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UNFOLDING HOMOGENIZATION METHOD APPLIED TO PHYSIOLOGICAL AND PHENOMENOLOGICAL BIDOMAIN MODELS IN ELECTROCARDIOLOGY

MOSTAFA BENDAHDANE, FATIMA MROUE, MAZEN SAAD, AND RAAFAT TALHOUK

ABSTRACT. In this paper, we apply a rigorous homogenization method based on unfolding operators to a microscopic bidomain model representing the electrical activity of the heart at a cellular level. The heart is represented by an arbitrary open bounded connected domain with smooth boundary and the cardiac cells' (myocytes) domain is viewed as a periodic region. We start by proving the well posedness of the microscopic problem by using Faedo-Galerkin method and L^2 -compactness argument on the membrane surface without any restrictive assumptions on the conductivity matrices. Using the unfolding method in homogenization, we show that the sequence of solutions constructed in the microscopic model converges to the solution of the macroscopic bidomain model. Because of the nonlinear ionic function, the proof is based on the surface unfolding method and Kolmogorov compactness argument.

1. INTRODUCTION

The heart is the muscular organ that contracts to pump blood throughout the body. Its contraction is initiated by an electrical signal called action potential. At a microscopic level, the cardiac tissue is a complex structure composed of elongated connected cells (cardiomyocytes) that have a cylindrical shape and that are aligned in preferential directions forming fibers. Cardiomyocytes are encapsulated in a dynamic cell membrane (the sarcolemma) that separates the interior of the cell from the surrounding medium and maintains a potential difference (the transmembrane potential) between the two media due to the different concentrations of various ionic species on both sides. The elongated cardiomyocytes are endowed with special end-to-end connections (the gap junctions) that form the long fiber structure of the muscle, as well as with lateral junctions that permit the connection between the intracellular spaces of the elongated fibers. Since those connections have a low resistance, the cardiac tissue can be viewed as a single intracellular connected domain, separated from the extracellular domain by the surface of the cell membrane [29]. Moreover, the sarcolemma consists of a phospholipid bilayer in which are embedded ionic channels that ensure the flow of ionic currents from the extra- to intracellular space or vice versa. As a consequence of this transfer of ionic species between the two-spaces (intra- and extracellular spaces) a current flows across the cell membrane (transmembrane current). The capacitive, diffusive and conductive effects contribute to this current flux across the membrane [29, 18, 38]. From a physical point of view, the cardiac tissue can be viewed as partitioned into two ohmic conducting volumes (intra- and extracellular spaces). The intra- and extracellular domains

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act as volume conductors and can be described by a quasi-static approximation of elliptic equations in both spaces. These equations are complemented by a dynamical boundary equation at the interface of the two regions. It is worth mentioning in the sequel that the approximation of the ionic current flow is based on Ohm's law and charge conservation and that these equations depend (at the microscopic level) on a small parameter ($0 < \varepsilon \ll 1$) whose order of magnitude is the ratio of the two macro- and microscopic space scales.

In this paper we derive a macroscopic bidomain model of cardiac electrophysiology based on a microscopic bidomain model, using a rigorous homogenization method. Indeed, the microscopic model is unsuitable for numerical computations due to the complexity of the underlying geometry, which highlights the importance of the rigorous derivation of the macroscopic model while taking into account the properties of the physiological and microscopic structure. 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 [16, 11]. There are now various mathematical methods related to this theory: the oscillating test functions method due to L. Tartar in [39], the two-scale convergence method introduced by G. Nguetseng in [34], and further developed by G. Allaire in [1] (see also [3]) and recently 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 [17]. **The idea of the unfolding operator was used in [13, 7, 43] under the name of periodic modulation or dilation operator. The name "unfolding operator" was then introduced in [17] and deeply studied in [15, 14].** 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, there is 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 [36]. Recently, the two-scale method has been used in [19, 27] to obtain the homogenized macroscopic model using different ionic models and assumptions on the conductivity matrices. **In [19], the authors derive a macroscopic bidomain model using simplified ionic models whereas in [27], 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 [19, 27], 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 [42], the author used Schauder's fixed point theorem and in [22], the authors used a variational approach to establish the well-posedness of the microscopic problem under different initial and boundary conditions. In the present work, we prove the existence of solution of 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 [12] **where the authors prove the existence of a local in time strong solution of the bidomain equations after introducing the so-called bidomain operator**). It is worth to mention that our approach is innovative and

cannot be found in the literature in the context of existence of solutions to the microscopic bidomain model. 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 [15, 17], for sequences of functions bounded in L^2 , H^1 or in $H^{1/2}$ on a micro-periodic domain. The difficulty of the homogenization problem for the bidomain equations is due, on one hand, to the degenerate structure of the equations, in combination with the highly oscillating underlying geometry. As a consequence, standard parabolic a priori estimates are not immediately available [22]. On the other hand, the (non-linear) 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 [4, 23]. We stress that we do 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 electroporabilization models. We cite for instance [6] where a dynamical homogenization scheme is obtained from a physiological cell model and [5] 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 [28], 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 under certain assumptions.

The plan of this paper is outlined as follows. The microscopic problem and the main assumptions used for homogenization are presented in Section 2 and the main result is stated. In Section 3, 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 4, 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 5. Then in Section 6, the macroscopic bidomain equations are recuperated from the limit equations obtained in Section 5 and the cell problem is decoupled. Finally, in Section 7, a microscopic bidomain model with physiological ionic model is homogenized to obtain the corresponding macroscopic model.

2. THE MICROSCOPIC BIDOMAIN MODEL

We first list in the following paragraphs the assumptions used in sections 3, 4, 5 and 6.

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 ap-

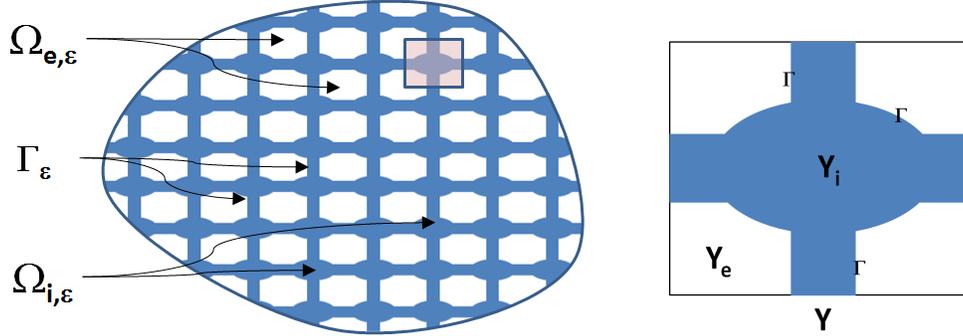


FIGURE 1. Left: A 2D section of the simplified periodic network of cells. Right: A 2D section of the reference cell Y .

proach of the 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 [14] for such domains.)

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.* [38, 44]):

$$-\operatorname{div}(\mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon}) = 0 \text{ in } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \quad (1a)$$

$$\varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, w_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m \text{ on } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \quad (1b)$$

$$\mathcal{I}_m = -\mathbf{M}_{i,\varepsilon} \nabla u_{i,\varepsilon} \cdot \mu_i = \mathbf{M}_{e,\varepsilon} \nabla u_{e,\varepsilon} \cdot \mu_e \text{ on } \Gamma_{\varepsilon,T}, \quad (1c)$$

$$\partial_t w_\varepsilon - H(v_\varepsilon, w_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}. \quad (1d)$$

We augment (1) with no-flux boundary conditions

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

and appropriate initial conditions for the transmembrane potential and gating variable

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

The conductivity tensors, the ionic functions, the source term and the initial data satisfy the following assumptions:

(E.1) 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 exists constants $m_1, m_2 > 0$ such that for $j = i, e$

$$m_1 |\zeta|^2 \leq \mathbf{M}_j(x, \xi) \zeta \cdot \zeta \leq m_2 |\zeta|^2, \quad (4a)$$

$$\mathbf{M}_j(x, \xi + e_k) = \mathbf{M}_j(x, \xi), \quad (4b)$$

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

(E.2) The ionic current $I_{\text{ion}}(u, w)$ is assumed to be decomposed into $I_{1,\text{ion}}(u)$ and $I_{2,\text{ion}}(w)$, where $I_{\text{ion}}(u, w) = I_{1,\text{ion}}(u) + I_{2,\text{ion}}(w)$. 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 exists $r \in (2, +\infty)$ and constants $\alpha_1, \alpha_2, \alpha_3, L > 0, l \geq 0$ such that

$$\frac{1}{\alpha_1} |v|^{r-1} \leq |I_{1,\text{ion}}(v)| \leq \alpha_1 (|v|^{r-1} + 1), \quad (5)$$

$$\text{and } I_{2,\text{ion}}(w)v - \alpha_2 H(v, w)w \geq \alpha_3 |w|^2,$$

$$\tilde{I}_{1,\text{ion}} : z \mapsto I_{1,\text{ion}}(z) + Lz + l \quad \text{is strictly increasing on } \mathbb{R} \text{ with } \lim_{z \rightarrow 0} \tilde{I}_{1,\text{ion}}(z)/z = 0 \quad (6a)$$

$$\text{and } \forall z, s \in \mathbb{R} \quad (\tilde{I}_{1,\text{ion}}(z) - \tilde{I}_{1,\text{ion}}(s))(z - s) \geq \frac{1}{C} (1 + |z| + |s|)^{r-2} |z - s|^2. \quad (6b)$$

Remark 2.1. 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 2.2. The function H in the ODE of (1)-(2) 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 [32]

$$H(v, w) = \frac{w_\infty(v/v_p) - w}{R_m c_m \eta_\infty(v/v_p)}, \quad (7a)$$

$$I_{\text{ion}}(v, w) = \frac{v_p}{R_m} \left(\frac{v}{v_p \eta_2} - \frac{v^2(1 - v/v_p)w}{v_p^2 \eta_1} \right), \quad (7b)$$

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 [21], often used by researchers to avoid computational difficulties. In this case,

$$H(v, w) = av - bw, \quad (8a)$$

$$I_{\text{ion}}(v, w) = \left(\lambda v(1 - v)(v - \theta) \right) + (-\lambda w) := I_{1,\text{ion}}(v) + I_{2,\text{ion}}(w), \quad (8b)$$

where a, b, λ, θ are given parameters with $a, b \geq 0$, $\lambda < 0$ and $0 < \theta < 1$. According to the Mitchell-Shaeffer and FitzHugh-Nagumo models, 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-Shaeffer membrane model, the gating variable w is bounded in L^∞). Assumptions (5), (6) 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-Shaeffer model.**

(E.3) There exists a constant C independent of ε such that the source term $I_{\text{app},\varepsilon}$ satisfies the following bound:

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

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

(E.4) The initial data $v_{0,\varepsilon}$ and $w_{0,\varepsilon}$ satisfy

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

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 (1) 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:

$$\int_{\Omega_{e,\varepsilon}} u_{e,\varepsilon}(t, x) dx = 0 \text{ for a.e. } t \in (0, T). \quad (11)$$

Finally, We end this section by stating the main results of the paper as given in the following theorems.

