Derivation of a bidomain model for bundles of myelinated axons

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Abstract

The work concerns the multiscale modeling of a nerve fascicle of myelinated axons. We present a rigorous derivation of a macroscopic bidomain model describing the behavior of the electric potential in the fascicle based on the FitzHugh-Nagumo membrane dynamics. The approach is based on the two-scale convergence machinery combined with the method of monotone operators.

Keywords: Nerve fascicle, myelinated axons, bidomain model, FitzHugh-Nagumo model, multiscale analysis, degenerate evolution equation.

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1. Introduction

Modeling the electrical stimulation of nerves requires biophysically consistent descriptions amenable also for computational purposes. A typical nerve in the peripheral nervous system contains several grouped fascicles, each of them comprising hundreds of axons \cite{1}. This complex microstructure of neural tissue presents an obvious problem for those attempting to describe its macroscopic response to electrical excitation. Specifically, one needs to know both how signals propagate along a single axon and how axons influence each other in a bundle.

Electric currents along individual axons are usually modeled via cable theory, which dates back to works of W. Thomson (Lord Kelvin). Fundamental insights into nerve cell excitability were made by A. Hodgkin and A. Huxley, who proposed a model that describes ionic mechanisms underlying the initiation and propagation of action potentials in axons \cite{2}. Later a more simple model for nonlinear dynamics in axons was introduced in \cite{3}, known as the FitzHugh–Nagumo model.

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Multiscale homogenization techniques were used in recent works [4, 5] to derive an effective cable equation describing propagation of signals in myelinated axons. Ideas of homogenization theory can also be naturally applied to account for ephaptic coupling in bundles of axons, where neighboring axons can communicate via current flow through the extracellular space. In 1978, experiments on giant squid axons were conducted [6] revealing evidence of ephaptic events and their physiological importance. Ephaptic interactions might be modelled by coupled systems of a large number of cable equations (as, e.g., in [7], [8]), but a continuous mathematical model for a fascicle of myelinated axons, to our best knowledge, has not been rigorously derived. An analogous phenomenon of coupling is observed in the electrical conductance of cardiac tissues [9], leading to the celebrated bidomain model. It was first derived by J. Neu and W. Krassowska [10]. In [11] the authors study the well-posedness of the reaction-diffusion systems modeling cardiac electric activity at the micro- and macroscopic level. They focus on the FitzHugh-Nagumo model (with recovery variable), and present a formal derivation of the effective bidomain model. The homogenization procedure is justified in [12] where Γ-convergence is used for asymptotic analysis. Homogenization techniques based on two-scale convergence and unfolding are applied in, e.g., [13], [14], [15], [16] for modeling of syncytial tissues.

The multiscale analysis of syncytial tissues includes the well-posedness of the microscopic problem, the homogenization procedure, and the well-posedness of the effective bidomain model. The latter question is interesting by itself, with solvability proven using different approaches depending on the nonlinearity. The solvability for a bidomain model in [11] is based on a reformulation as a Cauchy problem for a variational evolution inequality in a properly chosen Sobolev space. This approach applies to the case of the FitzHugh-Nagumo equations. In [17] existence and uniqueness are given for solutions of a wide class of models, including the classical Hodgkin-Huxley model, the first membrane model for ionic currents in an axon, and the Phase-I Luo-Rudy (LR1) model. In [18] the authors reformulate the coupled parabolic and elliptic PDEs into a single parabolic PDE by the introduction of a bidomain operator, which is a non-differential and non-local operator. This approach applies to fairly general ionic models, such as the Aliev-Panfilov and MacCulloch models.

