlinear hyperbolic equation given by finite volume schemes. *IMA Journal of Numerical Analysis*, 18(4):563–594, 1998. 23, 143
- [EGH00] R. Eymard, T. Gallouët, and R. Herbin. Finite volume methods. *Handbook of numerical analysis*, 7:713–1018, 2000. 23, 105, 122, 144
- [Emm99] E. Emmrich. Discrete versions of Gronwall’s lemma and their application to the numerical analysis of parabolic problems. 1999. 119
- [Eva98] L.C. Evans. *Partial Differential Equations*, volume 19 of *Graduate Studies in Mathematics*. American Mathematical Society, Providence, Rhode Island, 1998. 188, 189
- [FFLM97] M. Feistauer, J. Felcman, and M. Lukávcová-Medvid’ová. On the convergence of a combined finite volume-finite element method for nonlinear convection-diffusion problems. *Numerical Methods for Partial Differential Equations: An International Journal*, 13(2):163–190, 1997. 102
- [Fit61] R. FitzHugh. Impulses and physiological states in theoretical models of nerve membrane. *Biophysical journal*, 1(6):445–466, 1961. 42, 43, 64
- [FM79] P.C. Franzone and E. Magenes. On the inverse potential problem of electrocardiology. *Calcolo*, 16(4):459–538, 1979. 11
- [FS02a] P.C. 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. 163
- [FS02b] P.C. Franzone and G. Savaré. Degenerate evolution systems modeling the cardiac electric field at micro- and macroscopic level. In *Evolution equations, semigroups and functional analysis*, pages 49–78. Springer, 2002. 56, 57

- [FSS99] M. Feistauer, J. Slavík, and P. Stupka. On the convergence of a combined finite volume–finite element method for nonlinear convection–diffusion problems. explicit schemes. *Numerical Methods for Partial Differential Equations: An International Journal*, 15(2):215–235, 1999. 102
- [Gal08] C. Gal. Well-posedness and long time behavior of the non-isothermal viscous Cahn-Hilliard equation with dynamic boundary conditions. *Dynamics of Partial Differential Equations*, 5(1):39–67, 2008. 67
- [GGBM72] P. Gould, D. Ghista, L. Brombolich, and I. Mirsky. In vivo stresses in the human left ventricular wall: analysis accounting for the irregular 3-dimensional geometry and comparison with idealised geometry analyses. *Journal of biomechanics*, 5(5):521–539, 1972. 48
- [GK10] 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. 12, 49, 58, 164
- [GK18] E. Grandelius and K.H. Karlsen. The cardiac bidomain model and homogenization. *arXiv preprint arXiv:1811.07524*, 2018. 56
- [GNR16] M. Gahn and M. Neuss-Radu. A characterization of relatively compact sets in $L^p(\Omega, B)$. *Stud. Univ. Babeş-Bolyai Math*, 61(3):279–290, 2016. 56, 82
- [GNRK16] M. Gahn, M. Neuss-Radu, and P. Knabner. Homogenization of reaction–diffusion processes in a two-component porous medium with nonlinear flux conditions at the interface. *SIAM Journal on Applied Mathematics*, 76(5):1819–1843, 2016. 85, 88
- [GP14] I. Graf and M.A. Peter. A convergence result for the periodic unfolding method related to fast diffusion on manifolds. *Comptes Rendus Mathematique*, 352(6):485–490, 2014. 81
- [GT15] D. Gilbarg and N.S. Trudinger. *Elliptic partial differential equations of second order*. Springer, 2015. 60
- [Gur82] M. Gurtin. An introduction to continuum mechanics, 1982. 43, 44, 46
- [Hen93] C.S. Henriquez. Simulating the electrical behavior of cardiac tissue using the bidomain model. *Critical Reviews in Biomedical Engineering*, 21(1):1–77, 1993. 38, 57
- [HH52] A.L. Hodgkin and A.F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, 117(4):500–544, 1952. 11, 38
- [HH97] D.M. Harrild and C.S. Henriquez. A finite volume model of cardiac propagation. *Annals of Biomedical Engineering*, 25(2):315–334, 1997. 101
- [HH08] R. Herbin and F. Hubert. Benchmark on discretization schemes for anisotropic diffusion problems on general grids. *Finite Volumes for Complex Applications V*, pages 659–692, 2008. 102
- [HKT06] M. Hanslien, K.H. Karlsen, and A. Tveito. On a finite difference scheme for a beeler-reuter based model of cardiac electrical activity. *International Journal of Numerical Analysis and Modelling*, 3:395–412, 2006. 104