Theorem 2.1 (Microscopic Bidomain Model). *Assume conditions (E.1), ..., (E.4) hold. Then the microscopic bidomain problem (1), (2), (3) possesses a unique weak solution in the sense of Definition 3.1.*

Theorem 2.2 (Macroscopic Bidomain Model). *A sequence of solutions $(u_{i,\varepsilon}, u_{e,\varepsilon}, w_\varepsilon)_\varepsilon$ of the microscopic system (1)-(3) (obtained in Theorem 2.1) 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*

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

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

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

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

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

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

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

Herein, \mathbf{n} is the outward unit normal to the boundary of Ω and the tensors \mathcal{M}_i and \mathcal{M}_e are defined by

$$\mathcal{M}_j := \int_{Y_j} (\mathbf{M}_j + \mathbf{M}_j \nabla_y f_j)$$

for $j = i, e$, where the components $f_{k,j}$ of f_j ($k = 1, 2, 3$) are the corrector functions, solutions of the cell problems

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

3. EXISTENCE OF SOLUTIONS TO 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 3.1 (Weak Formulation). A solution of problem (1), (2), (3) 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. $t \in (0, T)$

$$\int_{\Gamma_\varepsilon} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, dx \quad (15)$$

$$+ \int_{\Gamma_\varepsilon} \varepsilon I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \varphi \, ds(x) = \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x),$$

$$\int_{\Gamma_\varepsilon} \partial_t w_\varepsilon \zeta \, ds(x) - \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon) \zeta \, ds(x) = 0, \quad (16)$$

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 2.1.

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 [25, 37] for similar approaches.

It follows from a well-known result (see e.g. [40] 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

$$\begin{pmatrix} u_{j,n} \\ \bar{u}_{j,n} \end{pmatrix} = \sum_{k=1}^n d_{j,k}(t) \begin{pmatrix} \phi_{j,k} \\ \psi_{j,k} \end{pmatrix}, \quad j = i, e, \quad \text{with } \phi_{j,k}|_{\Gamma_\varepsilon} = \psi_{j,k} \quad \text{and } w_n = \sum_{k=1}^n c_k(t) \zeta_k(x), \quad (17)$$

solving the approximate regularized problem:

$$\begin{aligned} & (\varepsilon + \delta_n) \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{i,n} \psi_i ds(x) - \varepsilon \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{e,n} \psi_i ds(x) + \delta_n \int_{\Omega_{i,\varepsilon}} \partial_t u_{i,n} \phi_i dx \\ & = \int_{\Gamma_\varepsilon} (-I_{\text{ion}}(v_n, w_n) + I_{\text{app},\varepsilon}) \psi_i ds(x) - \int_{\Omega_{i,\varepsilon}} \mathbf{M}_{i,\varepsilon}(x) \nabla u_{i,n} \cdot \nabla \phi_i dx \\ & - \varepsilon \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{i,n} \psi_e ds(x) + (\varepsilon + \delta_n) \int_{\Gamma_\varepsilon} \partial_t \bar{u}_{e,n} \psi_e ds(x) + \delta_n \int_{\Omega_{e,\varepsilon}} \partial_t u_{e,n} \phi_e dx \\ & = \int_{\Gamma_\varepsilon} (I_{\text{ion}}(v_n, w_n) - I_{\text{app},\varepsilon}) \psi_e |_{\Gamma_\varepsilon} ds(x) - \int_{\Omega_{e,\varepsilon}} \mathbf{M}_{e,\varepsilon}(x) \nabla u_{e,n} \cdot \nabla \phi_e dx \end{aligned} \quad (18)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_n \zeta ds(x) = \int_{\Gamma_\varepsilon} H(v_n, w_n) \zeta ds(x), \quad (20)$$

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 $\delta_n \int_{\Omega_{j,\varepsilon}} \partial_t u_{j,n} \phi_j dx$, $j = i, e$ were added to overcome the degeneracy in (15).

We aim to apply the 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 (17) to 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:

$$\begin{cases} (\delta_n + \varepsilon) \bar{\mathbb{A}}_{ii} \mathbf{d}'_i - \varepsilon \bar{\mathbb{A}}_{ie} \mathbf{d}'_e + \delta_n \mathbb{A}_{ii} \mathbf{d}'_i & = \mathbb{F}_i(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}) \\ -\varepsilon \bar{\mathbb{A}}_{ie} \mathbf{d}'_i + (\delta_n + \varepsilon) \bar{\mathbb{A}}_{ee} \mathbf{d}'_e + \delta_n \mathbb{A}_{ee} \mathbf{d}'_e & = \mathbb{F}_e(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}) \\ \mathbb{G} \mathbf{c}'(t) & = \mathbb{H}(t, \mathbf{d}_i, \mathbf{d}_e, \mathbf{c}), \end{cases} \quad (21)$$

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 $\bar{\mathbb{A}}_{jj}$, $j = i, e$ 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 (18)-(20).

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 (21) can be written in the following form:

$$\left(\delta_n \begin{bmatrix} \bar{\mathbb{A}}_{ii} + \mathbb{A}_{ii} & 0 \\ 0 & \bar{\mathbb{A}}_{ee} + \mathbb{A}_{ee} \end{bmatrix} + \varepsilon \begin{bmatrix} \bar{\mathbb{A}}_{ii} & -\bar{\mathbb{A}}_{ie} \\ -\bar{\mathbb{A}}_{ie}^T & \bar{\mathbb{A}}_{ee} \end{bmatrix} \right) \begin{bmatrix} \mathbf{d}'_i \\ \mathbf{d}'_e \end{bmatrix} = \begin{bmatrix} \mathbb{F}_i \\ \mathbb{F}_e \end{bmatrix}. \quad (22)$$

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 (22) may be written as

$$\mathbb{M} \begin{bmatrix} \mathbf{d}'_i \\ \mathbf{d}'_e \end{bmatrix} = \begin{bmatrix} \mathbb{F}_i \\ \mathbb{F}_e \end{bmatrix}, \quad \text{where } \mathbb{M} = \delta_n \begin{bmatrix} \mathbb{I}_{n \times n} & 0 \\ 0 & \mathbb{I}_{n \times n} \end{bmatrix} + \varepsilon \begin{bmatrix} \bar{\mathbb{A}}_{ii} & -\bar{\mathbb{A}}_{ie} \\ -\bar{\mathbb{A}}_{ie}^T & \bar{\mathbb{A}}_{ee} \end{bmatrix}. \quad (23)$$

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

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

Thus the matrix \mathbb{M} is symmetric positive definite, hence invertible. Consequently, the whole system (21) 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

$$\begin{aligned} u_{i,n}(0, x) &= u_{0,i,n}(x) := \sum_{l=1}^n d_{i,l}(0) \phi_{i,l}(x), \\ \bar{u}_{i,n}(0, x) &= \bar{u}_{0,i,n}(x) := \sum_{l=1}^n d_{i,l}(0) \psi_{i,l}(x), \quad d_{i,l}(0) := \left\langle \begin{pmatrix} u_{i,0} \\ \bar{u}_{i,0} \end{pmatrix}, \Theta_{i,l} \right\rangle_{V_{i,0}}, \\ u_{e,n}(0, x) &= u_{0,e,n}(x) := \sum_{l=1}^n d_{e,l}(0) \phi_{e,l}(x), \\ \bar{u}_{e,n}(0, x) &= \bar{u}_{0,e,n}(x) := \sum_{l=1}^n d_{e,l}(0) \psi_{e,l}(x), \quad d_{e,l}(0) := \left\langle \begin{pmatrix} u_{e,0} \\ \bar{u}_{e,0} \end{pmatrix}, \Theta_{e,l} \right\rangle_{V_{e,0}}, \\ w_n(0, x) &= w_{0,n}(x) := \sum_{l=1}^n c_{n,l}(0) \zeta_l(x), \quad c_{n,l}(0) := (w_0, \zeta_l)_{L^2(\Gamma_\varepsilon)}. \end{aligned} \quad (24)$$

Proceeding exactly as in Ref. [9], 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. [9].

Step 3: Energy estimates

Note that the Galerkin solutions satisfy the following weak formulations:

$$\begin{aligned} & \int_{\Gamma_\varepsilon} \varepsilon \partial_t v_n \varphi_n ds(x) + \sum_{i,e} \int_{\Gamma_\varepsilon} \delta_n \varepsilon \partial_t \bar{u}_{j,n} \bar{\varphi}_{j,n} ds(x) + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} \delta_n \partial_t u_{j,n} \varphi_{j,n} dx \\ & \quad + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,n} \cdot \nabla \varphi_{j,n} dx + \int_{\Gamma_\varepsilon} \varepsilon I_{\text{ion}}(v_n, w_n) \varphi_n ds(x) \\ & = \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} \varphi_n ds(x), \end{aligned} \quad (25)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_n e_n ds(x) - \int_{\Gamma_\varepsilon} H(v_n, w_n) e_n ds(x) = 0, \quad (26)$$

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 (25) and (26), respectively, integrating over $(0, s)$ for $s \in (0, T]$ and summing the resulting equations, one obtains upon using (5) and (6), Young's inequality, the uniform ellipticity of $\mathbf{M}_{j,\varepsilon}$ and the L^2 bound on $I_{\text{app},\varepsilon}$:

$$\begin{aligned} & \frac{1}{2} \left(\|\varepsilon^{1/2} v_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 + \alpha_2 \|\varepsilon^{1/2} w_n(s)\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\varepsilon^{1/2} \delta_n^{1/2} \bar{u}_{j,n}(s)\|_{L^2(\Gamma_\varepsilon)}^2 \right. \\ & \quad \left. + \sum_{i,e} \|\delta_n^{1/2} u_{j,n}(s)\|_{L^2(\Omega_{j,\varepsilon})}^2 \right) + m_1 \sum_{i,e} \|\nabla u_{j,n}\|_{L^2(\Omega_{j,\varepsilon,s})}^2 + \|\varepsilon \tilde{I}_{1,\text{ion}}(v_n) v_n\|_{L^1(\Gamma_{\varepsilon,s})} \\ & \leq \frac{1}{2} \left(\|\varepsilon^{1/2} v_{0,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \|w_{0,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\varepsilon^{1/2} \delta_n^{1/2} \bar{u}_{0,j,n}\|_{L^2(\Gamma_\varepsilon)}^2 + \sum_{i,e} \|\delta_n^{1/2} u_{0,j,n}\|_{L^2(\Omega_{j,\varepsilon})}^2 \right) \\ & \quad + \int_0^s \int_{\Gamma_\varepsilon} \varepsilon I_{\text{app},\varepsilon} v_n ds(x) dt - \int_0^s \int_{\Gamma_\varepsilon} \varepsilon I_{2,\text{ion}}(w_n) v_n ds(x) dt \\ & \quad + \alpha_2 \varepsilon \int_0^s \int_{\Gamma_\varepsilon} H(v_n, w_n) w_n ds(x) dt + \int_0^s \int_{\Gamma_\varepsilon} \varepsilon (L v_n + l) v_n ds(x) dt \\ & \leq C \left(\int_0^s (\|\varepsilon^{1/2} v_n\|_{L^2(\Gamma_\varepsilon)}^2 + \|\varepsilon^{1/2} w_n\|_{L^2(\Gamma_\varepsilon)}^2) dt + 1 \right), \end{aligned} \quad (27)$$