The asymptotic analysis of a nerve fascicle with a large number of axons also leads to a bidomain model. In [19] a linear model is considered without recovery variables. Therein, it is hypothesized that the homogenization procedure in [12] leading to a macroscopic bidomain model for syncytical tissues can also be carried out for a fascicle of unmyelinated axons. We extend this result to a nonlinear case and rigorously derive a bidomain model for a fascicle of myelinated axons. In particular, we consider the propagation of signals in a fascicle formed by a large number of axons. The microstructure of the fascicle is depicted as a set of closely packed thin cylinders—axons—with myelin sheaths arranged periodically in the surrounding extracellular matrix. The characteristic microscale of the structure is given by a small parameter \( \varepsilon > 0 \). Distances between neighboring axons, their diameters and the spacing of unmyelinated
parts of the axon’s membrane—Ranvier nodes—are assumed to be of order $\varepsilon$.
By means of two-scale analysis we derive a bidomain model that describes the
asymptotic behavior of the transmembrane potential on Ranvier nodes when $\varepsilon$
is sufficiently small. We adopt the FitzHugh-Nagumo dynamics on the unmyelinated
membrane. Main technical difficulties come from the nonlinear dynamics
and the lack of a priori estimates ensuring strong convergence of the membrane
potential on the Ranvier nodes. This lack of compactness is caused by the fact that the axons form a disconnected microstructure inside the fascicle,
which stands in the contrast with connected microstructure of syncytial tissues.
In order to derive the homogenized problem we transform problem to a form
allowing us to combine two-scale convergence machinery with the method of
monotone operators. Well-posedness of the micro- and macroscopic problems
are also shown via reduction to parabolic equations with monotone operators.

2. Microscopic model

2.1. Problem setup

A nerve fascicle is modeled by the cylinder $\Omega := (0, L) \times \varOmega \subset \mathbb{R}^3$ with length
$L > 0$ and cross section $\varOmega \subset \mathbb{R}^2$, being a bounded domain in $\mathbb{R}^2$ with a Lipschitz
boundary $\partial \varOmega$ (see Figure 1). The lateral boundary of the cylinder is denoted
by $\Sigma := [0, L] \times \partial \varOmega$, with bases $S_0 := \{0\} \times \varOmega$, $S_L := \{L\} \times \varOmega$. The bulk of the
cylinder consists of an intracellular part formed by thin cylinders (axons), an
extracellular part, and myelin sheaths. To describe the microstructure of the
fascicle, we introduce a periodicity cell $Y := [-\frac{1}{2}, \frac{1}{2}) \times [-R_0, R_0]^2$, consisting of three disjoint Lipschitz domains: (i) an intracellular part $Y_i := [-\frac{1}{2}, \frac{1}{2}) \times D_0$,
where $D_0$ is the disk with radius $0 < r_0 < \frac{1}{2}$; (ii) a myelin sheath $Y_m$; (iii) an extracellular domain $Y_e$. The real positive radii satisfy $r_0 < R_0$. We denote
by $\Gamma_{mi} := Y_i \cap Y_m$ the interface between $Y_i$ and $Y_m$. The interface between the extracellular domain $Y_e$ and a myelin sheath $Y_m$ is $\Gamma_{me} := Y_e \cap Y_m$. The unmyelinated part of the boundary of $Y_i$ (the Ranvier node) will be denoted by
$\Gamma = Y_i \cap Y_e$ (see Figure 1). We will assume that $\Gamma$ does not degenerate, and, for simplicity, that $\Gamma$ is connected.

The periodicity cell is translated by vertices of the lattice $\mathbb{Z} \times (2R_0\mathbb{Z})^2$ to form a $Y$-periodic structure, and then scaled by a small parameter $\varepsilon > 0$. We take only those axons that are entirely contained in $\Omega$. As a result, the domain is the union of three disjoint parts $\Omega^i_\varepsilon, \Omega^e_\varepsilon, \Omega^m_\varepsilon$, and their boundaries (see Figure 1). The unmyelinated part of the boundary of $\Omega^i_\varepsilon$ is denoted by $\Gamma_\varepsilon$. The boundary of the myelin is denoted by $\Gamma^m_\varepsilon$.