- [HO09] 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. 164
- [HP10] P.E. Hand and C.S. Peskin. Homogenization of an electrophysiological model for a strand of cardiac myocytes with gap-junctional and electric-field coupling. *Bulletin of Mathematical Biology*, 72(6):1408–1424, 2010. 58
- [HSY90] J.D. Humphrey, R.K. Strumpf, and F.C.P. Yin. Determination of a constitutive relation for passive myocardium: I. a new functional form. *Journal of Biomechanical Engineering*, 112(3):333–339, 1990. 48
- [Hun75] P.J. Hunter. *Finite Element Analysis of Cardiac Muscle Mechanics*. PhD thesis, University of Oxford, 1975. 11
- [HY09] C.S. Henriquez and W. Ying. The bidomain model of cardiac tissue: from microscale to macroscale. In *Cardiac Bioelectric Therapy*, pages 401–421. Springer, 2009. 57, 58
- [JMM⁺07] P.-S. Jouk, A. Mourad, V. Milisic, G. Michalowicz, A. Raoult, D. Caillerie, and Y. Usson. Analysis of the fiber architecture of the heart by quantitative polarized light microscopy. accuracy, limitations and contribution to the study of the fiber architecture of the ventricles during fetal and neonatal life. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*, 31:915–21, 06 2007. 39
- [JNT83] J.J.B. Jack, D. Noble, and R.W. Tsien. Electrical current flow in excitable cells, 1983. 57
- [Kat10] A.M. Katz. *Physiology of the Heart*. Lippincott Williams & Wilkins, 2010. 13, 35, 207
- [Kro11] M. Kroon. Simulation of cerebral aneurysm growth and prediction of evolving rupture risk. *Modelling and Simulation in Engineering*, 2011:3, 2011. 11
- [KS98] J.P. Keener and J. Sneyd. *Mathematical Physiology*, volume 1. Springer, 1998. 38, 41
- [KS09] B.M. Koeppen and B.A. Stanton. *Berne & Levy Physiology, Updated Edition E-Book*. Elsevier Health Sciences, 2009. 14, 36, 207
- [KSMSU06] P. Krejčí, J. Sainte-Marie, M. Sorine, and J.M. Urquiza. Solutions to muscle fiber equations and their long time behaviour. *Nonlinear Analysis: Real World Applications*, 7(4):535 – 558, 2006. 164
- [LAVH12] P. Lafortune, R. Arís, M. Vázquez, and G. Houzeaux. Coupled electromechanical model of the heart: Parallel finite element formulation. *Int. J. Numer. Methods Biomed. Engrg.*, 28(1):72–86, 2012. 12, 49, 164
- [Lio69] J.-L. Lions. *Quelques méthodes de résolution des problèmes aux limites non linéaires*. Dunod; Gauthier-Villars, Paris, 1969. 89, 110, 186, 187, 188
- [LR94] C.-H. Luo and Y. 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. 11, 19, 91, 164, 167

- [LRBQ13] 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. 51
- [LSC⁺95] I.J. LeGrice, B.H. Smaill, L.Z. Chai, S.G. Edgar, J.B. Gavin, and P.J. Hunter. Laminar structure of the heart: ventricular myocyte arrangement and connective tissue architecture in the dog. *American Journal of Physiology-Heart and Circulatory Physiology*, 269(2):H571–H582, 1995. 39, 48
- [LY98] D.H.S. Lin and F.C.P. Yin. A multiaxial constitutive law for mammalian left ventricular myocardium in steady-state barium contracture or tetanus. *Journal of Biomechanical Engineering*, 120(4):504–517, 1998. 48
- [McC86] A.D. McCulloch. *Deformation and stress in the passive heart*. PhD thesis, University of Auckland, 1986. 48
- [MG78] W.T. Miller and D.B. Geselowitz. Simulation studies of the electrocardiogram I. The normal heart. *Circulation Research*, 43(2):301–315, 1978. 38
- [MM11] 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. 163
- [Mor06] Y. Mori. *A three-dimensional model of cellular electrical activity*. PhD thesis, New York University, Graduate School of Arts and Science, 2006. 57
- [Mou03] A. Mourad. *Description topologique de l'architecture fibreuse et modélisation mécanique du myocarde*. PhD thesis, Institut National Polytechnique de Grenoble, 2003. 51
- [MS03] C.C. Mitchell and D.G. Schaeffer. A two-current model for the dynamics of cardiac membrane. *Bulletin of Mathematical Biology*, 65(5):767–793, 2003. 64
- [NAY62] J. Nagumo, S. Arimoto, and S. Yoshizawa. An active pulse transmission line simulating nerve axon. *Proceedings of the IRE*, 50(10):2061–2070, 1962. 42, 43
- [Nc66] J. Nečas. Sur les normes équivalentes dans $W_p^k(\Omega)$ et sur la coercivité des formes formellement positives. *Les presses de l'Université de Montréal*, 1966. 191
- [Nc11] J. Nečas. *Direct methods in the theory of elliptic equations*. Springer Science & Business Media, 2011. 191
- [Ngu89] G. Nguetseng. A general convergence result for a functional related to the theory of homogenization. *SIAM Journal on Mathematical Analysis*, 20(3):608–623, 1989. 55
- [NH00] 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. 48, 49, 51, 164
- [NK93] J.C. Neu and W. Krassowska. Homogenization of syncytial tissues. *Critical Reviews in Biomedical Engineering*, 21(2):137–199, 1993. 58
- [NNN⁺11] 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(1–3):77–88, 2011. 12, 50, 164