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 (27), 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 (27), one obtains

$$\|\sqrt{\varepsilon}v_n\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} + \sum_{j=i,e} \left\| \sqrt{\delta_n} \sqrt{\varepsilon} \bar{u}_{j,n} \right\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \quad (28)$$

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

$$\|\varepsilon \tilde{I}_{1,\text{ion}}(v_n)v_n\|_{L^1(\Gamma_\varepsilon,T)} + \sum_{j=i,e} \|\nabla u_{j,n}\|_{L^2(\Omega_{j,\varepsilon,T})} \leq C, \quad (29)$$

$$\|\varepsilon^{1/r}v_n\|_{L^r(\Gamma_\varepsilon,T)} \leq C, \quad (30)$$

$$\|\sqrt{\varepsilon}v_n\|_{L^2(\Gamma_\varepsilon,T)} + \|\sqrt{\varepsilon}w_n\|_{L^2(\Gamma_\varepsilon,T)} \leq C, \quad (31)$$

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 (25), and integrate in time to deduce

$$\begin{aligned} & \varepsilon \iint_{\Gamma_\varepsilon,T} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_\varepsilon,T} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 dx dt \\ & + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,n} \cdot \nabla (\partial_t u_{j,n}) dx dt + \varepsilon \iint_{\Gamma_\varepsilon,T} I_{1,\text{ion}}(v_n) \partial_t v_n ds(x) dt \\ & + \varepsilon \iint_{\Gamma_\varepsilon,T} I_{2,\text{ion}}(w_n) \partial_t v_n ds(x) dt = \varepsilon \iint_{\Gamma_\varepsilon,T} I_{\text{app},\varepsilon} \partial_t v_n ds(x) dt. \end{aligned} \quad (32)$$

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

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

and

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

Using this and Young's inequality, one gets from (32)

$$\begin{aligned}
& \varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_{\varepsilon,T}} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 dx dt \\
& \quad + \sum_{j=i,e} \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(T) + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(T, y)) ds(x) \\
& \leq -\varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{2,\text{ion}}(w_n) \partial_t v_n ds(x) dt + \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0) + \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, y)) ds(x) \\
& \quad + \varepsilon \iint_{\Gamma_{\varepsilon,T}} I_{\text{app},\varepsilon} \partial_t v_n ds(x) dt \\
& \leq \frac{\varepsilon}{2} \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + C\varepsilon \iint_{\Gamma_{\varepsilon,T}} |w_n|^2 ds(x) dt + \mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0) \\
& \quad + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, y)) ds(x) + C \int_{\Gamma_{\varepsilon,T}} |I_{\text{app},\varepsilon}|^2 ds(x) dt,
\end{aligned} \tag{33}$$

for some constant $C > 0$ not depending on ε and δ_n (recall that $0 < \varepsilon \leq 1$). **Note that by the monotonicity of $\tilde{I}_{1,\text{ion}}$ (see (6)), one can obtain**

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

Finally, use

$$\begin{aligned}
& \sum_{j=i,e} |\mathcal{P}_{\mathbf{M}_{j,\varepsilon}}(0)| + \varepsilon \int_{\Gamma_\varepsilon} \mathcal{I}_1(v_n(0, y)) ds(x) \\
& \leq C \sum_{j=i,e} \int_{\Omega_{j,\varepsilon}} |\nabla u_{j,n}(0, x)|^2 dx + \varepsilon \int_{\Gamma_\varepsilon} |v_n(0, y)|^r ds(x),
\end{aligned}$$

(for some constant $C > 0$) and estimates (28) and (29) to get from (33)

$$\varepsilon \iint_{\Gamma_{\varepsilon,T}} |\partial_t v_n|^2 ds(x) dt + \sum_{j=i,e} \iint_{\Gamma_{\varepsilon,T}} \delta_n \varepsilon (\partial_t \bar{u}_{j,n})^2 ds(x) dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \delta_n (\partial_t u_{j,n})^2 dx dt \leq C, \tag{34}$$

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

$$\sqrt{\varepsilon} \|\partial_t v_n\|_{L^2(0,T;L^2(\Gamma_\varepsilon))} + \sum_{i,e} \sqrt{\delta_n} \sqrt{\varepsilon} \|\partial_t \bar{u}_{j,n}\|_{L^2(0,T;L^2(\Gamma_\varepsilon))} \leq C, \tag{35}$$

for some constant $C > 0$ not depending on n . Also, exploiting the structure of (26) along with estimate (31), one obtains

$$\|\sqrt{\varepsilon} \partial_t w_n\|_{L^2(\Gamma_{\varepsilon,T})} \leq C, \tag{36}$$

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 (11), an application of Poincaré's inequality (see for instance [14]) implies that

$$\|u_{e,n}\|_{L^2(0,T;H^1(\Omega_{e,\varepsilon}))} \leq C. \quad (37)$$

Furthermore, making use of the trace inequality as stated in [2], 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

$$\varepsilon \|\bar{u}_{e,n}\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C. \quad (38)$$

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

$$\varepsilon \|\bar{u}_{i,n}\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C. \quad (39)$$

Finally, making use of this last inequality, of (29) and of Lemma C.2 in [5], one gets

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

Therefore, the following estimate holds

$$\|u_{i,n}\|_{L^2(0,T;H^1(\Omega_{i,\varepsilon}))} \leq C. \quad (40)$$

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. [9], so we omit the details.

Step 4: Passage to the limit and existence of solutions

From (40) and (37), 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 (31), (38) and (39) 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 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**)

$$\left\{ \begin{array}{l} v_n + (-1)^j \sqrt{\delta_n} \bar{u}_{j,n} \rightarrow v_{\varepsilon} \text{ a.e. in } \Gamma_{\varepsilon,T}, \text{ strongly in } L^2(\Gamma_{\varepsilon,T}), \\ \text{and weakly in } L^2(0, T; H^{1/2}(\Gamma_{\varepsilon})) \text{ for } j = i, e, \\ u_{j,n} \rightharpoonup u_{j,\varepsilon} \text{ weakly in } L^2(0, T; H^1(\Omega_{j,\varepsilon})) \text{ for } j = i, e, \\ v_n \rightarrow v_{\varepsilon} \text{ a.e. in } \Gamma_{\varepsilon,T}, \text{ strongly in } L^2(\Gamma_{\varepsilon,T}), \\ w_n \rightarrow w_{\varepsilon} \text{ a.e. in } \Gamma_{\varepsilon,T}, \text{ strongly in } L^2(\Gamma_{\varepsilon,T}), \\ I_{1,\text{ion}}(v_n) \rightarrow I_{1,\text{ion}}(v_{\varepsilon}) \text{ a.e. in } \Gamma_{\varepsilon,T} \text{ and weakly in } L^{r/(r-1)}(\Gamma_{\varepsilon,T}), \\ \partial_t v_n \rightharpoonup \partial_t v_{\varepsilon} \text{ weakly in } L^2(\Gamma_{\varepsilon,T}) \text{ and } \delta_n \partial_t \bar{u}_{j,n} \rightharpoonup 0 \text{ in } \mathcal{D}'(0, T; L^2(\Gamma_{\varepsilon})) \text{ for } j = i, e, \\ \partial_t w_n \rightharpoonup \partial_t w_{\varepsilon} \text{ weakly in } L^2(\Gamma_{\varepsilon,T}), \\ \delta_n \partial_t u_{j,n} \rightharpoonup 0 \text{ in } \mathcal{D}'(0, T; L^2(\Omega_{j,\varepsilon})) \text{ for } j = i, e. \end{array} \right. \quad (41)$$

Keeping in mind (41), (28) and (35) we infer, by letting $n \rightarrow \infty$ in (18), (19) and (20),

$$\begin{aligned} \varepsilon \int_{\Gamma_\varepsilon} \partial_t v_\varepsilon \varphi \, ds(x) + \sum_{i,e} \int_{\Omega_{j,\varepsilon}} M_j^\varepsilon(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, dx \\ + \varepsilon \int_{\Gamma_\varepsilon} I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \varphi \, ds(x) = \varepsilon \int_{\Gamma_\varepsilon} I_{\text{app},\varepsilon} \varphi \, ds(x), \end{aligned} \quad (42)$$

$$\int_{\Gamma_\varepsilon} \partial_t w_\varepsilon \phi \, ds(x) - \int_{\Gamma_\varepsilon} H(v_\varepsilon, w_\varepsilon) \phi \, ds(x) = 0, \quad (43)$$

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 (42)-(43), with $v_{\varepsilon,k} = (u_{i,\varepsilon,k} - u_{e,\varepsilon,k}) |_{\Gamma_\varepsilon}$ for $k = 1, 2$ and with ‘‘data’’ $v_{\varepsilon,0} = v_{\varepsilon,0,1}$, $w_{\varepsilon,0} = w_{\varepsilon,0,1}$ and $v_{\varepsilon,0} = v_{\varepsilon,0,2}$, $w_{\varepsilon,0} = w_{\varepsilon,0,2}$ 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 $\phi \in L^2(\Gamma_\varepsilon, T)$:

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

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

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

Now using (4), one has for $j = i, e$

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

Also, by (6) 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

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

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

4. 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.

4.1. Energy estimates for the microscopic solutions. The following estimates follow from the estimates on the Faedo-Galerkin solutions obtained in the previous section.