Let $u_\varepsilon$ denotes the electric potential $u_\varepsilon = u^l_\varepsilon$ in $\Omega^l_\varepsilon$, $l = i, e$. We assume that
$u_\varepsilon$ satisfies homogeneous Neumann boundary conditions on the boundary of the
myelin sheath $\Gamma^m_\varepsilon$, i.e the myelin sheath is assumed to be a perfect insulator
(see [4] for other insulation assumptions). The transmembrane potential $v_\varepsilon = [u_\varepsilon] = u^l_\varepsilon - u^e_\varepsilon$ is the potential jump across the Ranvier nodes $\Gamma_\varepsilon$. We assume
that the conductivity is a piecewise constant function:

\[
 a_\varepsilon = \begin{cases} 
 a_e & \text{in } \Omega^i_\varepsilon, \\
 a_i & \text{in } \Omega^o_\varepsilon.
\end{cases}
\]

On \( \Gamma_\varepsilon \) we further assume current continuity, and FitzHugh-Nagumo [3, 20] dynamics for the transmembrane potential. Namely, the ionic current is described as

\[
 I_{\text{ion}}(v_\varepsilon, g_\varepsilon) = \frac{v_\varepsilon^3}{3} - v_\varepsilon - g_\varepsilon,
\]

where \( g_\varepsilon \) is the recovery variable whose evolution is governed by the ordinary differential equation

\[
 \partial_t g_\varepsilon = \theta v_\varepsilon + a - b g_\varepsilon
\]

with constant coefficients \( \theta, a, b > 0 \). Thus, the electric activity in the bundle \( \Omega \) is described by the following system of equations for the unknowns \( v_\varepsilon \) and \( g_\varepsilon \):

\[
 - \text{div} (a_\varepsilon \nabla u_\varepsilon) = 0, \quad (t, x) \in (0, T) \times (\Omega^i_\varepsilon \cup \Omega^o_\varepsilon),
\]

\[
 a_\varepsilon \nabla u_\varepsilon \cdot \nu = a_i \nabla u^i_\varepsilon \cdot \nu, \quad (t, x) \in (0, T) \times \Gamma_\varepsilon,
\]

\[
 \varepsilon (c_m \partial_t u_\varepsilon) + I_{\text{ion}}(u_\varepsilon, g_\varepsilon) = -a_i \nabla u^i_\varepsilon \cdot \nu, \quad (t, x) \in (0, T) \times \Gamma_\varepsilon,
\]

\[
 \partial_t g_\varepsilon = \theta u_\varepsilon + a - b g_\varepsilon, \quad (t, x) \in (0, T) \times \Gamma_\varepsilon,
\]

\[
 u_\varepsilon = 0, \quad (t, x) \in (0, T) \times (S_0 \cup S_L),
\]

\[
 a_\varepsilon \nabla u_\varepsilon \cdot \nu = J^e_\varepsilon(t, x), \quad (t, x) \in (0, T) \times \Sigma,
\]

\[
 \nabla u_\varepsilon \cdot \nu = 0, \quad (t, x) \in (0, T) \times \Gamma^m_\varepsilon,
\]

\[
 [u_\varepsilon](0, x) = V^0_\varepsilon(x), \quad g_\varepsilon(0, x) = G^0_\varepsilon(x), \quad x \in \Gamma_\varepsilon,
\]

where \( \nu \) denotes the unit normal on \( \Gamma_\varepsilon \), \( \Gamma^m_\varepsilon \), and \( \Sigma \), exterior to \( \Omega^i_\varepsilon \), \( \Omega^m_\varepsilon \), and \( \Omega \), respectively. The function \( J^e_\varepsilon(t, x) \) models an external boundary excitation of the nerve fascicle.

We study the asymptotic behavior of \( u_\varepsilon \), as \( \varepsilon \to 0 \), and derive a macroscopic model describing the potential \( u_\varepsilon \) in the fascicle, under the following conditions:
(H1) The initial data is such that $\|V_0^\varepsilon\|_{L^4(\Gamma, \varepsilon)} \leq C$. Moreover, we assume that $V_0^\varepsilon = V_l^\varepsilon - V_e^\varepsilon$, where $V_l^\varepsilon$, $l = i,e$, can be extended to the whole $\Omega$ such that, keeping the same notation for the extension, $\|V_l^\varepsilon\|_{H^1(\Omega)} \leq C$ and $V_l^\varepsilon = 0$ on $S_0 \cup S_L$. We also assume that there exist weak limits of $V_l^\varepsilon \rightharpoonup V^l$ in $H^1(\Omega)$, $l = i,e$.