- [Nob62] D. Noble. A modification of the Hodgkin—Huxley equations applicable to Purkinje fibre action and pacemaker potentials. *The Journal of Physiology*, 160(2):317–352, 1962. 11
- [NP04] M.P. Nash and A.V. Panfilov. Electromechanical model of excitable tissue to study reentrant cardiac arrhythmias. *Progr. Biophys. Molec. Biol.*, 85(2–3):501–522, 2004. 12, 49, 164
- [NQRB12] 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. 29, 50, 165
- [NRJ07] M. Neuss-Radu and W. Jäger. Effective transmission conditions for reaction-diffusion processes in domains separated by an interface. *SIAM Journal on Mathematical Analysis*, 39(3):687–720, 2007. 88
- [NT07] P. Nardinocchi and L. Teresi. On the active response of soft living tissues. *J. Elasticity*, 88(1):27–39, 2007. 49, 163
- [OC88] J. Ohayon and R.S. Chadwick. Effects of collagen microstructure on the mechanics of the left ventricle. *Biophysical Journal*, 54(6):1077–1088, 1988. 48
- [Ogd03] R.W. Ogden. Nonlinear elasticity, anisotropy, material stability and residual stresses in soft tissue. In *Biomechanics of soft tissue in cardiovascular systems*, pages 65–108. Springer, 2003. 43, 47, 48
- [OSY09] O.A. Oleinik, A.S. Shamaev, and G.A. Yosifian. *Mathematical problems in elasticity and homogenization*, volume 2. Elsevier, 2009. 60, 90
- [Pag62] E. Page. Cat heart muscle in vitro: III. The extracellular space. *The Journal of general physiology*, 46(2):201–213, 1962. 40
- [PB84] R. Plonsey and R.C. Barr. Current flow patterns in two-dimensional anisotropic bisyncytia with normal and extreme conductivities. *Biophysical Journal*, 45(3):557–571, 1984. 38
- [PCGW10] P. Pathmanathan, S.J. Chapman, D.J. Gavaghan, and J.P. Whiteley. Cardiac electromechanics: the effect of contraction model on the mathematical problem and accuracy of the numerical scheme. *Quart. J. Mech. Appl. Math.*, 63(3):375–399, 2010. 12, 164
- [PDR⁺06] M. Potse, B. Dubé, J. Richer, A. Vinet, and R.M. Gulrajani. A comparison of monodomain and bidomain reaction-diffusion models for action potential propagation in the human heart. *IEEE Transactions on Biomedical Engineering*, 53(12):2425–2435, 2006. 101
- [Pes77] C.S. Peskin. Numerical analysis of blood flow in the heart. *Journal of Computational Physics*, 25(3):220–252, 1977. 11
- [PHLHM13] Olivier Pironneau, Frédéric Hecht, Antoine Le Hyaric, and J Morice. Freefem++, 2013. 33
- [POK13] P. Pathmanathan, C. Ortner, and D. Kay. Existence of solutions of partially degenerate visco-elastic problems, and applications to modelling muscular contraction and cardiac electro-mechanical activity. *Submitted*, 2013. 12, 50, 164