Lemma 4.1. *Assume that conditions $(\mathbf{E.1}), \dots, (\mathbf{E.1})$ and (1) and (2) hold. Then there exist constants $c_1, c_2, c_3, c_4 > 0$, not depending on ε such that*

$$\left\| \sqrt{\varepsilon} v_\varepsilon \right\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} + \left\| \sqrt{\varepsilon} w_\varepsilon \right\|_{L^\infty(0,T;L^2(\Gamma_\varepsilon))} \leq c_1, \quad (44)$$

$$\sum_{j=i,e} \|u_{j,\varepsilon}\|_{L^2(0,T;H^1(\Omega_{j,\varepsilon}))} \leq c_2 \quad (45)$$

$$\left\| \varepsilon^{1/r} v_\varepsilon \right\|_{L^r(\Gamma_{\varepsilon,T})} \leq c_3 \quad \text{and} \quad \left\| \varepsilon^{(r-1)/r} I_{1,\text{ion}}(v_\varepsilon) \right\|_{L^{r/(r-1)}(\Gamma_{\varepsilon,T})} \leq c_4. \quad (46)$$

If $v_{\varepsilon,0} \in H^{1/2}(\Gamma_\varepsilon) \cap L^r(\Gamma_\varepsilon)$, then there exists a constant $c_5 > 0$ not depending on ε such that

$$\left\| \sqrt{\varepsilon} \partial_t v_\varepsilon \right\|_{L^2(\Gamma_{\varepsilon,T})} \leq c_5. \quad (47)$$

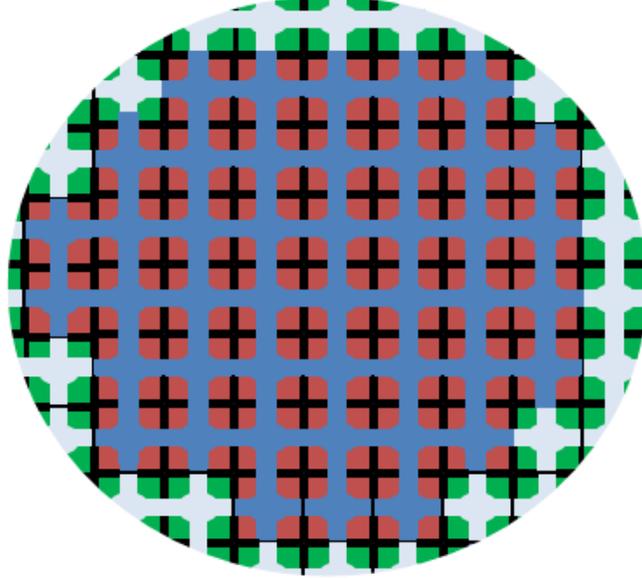


FIGURE 2. The set $\hat{\Omega}_\varepsilon^e$ in dark red, the set $\hat{\Omega}_\varepsilon^i$ in dark blue and the region Λ_ε in dark green and light blue.

4.2. Unfolded 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 [14]. First, we define the following sets in \mathbb{R}^3 (see Figure 2):

$$\begin{aligned} \Xi_\varepsilon &= \{\ell \in \mathbf{Z}^n, \varepsilon(\ell + Y) \subset \Omega\}, & \hat{\Omega}_\varepsilon &= \text{interior} \left\{ \bigcup_{\ell \in \Xi_\varepsilon} \varepsilon(\ell + \bar{Y}) \right\}, \\ \hat{\Omega}_\varepsilon^j &= \text{interior} \left\{ \bigcup_{\ell \in \Xi_\varepsilon} \varepsilon(\ell + \bar{Y}_j) \right\}, \quad j = i, e & \hat{\Omega}_{\varepsilon, T} &= (0, T) \times \hat{\Omega}_\varepsilon, \\ \hat{\Omega}_{\varepsilon, T}^j &= (0, T) \times \hat{\Omega}_\varepsilon^j, & \hat{\Gamma}_\varepsilon &:= \{y \in \Gamma_\varepsilon : y \in \hat{\Omega}_\varepsilon\}, \\ \Lambda_\varepsilon &= \Omega \setminus \hat{\Omega}_\varepsilon, & \Lambda_{\varepsilon, T} &= (0, T) \times \Omega \setminus \hat{\Omega}_\varepsilon. \end{aligned}$$

Secondly, we recall the definition of the time dependent unfolding operator in perforated domains.

Definition 4.1. For any function ϕ Lebesgue-measurable on $(0, T) \times \Omega_{j,\varepsilon}$, the unfolding operator is defined by

$$\mathcal{T}_\varepsilon^j(\phi)(t, x, y) = \begin{cases} \phi\left(t, \varepsilon \left[\frac{x}{\varepsilon} \right]_Y + \varepsilon y\right) & \text{a.e. for } (t, x, y) \in \hat{\Omega}_{\varepsilon, T} \times Y_j \\ 0 & \text{a.e. for } (t, x, y) \in (0, T) \times \Omega \setminus \hat{\Omega}_\varepsilon \times Y_j, \end{cases} \quad (48)$$

where $[\cdot]$ denotes the Gauß-bracket. Observe that the function $\varepsilon \left[\frac{x}{\varepsilon} \right]$ represents the lattice translation point of the ε -cellular medium containing x . For the sake of completeness, we recall some properties of the aforementioned operator and we refer the reader to [17, 14] for details.

Proposition 4.2. 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) $\int_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(\phi)(t, x, y) dx dy = \int_{\hat{\Omega}_{j,\varepsilon}} \phi(t, x) dx$,
- (3) $\|\mathcal{T}_\varepsilon^j(w)\|_{L^p(\Omega \times Y_j)} = \|w1_{\hat{\Omega}_{j,\varepsilon}^j}\|_{L^p(\Omega_{j,\varepsilon})} \leq \|w\|_{L^p(\Omega_{j,\varepsilon})}$.

Furthermore, since the dynamic equations are defined on the surface Γ_ε , we resort to the use of the boundary unfolding operator, developed in [17, 14] and defined as follows (recall that $\Gamma_{\varepsilon,T} = (0, T) \times \Gamma_\varepsilon$):

$$\mathcal{T}_\varepsilon^b : L^2(\Gamma_{\varepsilon,T}) \rightarrow L^2(\Omega_T \times \Gamma)$$

such that

$$\mathcal{T}_\varepsilon^b u(t, x, y) = \begin{cases} u(t, \varepsilon([\frac{x}{\varepsilon}] + y)), & \text{a.e. for } (t, x, y) \in \hat{\Omega}_{\varepsilon,T} \times \Gamma, \\ 0, & \text{a.e. for } (t, x, y) \in (0, T) \times \Omega \setminus \hat{\Omega}_\varepsilon \times \Gamma. \end{cases} \quad (49)$$

We also list herein some properties of the boundary unfolding operator as given in [14].

Proposition 4.3. *The boundary unfolding operator has the following properties:*

- (1) $\mathcal{T}_\varepsilon^b$ is a linear operator.
- (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

$$\int_{\hat{\Gamma}_\varepsilon} \phi(t, x) ds(x) = \frac{1}{\varepsilon} \int_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(\phi)(t, x, y) dx ds(y).$$

- (4) For every $\phi \in L^p(\hat{\Gamma}_{\varepsilon,T})$ with $p \in (1, +\infty)$, one has

$$\|\mathcal{T}_\varepsilon^b(\phi)\|_{L^p(\Omega_T \times \Gamma)} = \varepsilon^{1/p} \|\phi\|_{L^p((0,T) \times \hat{\Gamma}_\varepsilon)}.$$

- (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

$$\int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t w) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt = - \int_0^T \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(w) \mathcal{T}_\varepsilon^b(\partial_t \varphi) ds(y) dx dt.$$

Remark 4.1. Note that the last property (which is not listed in [14]) 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 4.3.

Now, in order to make use of the unfolding method in the homogenization of the microscopic problem, we rewrite the corresponding equations (42) and (43) in the ‘‘unfolded’’ form. We have the following identities:

$$\begin{aligned} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j dx dt &= \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) dx dy dt \\ &\quad + \iint_{(0,T) \times \Lambda_\varepsilon^j} \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j dx dy dt \\ &:= \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) dx dy dt + r_1, \end{aligned}$$

$$\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) \, dx \, 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) \, dx \, dt + r_2, \\
\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) \, dx \, dt + r_3, \\
\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 + \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) \, dx \, dt + r_4, \\
\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 + \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) \, dx \, 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) \, dx \, dt + r_5
\end{aligned}$$

Due to the above equalities, one obtains the following equivalent ‘‘unfolded’’ formulation of (42):

$$\begin{aligned}
&\iiint_{\Omega_T \times \Gamma} \mathcal{T}_{\varepsilon}^b(\partial_t v_{\varepsilon}) \mathcal{T}_{\varepsilon}^b(\varphi) \, ds(y) \, dx \, dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathcal{T}_{\varepsilon}^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_{\varepsilon}^j(\nabla u_{j,\varepsilon}) \mathcal{T}_{\varepsilon}^j(\nabla \varphi_j) \, dx \, dy \, dt \\
&- \lambda \iiint_{\Omega_T \times \Gamma} \mathcal{T}_{\varepsilon}^b(w_{\varepsilon}) \mathcal{T}_{\varepsilon}^b(\varphi) \, ds(y) \, dx \, dt + \iiint_{\Omega_T \times \Gamma} \mathcal{T}_{\varepsilon}^b(I_{1,\text{ion}}(v_{\varepsilon})) \mathcal{T}_{\varepsilon}^b(\varphi) \, ds(y) \, dx \, dt \\
&= \iiint_{\Omega_T \times \Gamma} \mathcal{T}_{\varepsilon}^b(I_{\text{app},\varepsilon}) \mathcal{T}_{\varepsilon}^b(\varphi) \, ds(y) \, dx \, dt + r_2 - r_5 - r_4 - r_3 - r_1.
\end{aligned} \tag{50}$$

Similarly, the ‘‘unfolded’’ formulation of (43) is given by:

$$\begin{aligned}
&\iiint_{\Omega_T \times \Gamma} \mathcal{T}_{\varepsilon}^b(\partial_t w_{\varepsilon}) \mathcal{T}_{\varepsilon}^b(\phi) \, ds(y) \, dx \, dt - \iiint_{\Omega_T \times \Gamma} H(\mathcal{T}_{\varepsilon}^b(v_{\varepsilon}), \mathcal{T}_{\varepsilon}^b(w_{\varepsilon})) \mathcal{T}_{\varepsilon}^b(\phi) \, ds(y) \, dx \, dt \\
&= -\varepsilon \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} \partial_t w_{\varepsilon} \phi \, ds(x) \, dt + \varepsilon \iint_{\Gamma_{\varepsilon,T} \cap \Lambda_{\varepsilon,T}} H(v_{\varepsilon}, w_{\varepsilon}) \phi \, ds(x) \, dt \\
&:= r_6 + r_7.
\end{aligned} \tag{51}$$