- [PSF05] M. Pennacchio, G. Savaré, and P.C. Franzone. Multiscale modeling for the bioelectric activity of the heart. *SIAM Journal on Mathematical Analysis*, 37(4):1333–1370, 2005. 56, 58
- [PW85] A.V. Panfilov and A.T. Winfree. Dynamical simulations of twisted scroll rings in three-dimensional excitable media. *Physica D: Nonlinear Phenomena*, 17(3):323–330, 1985. 11
- [RB13] M. Rioux and Y. Bourgault. A predictive method allowing the use of a single ionic model in numerical cardiac electrophysiology. *ESAIM: Mathematical Modelling and Numerical Analysis*, 47(4):987–1016, 2013. 58
- [RBAP⁺13] R. Ruiz-Baier, D. Ambrosi, S. Pezzuto, S. Rossi, and A. Quarteroni. Activation models for the numerical simulation of cardiac electromechanical interactions. In G.A. Holzapfel and E. Kuhl, editors, *Computer Models in Biomechanics: From nano to macro*, pages 189–201. Springer-Verlag, Heidelberg, 2013. 51
- [RBGR⁺14] 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. 50, 51
- [RFS86] T.F. Robinson, S.M. Factor, and E.H. Sonnenblick. The heart as a suction pump. *Scientific American*, 254(6):84–91, 1986. 37, 207
- [RLRB⁺14] S. Rossi, T. Lassila, R. Ruiz-Baier, A. Sequeira, and A. Quarteroni. Thermodynamically consistent orthotropic activation model capturing ventricular systolic wall thickening in cardiac electromechanics. *Eur. J. Mechanics A/Solids*, 48:129–142, 2014. 28, 50, 165
- [RM94] J.M. Rogers and A.D. McCulloch. A collocation-galerkin finite element model of cardiac action potential propagation. *IEEE Transactions on Biomedical Engineering*, 41(8):743–757, 1994. 43
- [RRBPQ12] 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. 164
- [RTCL98] P.-A. Raviart, J.-M. Thomas, P.G. Ciarlet, and J.-L. Lions. *Introduction à l'analyse numérique des équations aux dérivées partielles*, volume 2. Dunod Paris, 1998. 169
- [RZ03] R. Racke and S. Zheng. The cahn-hilliard equation with dynamic boundary conditions. *Advances in Differential Equations*, 8(1):83–110, 2003. 67
- [San96] G. Sands. *Mathematical model of ventricular activation in an anatomically accurate deforming heart*. PhD thesis, University of Auckland, 1996. 41
- [SBHMC15] T. Stiehl, N. Baran, A.D. Ho, and A. Marciniak-Czochra. Cell division patterns in acute myeloid leukemia stem-like cells determine clinical course: a model to predict patient survival. *Cancer Research*, 75(6):940–949, 2015. 11
- [Sch69] O.H. Schmitt. Biological information processing using the concept of interpenetrating domains. In *Information processing in the nervous system*, pages 325–331. Springer, 1969. 38
- [SD63] H. Sandler and H.T. Dodge. Left ventricular tension and stress in man. *Circulation research*, 13(2):91–104, 1963. 48

- [SH91] B. Smaill and P. Hunter. Structure and function of the diastolic heart: material properties of passive myocardium. In *Theory of heart*, pages 1–29. Springer, 1991. 48
- [Sim93] J. Simon. Démonstration constructive d’un théorème de G. de Rham. *CR Acad. Sci. Paris Sér. I Math*, 316(11):1167–1172, 1993. 191
- [SLC⁺07] 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. Springer Science & Business Media, 2007. 15, 50, 63
- [SWO⁺14] J. Sundnes, S. Wall, H. Osnes, T. Thorvaldsen, and A.D. McCulloch. Improved discretisation and linearisation of active tension in strongly coupled cardiac electro-mechanics simulations. *Comput. Meth. Biomech. Biomed. Engrg.*, 17(6):604–615, 2014. 164
- [Tar76] L. Tartar. Quelques remarques sur l’homogénéisation. In *Functional Analysis and Numerical Analysis, Proceedings of the Japan-France Seminar*, pages 469–482, 1976. 55
- [Tem01] R. Temam. *Navier-Stokes equations: theory and numerical analysis*, volume 343. American Mathematical Society, 2001. 191
- [Tem12] R. Temam. *Infinite-dimensional dynamical systems in mechanics and physics*, volume 68. Springer Science & Business Media, 2012. 67
- [TLGSP05] M. Trew, I. Le Grice, B. Smaill, and A. Pullan. A finite volume method for modeling discontinuous electrical activation in cardiac tissue. *Annals of Biomedical Engineering*, 33(5):590–602, 2005. 101
- [Tra11] N.A. Trayanova. Whole-heart modeling: Applications to cardiac electrophysiology and electromechanics. *Circulation Research*, 108:113–128, 2011. 12, 49, 164
- [Tun78] L. Tung. *A bi-domain model for describing ischemic myocardial dc potentials*. PhD thesis, Massachusetts Institute of Technology, 1978. 11, 38, 163
- [UMM00] T.P. Usyk, R. Mazhari, and A.D. McCulloch. Effect of laminar orthotropic myofiber architecture on regional stress and strain in the canine left ventricle. *Journal of elasticity and the physical science of solids*, 61(1-3):143–164, 2000. 48
- [Ven06] M. Veneroni. Reaction–diffusion systems for the microscopic cellular model of the cardiac electric field. *Mathematical Methods in the Applied Sciences*, 29(14):1631–1661, 2006. 56, 93
- [Ven09] M. Veneroni. Reaction–diffusion systems for the macroscopic bidomain model of the cardiac electric field. *Nonlinear Analysis: Real World Applications*, 10(2):849–868, 2009. 12, 90, 91, 163, 164, 167, 175
- [Vog82] C. Vogt. *A homogenization theorem leading to a Volterra-integro-differential equation for permeation chromatography*. SFB 123, University of Heidelberg,, 1982. 55
- [Wan93] X. Wang. A remark on the characterization of the gradient of a distribution. *Applicable Analysis*, 51(1-4):35–40, 1993. 191