5. ‘‘UNFOLDING’’ COMPACTNESS

In this section, we establish the passage to the limit in (50) and (51). First, note that by estimates (44)-(47) obtained above one has

$$r_1, \dots, r_7 \rightarrow 0 \text{ as } \varepsilon \rightarrow 0.$$

Also, 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

$$\mathcal{T}_\varepsilon^j \varphi_j \rightarrow \varphi_j \text{ strongly in } L^2(\Omega_T \times Y_j).$$

Now, consider Ψ_j and θ_j in $D(\Omega_T)$ and $\psi_j = \psi_j(\xi)$ in $H_{per}^1(Y_j)$ such that $\int_{Y_j} \psi_j = 0$ and test equation (50) 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. [14]). 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 [14] (see also [26]), there holds

$$\begin{aligned} \mathcal{T}_\varepsilon^j(\varphi_j^\varepsilon) &\rightarrow \Psi_j \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \mathcal{T}_\varepsilon^j(\theta_j \psi_{j,\varepsilon}) &\rightarrow \theta_j(x) \psi_j(\xi) \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \mathcal{T}_\varepsilon^j(\nabla \varphi_j^\varepsilon) &\rightarrow \nabla \Psi_j + \theta_j \nabla_\xi \psi_j \text{ strongly in } L^2(\Omega_T \times Y_j), \\ \text{and } \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) &\rightarrow \Psi \text{ strongly in } L^2(\Omega_T \times \Gamma), \end{aligned} \tag{52}$$

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 (50) and (51), we need to verify that the remaining terms of the equations are weakly convergent.

Now, making use of estimate (29), 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 (see for instance theorem 3.12 in [14]), 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 (52))

$$\begin{aligned} &\sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla u_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) dy dx dt \\ &\rightarrow \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j(\nabla u_j + \nabla_\xi \hat{u}_j)(\nabla \Psi_j + \theta_j \nabla_\xi \psi_j(\xi)) dy dx dt \text{ as } \varepsilon \rightarrow 0. \end{aligned}$$

Furthermore, since

$$\|\mathcal{T}_\varepsilon^b(w_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq |Y|^{1/2} \varepsilon^{1/2} \|w_\varepsilon\|_{L^2(\Gamma_{\varepsilon,T})} \leq C,$$

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 $I_{2,\text{ion}}$,

$$\iiint_{\Omega_T \times \Gamma} I_{2,\text{ion}}(\mathcal{T}_\varepsilon^b(w_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{2,\text{ion}}(w) \Psi ds(y) dx dt.$$

Similarly, exploiting assumption (9), one obtains

$$\iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{\text{app}} \Psi ds(y) dx dt.$$

In order to establish the convergence of $\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon)$, first note that

$$\|\mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon)\|_{L^2(\Omega_T \times \Gamma)} \leq |Y|^{1/2} \varepsilon^{1/2} \|\partial_t v_\varepsilon\|_{L^2 \Gamma_{\varepsilon,T}} \leq C.$$

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 $L^2(\Omega_T \times \Gamma)$. By a classical argument, one can identify h to $\partial_t v$. Therefore,

$$\iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi^\varepsilon) ds(y) dx dt \rightarrow \iiint_{\Omega_T \times \Gamma} \partial_t v \Psi ds(y) dx dt.$$

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

$$\mathcal{T}_\varepsilon^b \varphi^\varepsilon \rightarrow \Psi \text{ strongly in } L^r((0, T) \times \Omega \times \Gamma).$$

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 [23].

Proposition 5.1. *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 $\{\int_C f dx : f \in F\}$ 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 $\Omega_\delta^z := \{x \in \Omega_\delta : x + z \in \Omega_\delta\}$ and $\Omega_\delta := \{x \in \Omega : \text{dist}(x, \partial\Omega) > \delta\}$,

- (iii) *for $\delta > 0$, there holds $\sup_{f \in F} \int_{\Omega \setminus \Omega_\delta} |f(x)|^p dx \rightarrow 0$ 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 5.2. *Let $l \in \mathbb{Z}^3$ and $\varepsilon > 0$ such that $\varepsilon|l| \leq |z|$. Then the following estimate holds:*

$$\varepsilon \|v_\varepsilon(t, x + \varepsilon l) - v_\varepsilon(t, x)\|_{L^2(\Gamma_{\varepsilon, K})}^2 \leq C\varepsilon l, \quad (53)$$

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 (15). In the resulting equation, we make the substitution $x \mapsto x + \varepsilon l$, and we exploit the periodicity of the domain to get

$$\begin{aligned} & \varepsilon \int_{\Gamma_\varepsilon \cap K} \partial_t(\tau_{\varepsilon l} v_\varepsilon)(\varphi_i - \varphi_e) ds(x) + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K} \tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} \cdot \nabla \varphi_j dx \\ & + \varepsilon \int_{\Gamma_\varepsilon \cap K} I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon)(\varphi_i - \varphi_e) ds(x) = \int_{\Gamma_\varepsilon \cap K} \tau_{\varepsilon l} I_{\text{app},\varepsilon} \varphi ds(x). \end{aligned} \quad (54)$$

Noting that the last equality is valid for test functions with support in K' , let $\eta \in D(K')$ 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

$$\begin{aligned} & \frac{\varepsilon}{2} \frac{d}{dt} \int_{\Gamma_\varepsilon \cap K'} \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)^2 ds(x) \\ & + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\eta^2 (\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon}) \right) dx \\ & + \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon) - I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds(x) \\ & = \int_{\Gamma_\varepsilon \cap K'} (\tau_{\varepsilon l} I_{\text{app},\varepsilon} - I_{\text{app},\varepsilon}) \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds(x). \end{aligned} \quad (55)$$

First, we break up the second term in (55) as follows:

$$\begin{aligned} & \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\eta^2 (\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon}) \right) dx \\ & = \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) dx \\ & \quad + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} 2\eta \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} \nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \nabla u_{j,\varepsilon} \right) \cdot \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) \nabla \eta dx \\ & := T_1 + T_2, \end{aligned} \quad (56)$$

and we estimate T_1 exploiting the ellipticity of $\mathbf{M}_{j,\varepsilon}$ given in (4):

$$\begin{aligned} T_1 & = \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \mathbf{M}_{j,\varepsilon} \left(\nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \nabla u_{j,\varepsilon} \right) \cdot \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} - u_{j,\varepsilon} \right) dx \\ & \quad + \sum_{j=i,e} \int_{\Omega_{j,\varepsilon} \cap K'} \eta^2 \left(\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon} \right) \nabla \left(\tau_{\varepsilon l} u_{j,\varepsilon} \right) \cdot \left(\nabla \tau_{\varepsilon l} u_{j,\varepsilon} - \nabla u_{j,\varepsilon} \right) dx \\ & \geq 0 - C \sum_{j=i,e} \|\eta^2 (\tau_{\varepsilon l} \mathbf{M}_{j,\varepsilon} - \mathbf{M}_{j,\varepsilon})\|_{L^\infty(\Omega_{j,\varepsilon} \cap K')} \|\nabla u_{j,\varepsilon}\|_{L^2(\Omega_{j,\varepsilon} \cap K')}^2 \\ & \geq -\varepsilon |l| C \sum_{j=i,e} \|\nabla u_{j,\varepsilon}\|_{L^2(\Omega_{j,\varepsilon} \cap K')}^2. \end{aligned} \quad (57)$$

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 :

$$|T_2| \leq C \varepsilon |l| \sum_{j=i,e} \|u_{j,\varepsilon}\|_{H^1(\Omega_{j,\varepsilon} \cap K')}, \quad (58)$$

for some constant $C > 0$. On the other hand, the third term of (55) may be divided into two terms by making use of (8b) as follows:

$$\begin{aligned} & \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{\text{ion}}(\tau_{\varepsilon l} v_\varepsilon, \tau_{\varepsilon l} w_\varepsilon) - I_{\text{ion}}(v_\varepsilon, w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\ &= \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{1,\text{ion}}(\tau_{\varepsilon l} v_\varepsilon) - I_{1,\text{ion}}(v_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\ & \quad + \varepsilon \int_{\Gamma_\varepsilon \cap K'} \eta^2 \left(I_{2,\text{ion}}(\tau_{\varepsilon l} w_\varepsilon) - I_{2,\text{ion}}(w_\varepsilon) \right) (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds \\ &:= T_3 + T_4. \end{aligned} \quad (59)$$

By monotonicity (6), we estimate T_3 :

$$T_3 \geq -\varepsilon L \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2. \quad (60)$$

In addition, using the definition of η and the linearity of $I_{2,\text{ion}}$ (5), Cauchy-Schwarz and Young's inequalities, T_4 can be estimated by:

$$|T_4| \leq \varepsilon C (\|\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2), \quad (61)$$

for some constant $C > 0$. Furthermore, the source term in (55) satisfies the following inequality:

$$\left| \int_{\Gamma_\varepsilon \cap K'} (\tau_{\varepsilon l} I_{\text{app},\varepsilon} - I_{\text{app},\varepsilon}) \eta^2 (\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon) ds(x) \right| \leq C \varepsilon \|I_{\text{app},\varepsilon}\|_{L^2(\Gamma_\varepsilon)} \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}. \quad (62)$$

Gathering all these estimates, one obtains

$$\begin{aligned} \varepsilon \frac{d}{dt} \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 &\leq C_1 \varepsilon |l| + C_2 \varepsilon \left(\|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right. \\ &\quad \left. + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right). \end{aligned} \quad (63)$$

By a similar argument, one can also obtain from (16),

$$\varepsilon \frac{d}{dt} \|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \leq C_3 \varepsilon \left(\|\eta(\tau_{\varepsilon l} w_\varepsilon - w_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 + \|\eta(\tau_{\varepsilon l} v_\varepsilon - v_\varepsilon)\|_{L^2(\Gamma_\varepsilon \cap K')}^2 \right). \quad (64)$$

By Grönwall's inequality applied to the sum of (63) and (64), 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 (53) holds. \square

Now, we state and prove the strong convergence of $\mathcal{T}_{\varepsilon}^b(v_{\varepsilon})$ to v .

Lemma 5.3. *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 [24] but herein the domain is not the union of scaled and translated reference cells.

The proof is based on Proposition 5.1.

Condition (iii) follows from estimate (46), since

$$\int_{\Omega \setminus \Omega_{\delta}} |\mathcal{T}_{\varepsilon}^b(v_{\varepsilon})|^2 dx \leq |\Omega \setminus \Omega_{\delta}|^{\frac{r-2}{r}} \left(\int_{\Omega} |\mathcal{T}_{\varepsilon}^b(v_{\varepsilon})|^r dx \right)^{\frac{2}{r}} \leq C |\Omega \setminus \Omega_{\delta}|^{\frac{r-2}{r}}.$$

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 obtained on v_{ε} imply that 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 $L^2((0, T), L^2(\Gamma))$. Using the properties of the unfolding operator (see Proposition 4.3) and estimate (44) one can easily 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 $v_\varepsilon = (u_{i,\varepsilon} - u_{e,\varepsilon})\Big|_\Gamma$ 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 [2], 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 4.2-(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 4.2-(2) to obtain:

$$\int_{\hat{\Omega}_\varepsilon} \int_{Y_j} u_{j,\varepsilon} \left(t, \varepsilon[\frac{x}{\varepsilon}] + \varepsilon y \right) dy dx = |Y| \int_{\hat{\Omega}_{j,\varepsilon}} u_{j,\varepsilon}(t, x) dx,$$

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 (29) on $u_{j,\varepsilon}$, we obtain the required result.

It remains to prove condition (ii) of Proposition 5.1 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 [20, 33] as follows:

$$\begin{aligned} E_{1,\xi,\varepsilon} &= \sum_{i \in I} \int_0^T \int_{\varepsilon(Y+i)} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon\left[\frac{x+\xi}{\varepsilon}\right] + \varepsilon y\right) - v^\varepsilon\left(t, \varepsilon\left[\frac{x}{\varepsilon}\right] + \varepsilon y\right) \right|^2 ds(y) dx dt \\ &= \sum_{i \in I} \sum_{k \in \{0,1\}^3} \int_0^T \int_{\varepsilon(Y+i)^k} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon\left(i + k + \left[\frac{\xi}{\varepsilon}\right]\right) + \varepsilon y\right) - v^\varepsilon(t, \varepsilon i + \varepsilon y) \right|^2 ds(y) dx dt \\ &\leq \sum_{i \in I} \sum_{k \in \{0,1\}^3} \int_0^T \int_{\varepsilon(Y+i)} \int_\Gamma \left| v^\varepsilon\left(t, \varepsilon\left(i + k + \left[\frac{\xi}{\varepsilon}\right]\right) + \varepsilon y\right) - v^\varepsilon(t, \varepsilon i + \varepsilon y) \right|^2 ds(y) dx dt \\ &\leq \sum_{k \in \{0,1\}^3} \int_0^T \int_{\hat{\Omega}_\varepsilon} \int_\Gamma \left| \mathcal{T}_\varepsilon^b v^\varepsilon\left(t, x + \varepsilon\left(k + \left[\frac{\xi}{\varepsilon}\right]\right), y\right) - \mathcal{T}_\varepsilon^b v^\varepsilon(t, x, y) \right|^2 ds(y) dx dt \\ &\leq \sum_{k \in \{0,1\}^3} \varepsilon \int_0^T \int_{\Gamma_\varepsilon} \left| v^\varepsilon\left(t, x + \varepsilon\left(\left[\frac{\xi}{\varepsilon}\right] + k\right)\right) - v^\varepsilon(t, x) \right|^2 ds(x) dt, \end{aligned}$$

where in the last inequality we used the identity $i = \left[\frac{x}{\varepsilon}\right]$ and the integration formula of Proposition 4.3-(3). Moreover, using estimate (53), 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 [24]. 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 5.1.

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 [30]),

$$I_{1,\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon)) \rightharpoonup I_{1,\text{ion}}(v) \text{ weakly in } L^{r/(r-1)}(\Omega_T \times \Gamma).$$

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:

$$\begin{aligned} & |\Gamma| \iint_{\Omega_T} \partial_t v \Psi \, dx \, dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j[\nabla u_j + \nabla_\xi \hat{u}_j][\nabla \Psi_j + \theta_j \nabla_\xi \psi_j] \\ & + |\Gamma| \iint_{\Omega_T} I_{2,\text{ion}}(w) \Psi \, dx \, dt + |\Gamma| \iint_{\Omega_T} I_{1,\text{ion}}(v) \Psi \, dx \, dt \\ & = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi \, dx \, dt. \end{aligned} \tag{65}$$

Similarly, one can easily show that the limit of (51) as ε tends to 0, is given by

$$|\Gamma| \iint_{\Omega_T} \partial_t w \phi \, dx \, dt - |\Gamma| \iint_{\Omega_T} H(v, w) \phi \, dx \, dt = 0. \tag{66}$$

6. MACROSCOPIC BIDOMAIN MODEL (PROOF OF THEOREM 2.2)

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 (65) Ψ_i, Ψ_e and θ_e to 0, to get

$$\iiint_{\Omega_T \times Y_i} \mathbf{M}_i [\nabla u_i + \nabla_y \hat{u}_i] [\theta_i \nabla_y \psi_i] dy dx dt = 0,$$

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 [14]):

$$\hat{u}_i(t, x, y) = f_i(t, x, y) \cdot \nabla_x u_i + f_{0,i}(t, x) = \sum_{k=1}^3 \frac{\partial u_i}{\partial x_k} f_{k,i}(t, x, y) + f_{0,i}(t, x), \quad (67)$$

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

$$\begin{cases} -\nabla_y \cdot (\mathbf{M}_i \nabla_y f_{k,i}) = -\nabla_y \cdot (\mathbf{M}_i e_k) & \text{in } Y_i, \\ \mathbf{M}_i \nabla_y f_{k,i} \cdot \mu_i = \mathbf{M}_i e_k \cdot \mu_i & \text{on } \Gamma, \\ \int_{Y_i} f_{k,i} = 0, & f_{k,i} \text{ } Y \text{-periodic.} \end{cases} \quad (68)$$

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 [11] or [35]). Finally, inserting formula (67) into (65) and setting θ_i, Ψ_e and θ_e to 0, one obtains the weak formulation of the macroscopic bidomain model

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi_i dx dt + \iint_{\Omega_T} \mathcal{M}_i \nabla u_i \cdot \nabla \Psi_i + |\Gamma| \iint_{\Omega_T} I_{2,\text{ion}}(w) \Psi_i dx dt \\ + |\Gamma| \iint_{\Omega_T} I_{1,\text{ion}}(v) \Psi_i dx dt = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi_i dx dt, \end{aligned} \quad (69)$$

where \mathcal{M}_i is elliptic and defined by

$$\mathcal{M}_i := \int_{Y_i} (\mathbf{M}_i + \mathbf{M}_i \nabla_y f_i).$$

Similarly, one can decouple the cell problem in the extracellular domain and define the homogenized conductivity matrix \mathcal{M}_e .

Remark 6.1. 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 [9, 12] for the case of phenomenological models of FitzHugh-Nagumo type and to [41] for physiological models of Luo-Rudy type.

7. 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 (1d) 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 several gating and ionic concentration variables in Beeler-Reuter or Luo-Rudy ionic models [41, 8, 31].

(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

$$R_l(v, \mathbf{w}) = \alpha_l(v)(1 - w_l) - \beta_l(v)w_l \quad (70)$$

where α_l and β_l , $l = 1, \dots, k$ are positive rational functions of exponentials in v such that:

$$0 < \alpha_l(v), \beta_l(v) \leq C_{\alpha, \beta}(1 + |v|). \quad (71)$$

(A.2) The function $I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty) \rightarrow \mathbb{R}$ has the general form:

$$I_{\text{ion}}(v, \mathbf{w}, z) = \sum_{l=1}^k I_{\text{ion}}^l(v, w_l) + I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \quad (72)$$

where $I_{\text{ion}}^l \in C^0(\mathbb{R} \times \mathbb{R}^k) \cap \text{Lip}(\mathbb{R} \times [0, 1]^k)$ and satisfies the condition:

$$|I_{\text{ion}}^l(v, w_l)| \leq C_{1,I}(1 + |w_l| + |v|), \quad (73)$$

and I_{ion}^z is such that:

$$I_{\text{ion}}^z \in C^1(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}^+ \times \mathbb{R}) \cap \text{Lip}(\mathbb{R} \times [0, 1]^k \times \mathbb{R}^+ \times \mathbb{R}), \quad (74)$$

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

$$I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z) \geq C_{3,I} \sum_{l=1}^k (|v| + w_l + w_l \ln z), \quad (75)$$

$$0 < \underline{\Theta}(\mathbf{w}) \leq \frac{\partial}{\partial \zeta} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \leq \bar{\Theta}(\mathbf{w}), \quad (76)$$

$$\left| \frac{\partial}{\partial v} I_{\text{ion}}^z(v, \mathbf{w}, z, \zeta) \right| \leq L(\mathbf{w}), \quad (77)$$

$$\frac{\partial}{\partial w_l} I_{\text{ion}}^z \leq C_{4,I}(1 + |v| + |\ln z|), \quad \forall l = 1, \dots, k, \quad (78)$$

$$0 \leq \frac{\partial}{\partial z} I_{\text{ion}}^z \leq C_{5,I}, \quad (79)$$

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:

$$G(v, \mathbf{w}, z) = a_1(a_2 - z) - a_3 I_{\text{ion}}^z(v, \mathbf{w}, z, \ln z), \quad (80)$$

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:

$$-\operatorname{div}(\mathbf{M}_{j,\varepsilon}\nabla u_{j,\varepsilon}) = 0 \text{ in } \Omega_{j,\varepsilon,T} := (0, T) \times \Omega_{j,\varepsilon}, \quad (81a)$$

$$\varepsilon(\partial_t v_\varepsilon + I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) - I_{\text{app},\varepsilon}) = \mathcal{I}_m \text{ on } \Gamma_{\varepsilon,T} := (0, T) \times \Gamma_\varepsilon, \quad (81b)$$

$$\mathcal{I}_m = -\mathbf{M}_{i,\varepsilon}\nabla u_{i,\varepsilon} \cdot \boldsymbol{\mu}_i = \mathbf{M}_{e,\varepsilon}\nabla u_{e,\varepsilon} \cdot \boldsymbol{\mu}_e \text{ on } \Gamma_{\varepsilon,T}, \quad (81c)$$

$$\partial_t \mathbf{w}_\varepsilon - \mathbf{R}(v_\varepsilon, \mathbf{w}_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}, \quad (81d)$$

$$\partial_t z_\varepsilon - G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) = 0 \text{ on } \Gamma_{\varepsilon,T}. \quad (81e)$$