- [WHO16] Global health estimates 2015: Deaths by cause, age and sex, by country and by region, 2000-2015. http://www.who.int/healthinfo/global_burden_disease/en, 2016. Accessed: 2019-07-20. 35
- [WR68] A.Y.K. Wong and P.M. Rautaharju. Stress distribution within the left ventricular wall approximated as a thick ellipsoidal shell. *American Heart Journal*, 75(5):649–662, 1968. 48
- [Yin05] W. Ying. *A multilevel adaptive approach for computational cardiology*. Duke University, 2005. 15, 63

List of Figures

1	L'anatomie du cœur. https://www.drmani.com/what-is-the-heart/	13
2	Phases du potentiel d'action ventriculaire, adapté de [Kat10].	13
3	Diagramme montrant la structure d'une cellule cardiaque. (Extraite de Berne et Levy, [KS09])	14
4	Gauche: Une section 2D de l'organisation périodique des treillis. Droite: Section 2D du treilli de reference Y	16
5	Volumes de contrôle, centres et diamants (en lignes détachées).	24
1.1	Schematic of the activation sequence (Berne and Levy [KS09]).	36
1.2	(A): Cardiomyocytes in long section, (B): Cardiomyocytes in cross-section [BDMHB16].	37
1.3	A cardiomyocyte surrounded by an extracellular matrix of collagen and connected to other myocytes [RFS86].	37
1.4	A schematic diagram describing the current flows across the cell membrane that are captured in the BR model. http://models.cellml.org/e/23a/beeler_reuter_1977.cellml/	42
2.1	The set $\hat{\Omega}_\varepsilon^e$ in dark red, the set $\hat{\Omega}_\varepsilon^i$ in dark blue and the region Λ_ε in dark green and light blue.	77
3.1	Triangular mesh \mathcal{T} (in blue), dual mesh \mathcal{M} (in green)	130
3.2	Relative L^2 -error in a log-log scale for Example 1.	152
3.3	Relative L^∞ -error in a log-log scale for Example 1.	152
3.4	Relative L^2 -error in a log-log scale for Example 2.	154
3.5	Relative L^∞ -error in a log-log scale for Example 2.	154
3.6	From top to bottom consecutively: The propagation of the action potential for $t = 10, 200, 350, 600$ ms respectively using CVFE scheme.	156
3.7	From top to bottom consecutively: The propagation of the action potential for $t = 10, 200, 350, 600$ ms respectively using the positive nonlinear CVFE scheme with $\ln(\cdot/(1 - \cdot))$	158
3.8	First Column: Action potentials obtained from the CVFE scheme (top), the positive nonlinear CVFE scheme (center) and the finite elements method (bottom) at the same point. Second column: the respective wave propagation at time $t = 250$ ms.	159
3.9	The mesh of the cross section using 1701 vertices and 2992 triangles, along with the points at which the action potential is drawn.	159
3.10	The propagation of the action potential using the conductivity Λ_1 at $t = 10, 45, 90, 200, 300$ and 500 ms from top left to bottom right respectively.	160
3.11	Action potentials recorded at the points A, B, C, D and E using conductivity Λ_1 .	160

- 3.12 The propagation of the action potential using the conductivity Λ_2 at $t = 10, 45, 90, 200, 300$ and 500 ms from top left to bottom right respectively. 161
- 3.13 Action potentials recorded at the points A, B, C, D and E using conductivity Λ_2 . 161

Titre : Couplage Électromécanique du cœur : modélisation, analyse mathématique et simulation numérique.