We augment (81) with no-flux boundary conditions

$$(\mathbf{M}_{j,\varepsilon}(x)\nabla u_{j,\varepsilon}) \cdot \boldsymbol{\mu}_j = 0 \text{ on } (0, T) \times (\partial\Omega_{j,\varepsilon} \setminus \Gamma_\varepsilon), \quad j \in \{e, i\}, \quad (82)$$

and appropriate initial conditions for the transmembrane potential, the gating variables and the concentration variable

$$v_\varepsilon(0, \cdot) = v_{0,\varepsilon}(\cdot), \quad \mathbf{w}_\varepsilon(0, \cdot) = \mathbf{w}_{0,\varepsilon}(\cdot), \quad z_\varepsilon(0, \cdot) = z_{0,\varepsilon}(\cdot) \text{ on } \Gamma_\varepsilon, \quad (83)$$

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 7.1. *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 (81),(82),(83) 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*

$$\begin{aligned} & \iint_{\Gamma_{\varepsilon,T}} \varepsilon \partial_t v_\varepsilon \varphi \, ds(x) \, dt + \sum_{j=i,e} \iint_{\Omega_{j,\varepsilon,T}} \mathbf{M}_{j,\varepsilon}(x) \nabla u_{j,\varepsilon} \cdot \nabla \varphi_j \, dx \, dt \\ & + \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \varphi \, ds(x) \, dt = \iint_{\Gamma_{\varepsilon,T}} \varepsilon I_{\text{app},\varepsilon} \varphi \, ds(x) \, dt, \end{aligned} \quad (84)$$

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t w_{l,\varepsilon} \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} R_l(v_\varepsilon, \mathbf{w}_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (85)$$

for $l = 1, \dots, k$ and

$$\iint_{\Gamma_{\varepsilon,T}} \partial_t z_\varepsilon \phi \, ds(x) \, dt - \iint_{\Gamma_{\varepsilon,T}} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \phi \, ds(x) \, dt = 0, \quad (86)$$

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 (similarly to section 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 available in [10]. We also refer to [42] where a fixed point approach was used. First, the recovery variables are shown to satisfy the physiological bounds.

Lemma 7.2. *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 $\omega \in L^2(\Gamma_\varepsilon)$:*

$$\int_{\Gamma_\varepsilon} \partial_t w_{l,\varepsilon} \omega = \int_{\Gamma_\varepsilon} R_l(v_\varepsilon, w_{l,\varepsilon}) \omega, \quad (87)$$

where $\mathbf{R}(v, \mathbf{w})$ is defined by (70). Assume that $0 \leq w_{l,0,\varepsilon} \leq 1$ a.e. in Γ_ε , then

$$0 \leq w_{l,\varepsilon} \leq 1, \quad \text{a.e. in } \Gamma_{\varepsilon,T}. \quad (88)$$

Secondly, one has to make sure that the concentration variable stays positive.

Lemma 7.3. *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 $\omega \in L^2(\Gamma_\varepsilon)$:*

$$\int_{\Gamma_\varepsilon} \partial_t z_\varepsilon \omega = \int_{\Gamma_\varepsilon} G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon) \omega, \quad (89)$$

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

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

Then for a.e. $(t, \mathbf{x}) \in [0, T] \times \Gamma_\varepsilon$, $z > 0$.

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 7.4. *Under the same assumptions as Lemma 7.3, the concentration variable z_ε satisfies the following estimates for a.e. $\mathbf{x} \in \Gamma_\varepsilon$, $t \in (0, T)$:*

$$|z_\varepsilon(t, \mathbf{x})| \leq C(1 + |z_{0,\varepsilon}(\mathbf{x})| + \|v_\varepsilon(\mathbf{x})\|_{L^2(0,t)}), \quad \forall t \in [0, T], \quad (90)$$

$$|\ln z_\varepsilon(t, \mathbf{x})| \leq C(1 + |z_{0,\varepsilon}(\mathbf{x})| + |v_\varepsilon(t, \mathbf{x})| + \|v_\varepsilon(\mathbf{x})\|_{L^2(0,t)}) \quad (91)$$

$$\int_0^t |\partial_s z_\varepsilon|^2 \leq C \left(1 + |z_{0,\varepsilon} \ln z_{0,\varepsilon}| + |z_{0,\varepsilon}|^2 + \|v_\varepsilon\|_{L^2(0,t)}^2 \right), \quad (92)$$

$$\int_0^t |\ln z_\varepsilon|^2 \leq C \left(1 + |z_{0,\varepsilon} \ln z_{0,\varepsilon}| + |z_{0,\varepsilon}|^2 + \|v_\varepsilon\|_{L^2(0,t)}^2 \right), \quad (93)$$

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 7.5. *Under the same conditions of Lemma 7.4, there exists a constant $C > 0$ (dependent on T) such that*

$$\|I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)\|_{L^2(\Gamma_{\varepsilon,T})}^2 \leq C(1 + \|v_\varepsilon\|_{L^2(\Gamma_{\varepsilon,T})}^2). \quad (94)$$

Based on the previous Lemmata, and proceeding in a similar way as in Section 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 [10]).

Lemma 7.6. *There exist constants \mathcal{C}_1 , \mathcal{C}_2 and \mathcal{C}_3 independent of ε such that*

$$\max_{t \in [0, T]} \left(\|\sqrt{\varepsilon} v_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 + \|\sqrt{\varepsilon} w_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 + \|\sqrt{\varepsilon} z_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 \right) \leq \mathcal{C}_1, \quad (95)$$

$$\sum_{j=i,e} \|u_{j,\varepsilon}\|_{L^2(0, T; H^1(\Omega_{j,\varepsilon}))} \leq \mathcal{C}_2, \quad (96)$$

$$\|\sqrt{\varepsilon} \partial_t v_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})} + \|\sqrt{\varepsilon} \partial_t \mathbf{w}_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})^k} + \|\sqrt{\varepsilon} \partial_t z_\varepsilon\|_{L^2(\Gamma_{\varepsilon, T})} \leq \mathcal{C}_3, \quad (97)$$

In order to exploit the unfolding method, the weak formulation is written in its ‘‘unfolded’’ form as in section 4.2 above. Equation (84) becomes:

$$\begin{aligned} & \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) dy dx dt \\ & + \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{ion}}(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt \\ & = \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app}, \varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt + r_{10}, \end{aligned} \quad (98)$$

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 (85) and (86) are given by:

$$\begin{aligned} & \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t w_{l,\varepsilon}) \mathcal{T}_\varepsilon^b(\phi) ds(y) dx dt - \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(R_l(v_\varepsilon, \mathbf{w}_\varepsilon)) \mathcal{T}_\varepsilon^b(\phi) ds(y) dx dt \\ & = r_{11}, \end{aligned} \quad (99)$$

for $l = 1, \dots, k$ and

$$\begin{aligned} & \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(\partial_t z_\varepsilon) \mathcal{T}_\varepsilon^b(\phi) ds(y) dx dt - \iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(G(v_\varepsilon, \mathbf{w}_\varepsilon, z_\varepsilon)) \mathcal{T}_\varepsilon^b(\phi) ds(y) dx dt \\ & = r_{12}, \end{aligned} \quad (100)$$

where r_{11} and r_{12} are remainder terms that tend to zero as $\varepsilon \rightarrow 0$.

Now, making use of Lemma 7.6, one can repeat the arguments in section 5 to show that there exist $u_j \in L^2(0, T; H^1(\Omega))$ and $\hat{u}_j \in L^2(0, T; L^2(\Omega, H_{\text{per}}^1(Y_j)))$ 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

$$\begin{aligned} & \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathcal{T}_\varepsilon^j(\mathbf{M}_j^\varepsilon) \mathcal{T}_\varepsilon^j(\nabla u_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_j) \\ & \rightarrow \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j(\nabla u_j + \nabla_y \hat{u}_j)(\nabla \Psi_j + \theta_j \nabla_y \psi_j(y)) \text{ as } \varepsilon \rightarrow 0. \end{aligned}$$

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 7.6), 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 5, 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 (9) on the source term $I_{\text{app},\varepsilon}$, one obtains

$$\iiint_{\Omega_T \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(\varphi) ds(y) dx dt \rightarrow \iiint_{\Omega_T \times \Gamma} I_{\text{app}} \Psi ds(y) dx dt.$$

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 7.5 and of Lemma 7.6, 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 49 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

$$\begin{aligned}I_{\text{ion}} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right) &\rightharpoonup \tilde{I}_{\text{ion}}, \text{ in } L^2(\Omega_T \times \Gamma), \\ \mathbf{R} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \right) &\rightharpoonup \tilde{\mathbf{R}}, \text{ in } L^2(\Omega_T \times \Gamma)^k, \\ \text{and } G \left(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon) \right) &\rightharpoonup \tilde{G}, \text{ in } L^2(\Omega_T \times \Gamma).\end{aligned}$$

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 7.1. One possibility is to proceed analogously to Section 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 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 7.7. *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 (84)-(86) as given in Theorem 7.1. 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

$$\begin{aligned} &(I_{\text{ion}}(v_1, \mathbf{w}_1, z_1) - I_{\text{ion}}(v_2, \mathbf{w}_2, z_2))(v_1 - v_2) - (\mathbf{R}(v_1, \mathbf{w}_1) - \mathbf{R}(v_2, \mathbf{w}_2)) \cdot (\mathbf{w}_1 - \mathbf{w}_2) \\ &- ((G(v_1, \mathbf{w}_1, z_1) - G(v_2, \mathbf{w}_2, z_2))(z_1 - z_2) \geq -K_I(|v_1 - v_2|^2 + |\mathbf{w}_1 - \mathbf{w}_2|^2 + |z_1 - z_2|^2). \end{aligned} \quad (101)$$

To obtain the result, we proceed as in [1, 19] for 2-scale convergence in nonlinear terms. Using the formulation of the unfolded equations (98)-(100) 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 dx 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) dx + \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) dx + \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) dx + \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) dx ds + \int_0^t e^{-\lambda s} (r_{10} + r_{11} + r_{12}) ds. \end{aligned} \quad (102)$$

By (101), 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 dx 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) dx + \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))) \cdot (\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) - \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) ds(y) dx \right. \\
& \quad \left. + \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) dx + \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{103}$$