Mots clés : Bidomaine, homogénéisation, éclatement périodique, volumes finis, CVFE, couplage électromécanique.

Résumé : Cette thèse est dédiée à l'analyse mathématique et la simulation numérique des équations intervenant dans la modélisation de l'électrophysiologie cardiaque.

D'abord, nous donnons une justification mathématique rigoureuse du processus d'homogénéisation périodique à l'aide de la méthode d'éclatement périodique. Nous considérons des conductivités électriques tensorielles qui dépendent de l'espace et des modèles ioniques non linéaires physiologiques et phénoménologiques. Nous montrons l'existence et l'unicité d'une solution du modèle microscopique en utilisant une approche constructive de Faedo-Galerkin suivie par un argument de compacité dans L^2 . Ensuite, nous montrons la convergence de la suite de solutions du problème microscopique vers la solution du problème macroscopique. À cause des termes non linéaires sur la variété oscillante, nous utilisons l'opérateur d'éclatement sur la surface et un argument de compacité de type Kolmogorov pour les modèles phénoménologiques et de type Minty pour les modèles physiologiques.

En outre, nous considérons le modèle monodomaine couplé au modèle physiologique de Beeler-Reuter. Nous proposons un schéma volumes finis et nous analysons sa convergence.

D'abord, nous dérivons la formulation variationnelle discrète correspondante et nous montrons l'existence et l'unicité de sa solution. Par compacité, nous obtenons la convergence de la solution discrète. Comme le schéma TPFA (two point flux approximation) est inefficace pour approcher les flux diffusifs avec des tenseurs anisotropes, nous proposons et analysons, ensuite, un schéma combiné non-linéaire qui préserve le principe de maximum. Ce schéma est basé sur l'utilisation d'un flux numérique de Godunov pour le terme de diffusion assurant que les solutions discrètes soient bornées sans restriction sur le maillage du domaine spatial ni sur les coefficients de transmissibilité. Enfin, dans la perspective d'étudier la solvabilité des modèles électromécaniques couplés avec des modèles ioniques physiologiques, nous considérons un modèle avec une description linéarisée de la réponse élastique passive du tissu cardiaque, une linéarisation de la contrainte d'incompressibilité et une approximation tronquée des diffusivités non linéaires intervenant dans les équations du modèle bidomaine. La preuve utilise des approximations par des systèmes non-dégénérés et la méthode Faedo-Galerkin suivie par un argument de compacité.

Title: Electromechanical coupling of the heart: modeling, mathematical analysis and numerical simulation.

Keywords: Bidomain, homogenization, unfolding, finite volumes, CVFE, electromechanical coupling.

Abstract: This thesis is concerned with the mathematical analysis and numerical simulation of cardiac electrophysiology models. We use the unfolding method of homogenization to rigorously derive the macroscopic bidomain equations. We consider tensorial and space dependent conductivities and physiological and simplified ionic models. Using the Faedo-Galerkin approach followed by compactness, we prove the existence and uniqueness of solution to the microscopic bidomain model. The convergence of a sequence of solutions of the microscopic model to the solution of the macroscopic model is then obtained. Due to the nonlinear terms on the oscillating manifold, the boundary unfolding operator is used as well as a Kolmogorov compactness argument for the simplified models and a Minty type argument for the physiological models. Furthermore, we consider the monodomain model coupled to Beeler-Reuter's ionic model. We propose a finite volume scheme and analyze its convergence.

First, we show existence and uniqueness of its solution. By compactness, the convergence of the discrete solution is obtained. Since the two-point flux approximation (TPFA) scheme is inefficient in approximating anisotropic diffusion fluxes, we propose and analyze a nonlinear combined scheme that preserves the maximum principle. In this scheme, a Godunov approximation to the diffusion term ensures that the solutions are bounded without any restriction on the transmissibilities or on the mesh. Finally, in view of addressing the solvability of cardiac electromechanics coupled to physiological ionic models, we considered a model 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 and the Faedo-Galerkin method followed by a compactness argument.