We want to use (102) to simplify the previous inequality. We introduce the following notation:

$$\begin{aligned}
A^\varepsilon & := \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \mathcal{T}_\varepsilon^b(I_{\text{app},\varepsilon}) \mathcal{T}_\varepsilon^b(v_\varepsilon) ds(y) dx dt + \frac{1}{2} \|\mathcal{T}_\varepsilon^b(v_{\varepsilon,0})\|_{L^2}^2 + \frac{1}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(w_{l,\varepsilon,0})\|_{L^2}^2 \\
& \quad + \frac{1}{2} \|\mathcal{T}_\varepsilon^b(z_{\varepsilon,0})\|_{L^2}^2 + \int_0^T e^{-\lambda t} (r_{10} + r_{11} + r_{12}) dt,
\end{aligned}$$

$$\begin{aligned}
D^\varepsilon & := \frac{1}{2} e^{-\lambda T} \iint_{\Omega \times \Gamma} \left(\mathcal{T}_\varepsilon^b(v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) + \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) + \mathcal{T}_\varepsilon^b(z_\varepsilon) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) \right) ds(y) dx \\
& \quad + \sum_{i,\varepsilon} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla(u_{j,\varepsilon})) \cdot \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) dy dx dt,
\end{aligned}$$

$$\begin{aligned}
E^\varepsilon & := \frac{1}{2} e^{-\lambda T} \left(\|\mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 + \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 + \|\mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \right) \\
& \quad + \sum_{i,\varepsilon} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} \mathcal{T}_\varepsilon^j(M_{j,\varepsilon}) \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) \cdot \mathcal{T}_\varepsilon^j(\nabla \varphi_{j,\varepsilon}) dy dx dt
\end{aligned}$$

$$\begin{aligned}
I^\varepsilon & := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} \left(-I_{\text{ion}}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) \right. \right. \\
& \quad \left. \left. - I_{\text{ion}}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) (\mathcal{T}_\varepsilon^b(v_\varepsilon) - \mathcal{T}_\varepsilon^b(\varphi_\varepsilon)) - \lambda \mathcal{T}_\varepsilon^b(v_\varepsilon) \mathcal{T}_\varepsilon^b(\varphi_\varepsilon) \right) ds(y) dx + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(\varphi_\varepsilon)\|_{L^2}^2 \right] dt,
\end{aligned}$$

$$\begin{aligned}
R^\varepsilon & := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} \left(\mathbf{R}(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon)) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) + \mathbf{R}(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) \cdot (\mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) - \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon)) \right. \right. \\
& \quad \left. \left. - \lambda \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon) \cdot \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon) \right) ds(y) dx + \frac{\lambda}{2} \sum_{l=1}^k \|\mathcal{T}_\varepsilon^b(\psi_{l,\varepsilon})\|_{L^2}^2 \right] dt,
\end{aligned}$$

and

$$G^\varepsilon := \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} G(\mathcal{T}_\varepsilon^b(v_\varepsilon), \mathcal{T}_\varepsilon^b(\mathbf{w}_\varepsilon), \mathcal{T}_\varepsilon^b(z_\varepsilon)) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) + G(\mathcal{T}_\varepsilon^b(\varphi_\varepsilon), \mathcal{T}_\varepsilon^b(\boldsymbol{\psi}_\varepsilon), \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) (\mathcal{T}_\varepsilon^b(z_\varepsilon) - \mathcal{T}_\varepsilon^b(\theta_\varepsilon)) - \mathcal{T}_\varepsilon^b(z_\varepsilon) \mathcal{T}_\varepsilon^b(\theta_\varepsilon) ds(y) dx + \frac{\lambda}{2} \|\mathcal{T}_\varepsilon^b(\theta_\varepsilon)\|_{L^2}^2 \right] dt.$$

Substituting (102) into (103), we obtain

$$A^\varepsilon - 2D^\varepsilon + E^\varepsilon + I^\varepsilon + R^\varepsilon + G^\varepsilon \geq 0. \quad (104)$$

Now, we set for any positive scalar τ , the following test functions

$$\begin{aligned} \psi_{l,\varepsilon}(t, x) &= \psi_{l,0}(t, x, \frac{x}{\varepsilon}) + \tau \psi_l(t, x, \frac{x}{\varepsilon}), & \theta_\varepsilon(t, x) &= \theta_0(t, x, \frac{x}{\varepsilon}) + \tau \theta(t, x, \frac{x}{\varepsilon}), \\ \varphi_j^\varepsilon(t, x) &= \varphi_j^0(t, x) + \varepsilon \varphi_j^1(t, x, \frac{x}{\varepsilon}) + \tau \varphi_j(t, x), & \varphi^\varepsilon &= (\varphi_i^\varepsilon - \varphi_e^\varepsilon)|_{\Gamma_\varepsilon}. \end{aligned}$$

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 (104), showing the limit of each term separately.

$$\begin{aligned} A^0 &:= \lim_{\varepsilon \rightarrow 0} A^\varepsilon \\ &= |\Gamma| \int_0^T e^{-\lambda t} \int_\Omega I_{\text{app},\varepsilon} v dx dt + \frac{|\Gamma|}{2} \left(\|v_0\|_{L^2(\Omega)}^2 + \sum_{l=1}^k \|w_{l,0}\|_{L^2(\Omega)}^2 + \|z_0\|_{L^2(\Omega)}^2 \right). \\ D^0 &:= \lim_{\varepsilon \rightarrow 0} D^\varepsilon \\ &= \frac{|\Gamma|}{2} e^{-\lambda t} \int_\Omega \left(v(\varphi^0 + \tau \varphi) + \mathbf{w} \cdot (\boldsymbol{\psi}_0 + \tau \boldsymbol{\psi}) + z(\theta_0 + \tau \theta) \right) dx \\ &\quad + \sum_{i,e} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} M_j(\nabla u_j + \nabla_y \hat{u}_j)(\nabla(\varphi_j^0 + \tau \nabla \varphi) + \nabla_y \varphi_j^1) dy dx, \\ E^0 &:= \lim_{\varepsilon \rightarrow 0} E^\varepsilon \\ &= \frac{|\Gamma|}{2} e^{-\lambda T} \left(\|(\varphi^0 + \tau \varphi)(T)\|_{L^2(\Omega)}^2 + \sum_{l=1}^k \|(\psi_{l,0} + \tau \psi_l)(T)\|_{L^2(\Omega)}^2 + \|(\theta^0 + \tau \theta)(T)\|_{L^2(\Omega)}^2 \right) \\ &\quad + \sum_{i,e} \int_0^T e^{-\lambda t} \iint_{\Omega \times Y_j} M_j(\nabla(\varphi_j^0 + \tau \varphi_j) + \nabla_y \varphi_j^1) \cdot (\nabla(\varphi_j^0 + \tau \varphi_j) + \nabla_y \varphi_j^1) dy dx, \\ I^0 &:= \lim_{\varepsilon \rightarrow 0} I^\varepsilon \\ &= \int_0^T e^{-\lambda t} \left[\iint_{\Omega \times \Gamma} -\tilde{I}(\varphi^0 + \tau \varphi) - \left(I_{\text{ion}}(\varphi^0 + \tau \varphi, \boldsymbol{\psi}_0 + \tau \boldsymbol{\psi}, \theta_0 + \tau \theta)(v - \varphi^0 - \tau \varphi) ds(y) dx \right. \right. \\ &\quad \left. \left. - \lambda |\Gamma| \int_\Omega v(\varphi^0 + \tau \varphi) dx + \frac{\lambda |\Gamma|}{2} \|\varphi^0 + \tau \varphi\|_{L^2(\Omega)}^2 \right) \right] dt \end{aligned}$$

Similarly, the limits of R^ε and G^ε can be obtained to get from inequality (104)

$$A^0 - 2D^0 + E^0 + I^0 + R^0 + G^0 \geq 0. \quad (105)$$

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 (105)

using (102), to obtain

$$\begin{aligned} \tau \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v + \tau\varphi, \mathbf{w} + \tau\psi, z + \tau\theta) - \tilde{I} \right) \varphi + (\mathbf{R}(v + \tau\varphi, \mathbf{w} + \tau\psi) - \tilde{\mathbf{R}}) \cdot \boldsymbol{\psi} \\ + (G(v + \tau\varphi, \mathbf{w} + \tau\psi, z + \tau\theta) - \tilde{G}) \theta \, dx dy dt + \mathcal{O}(\tau^2) \geq 0 \end{aligned}$$

Dividing by τ and then letting τ tends to 0, we find that for all test functions φ , ψ and θ , there holds

$$\begin{aligned} \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v, \mathbf{w}, z) - \tilde{I} \right) \varphi + (\mathbf{R}(v, \mathbf{w}) - \tilde{\mathbf{R}}) \cdot \boldsymbol{\psi} \\ + (G(v, \mathbf{w}, z) - \tilde{G}) \theta \, dx dy dt \geq 0, \end{aligned}$$

Using $-\varphi$, $-\psi$ and $-\theta$ for φ , ψ and θ one also gets

$$\begin{aligned} \int_0^T e^{-\lambda t} \iint_{\Omega \times \Gamma} \left(I_{\text{ion}}(v, \mathbf{w}, z) - \tilde{I} \right) \varphi + (\mathbf{R}(v, \mathbf{w}) - \tilde{\mathbf{R}}) \cdot \boldsymbol{\psi} \\ + (G(v, \mathbf{w}, z) - \tilde{G}) \theta \, dx dy dt \leq 0, \end{aligned}$$

which gives the result of the proposition. \square

Collecting all the convergence results stated above, one obtains the following limiting problem:

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi \, dx \, dt + \sum_{i,e} \iiint_{\Omega_T \times Y_j} \mathbf{M}_j [\nabla u_j + \nabla_y \hat{u}_j] [\nabla \Psi_j + \theta_j \nabla_y \psi_j] \\ + |\Gamma| \iint_{\Omega_T} I_{\text{ion}}(v, \mathbf{w}, z) \Psi \, dx \, dt = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi \, dx \, dt, \end{aligned} \quad (106)$$

$$|\Gamma| \iint_{\Omega_T} \partial_t \mathbf{w} \phi \, dx \, dt - |\Gamma| \iint_{\Omega_T} \mathbf{R}(v, \mathbf{w}) \phi \, dx \, dt = 0, \quad (107)$$

and

$$|\Gamma| \iint_{\Omega_T} \partial_t z \phi \, dx \, dt - |\Gamma| \iint_{\Omega_T} G(v, \mathbf{w}, z) \phi \, dx \, dt = 0. \quad (108)$$

Finally, repeating the argument of section 6 one can easily decouple the limit equations to get the equations of the macroscopic bidomain model (as (69)):

$$\begin{aligned} |\Gamma| \iint_{\Omega_T} \partial_t v \Psi_i \, dx \, dt + \iint_{\Omega_T} \mathcal{M}_i \nabla u_i \cdot \nabla \Psi_i + |\Gamma| \iint_{\Omega_T} I_{\text{ion}}(v, \mathbf{w}, z) \Psi_i \, dx \, dt \\ = |\Gamma| \iint_{\Omega_T} I_{\text{app}} \Psi_i \, dx \, dt, \end{aligned} \quad (109)$$

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 (68).

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