(H2) There exists $G^0 \in L^2(\Omega)$, such that

- for any $\phi \in C(\overline{\Omega})$, it holds that
  $$\lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} G^0_\varepsilon(x) \phi(x) \, d\sigma = \frac{|\Gamma|}{|Y|} \int_{\Omega} G^0(x) \phi(x) \, dx;$$

- $\varepsilon \int_{\Gamma_\varepsilon} |G^0_\varepsilon|^2 \, d\sigma \to \frac{|\Gamma|}{|Y|} \int_{\Omega} |G^0|^2 \, dx$, $\varepsilon \to 0$.

(H3) The external excitation $J^\varepsilon \in L^2((0,T) \times \Sigma)$ converges weakly to $J^e(t,x)$, as $\varepsilon \to 0$, and

$$\int_{0}^{t} \int_{\Sigma} |\partial_\tau J^\varepsilon|^2 \, d\sigma d\tau \leq C.$$

Remark 1. Hypothesis (H2) actually assumes strong two-scale convergence (cf. Proposition 2.5 in [21]). Note that the hypothesis (H2) is satisfied if $G^0_\varepsilon$ is sufficiently regular, e.g. continuous, and independently of $\varepsilon$.

2.2. Main result

The main result of the paper is given in short form by Theorem 2.1, showing that the asymptotic behavior of solutions of the boundary value problem (1) is described by the following effective bidomain model in $\Omega$:

$$c_m \partial_t v_0 + I_{ion}(v_0, g_0) = \alpha_{v_0}^n \partial_{x_1}^2 u_0^i, \quad (t,x) \in (0,T) \times \Omega,$$

$$c_m \partial_t v_0 + I_{ion}(v_0, g_0) = -\text{div} \left( \alpha_{v_0}^n \nabla u_0^i \right), \quad (t,x) \in (0,T) \times \Omega,$$

$$\partial_\tau g_0 = \theta v_0 + a - b \, g_0, \quad (t,x) \in (0,T) \times \Omega,$$

$$u_0^i \cdot \nu = J^e, \quad (t,x) \in (0,T) \times (S_0 \cup S_L),$$

$$\alpha_{v_0}^e \nabla u_0^e \cdot \nu = J^e, \quad (t,x) \in (0,T) \times \Sigma,$$

$$v_0(0,x) = V^i(x) - V^e(x), \quad g_0(0,x) = G^0(x), \quad x \in \Omega,$$

Throughout, $C$ denotes a generic constant independent of $\varepsilon$, whose value may be different from line to line.
where \( v_0 = u_0^i - u_0^e \). The effective scalar coefficient \( a_i^{\text{eff}} \) is

\[
a_i^{\text{eff}} := \frac{|Y_i|}{|\Gamma|} a_i.
\]

The effective matrix \( a_e^{\text{eff}} \in \mathbb{R}^{3 \times 3} \) is given by

\[
(a_e^{\text{eff}})_{kl} := \frac{1}{|\Gamma|} \int_{Y_e} a_e (\partial_l N_k^e(y) + \delta_{kl}) \, dy, \quad k, l = 1, 2, 3,
\]

with the functions \( N_k^e, k = 1, 2, 3 \), solving the following auxiliary cell problems in \( Y_e \)

\[
-\Delta N_k^e = 0, \quad y \in Y_e, \\
\nabla N_k^e \cdot \nu = -\nu_k, \quad y \in \Gamma \cup \Gamma_m, \\
N_k^e(y) \text{ is } Y \text{-periodic.}
\]

**Theorem 2.1.** Under the hypothesis (H1)–(H3), the solutions \( v_\varepsilon = [u_\varepsilon^i, g_\varepsilon] \) of the microscopic problem \([1]\) converge to the solution \( v_0 = u_0^i - u_0^e, g_0 \) of the macroscopic one \([2]\) in the following sense:

(i) For any \( \Phi(t, x) \in C([0, T] \times \Omega) \), it holds that

\[
\lim_{\varepsilon \to 0} \varepsilon \int_0^T \int_{\Gamma_\varepsilon} v_\varepsilon(t, x) \Phi(t, x) \, d\sigma_x \, dt = \frac{|\Gamma|}{|Y|} \int_0^T \int_{\Omega} v_0(t, x) \Phi(t, x) \, dx \, dt.
\]

(ii) For any \( t \in [0, T] \), one has

\[
\lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} |v_\varepsilon|^2 \, d\sigma = \frac{|\Gamma|}{|Y|} \int_{\Omega} |v_0|^2 \, dx.
\]

(iii) For any \( \Phi(t, x) \in C([0, T] \times \Omega) \),

\[
\lim_{\varepsilon \to 0} \varepsilon \int_0^T \int_{\Gamma_\varepsilon} g_\varepsilon(t, x) \Phi(t, x) \, d\sigma_x \, dt = \frac{|\Gamma|}{|Y|} \int_0^T \int_{\Omega} g_0(t, x) \Phi(t, x) \, dx \, dt.
\]

(iv) For any \( t \in [0, T] \), \( \varepsilon \int_{\Gamma_\varepsilon} |g_\varepsilon|^2 \, d\sigma \to \frac{|\Gamma|}{|Y|} \int_{\Omega} |g_0|^2 \, dx \), as \( \varepsilon \to 0 \).

(v) \( \int_0^T \int_{\Omega_\varepsilon} |u_\varepsilon^i - u_0^i|^2 \, dx \, dt \to 0 \), as \( \varepsilon \to 0 \).

**Remark 2.** If \( v_0 \) is continuous, the convergence (i), (ii) implies strong convergence of \( v_\varepsilon \). Namely, for any \( t \in [0, T] \), one obtains

\[
\lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} |v_\varepsilon - v_0|^2 \, d\sigma = 0.
\]
In general, approximating \( v_0 \) in \( L^2(\Omega) \) by \( v_{0\delta} \in C(\Omega) \), we have

\[
\limsup_{\delta \to 0} \limsup_{\varepsilon \to 0} \int_{\Gamma_\varepsilon} |v_\varepsilon - v_{0\delta}|^2 \, d\sigma = 0.
\]

**Remark 3.** The result can be generalized to the case of a varying cross section, as in [5]. In such case, the solution \( N_i^j \) of the cell problem (26) is no longer constant, and the corresponding effective coefficient is given by

\[
a_i^{\text{eff}} = \frac{1}{|\Gamma|} \int_{Y_i} a_i(\partial_1 N^j_1 + 1) \, dy.
\]

**Remark 4.** Hypothesis (H2) can be generalized to the case of an oscillating initial function \( G_0^\varepsilon \). Namely, assume that there exists \( G_0(x,y) \in L^2(\Omega \times \Gamma) \), \( Y \)-periodic in \( y \) such that

- \( \lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} |G_0^\varepsilon| \phi(x,z) \, d\sigma = \frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |G_0^\varepsilon(x,y)| \phi(x,y) \, d\sigma_y \, dx; \)

- \( \varepsilon \int_{\Gamma_\varepsilon} |G_0^\varepsilon|^2 \, d\sigma \to \frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |G_0^\varepsilon(x,y)|^2 \, d\sigma_y \, dx, \varepsilon \to 0. \)

Then, the two-scale limit \( \tilde{g}_0(t,x,y) \) of \( g_\varepsilon \) does depend on the fast variable \( y \), and denoting \( g_0(t,x) = \frac{1}{|\Gamma|} \int_{\Gamma} \tilde{g}_0(t,x,y) \, d\sigma_y \), the effective problem reads

\[
\begin{align*}
    c_m \partial_t v_0 + I_{\text{ion}}(v_0, g_0) &= a_i^{\text{eff}} \partial^2_{x_1} u_0^i, & (t, x) &\in (0, T) \times \Omega, \\
    c_m \partial_t v_0 + I_{\text{ion}}(v_0, g_0) &= -\text{div} \left( a_i^{\text{eff}} \nabla u_0^i \right), & (t, x) &\in (0, T) \times \Omega, \\
    \partial_t \tilde{g}_0 &= \theta v_0 + a - b \tilde{g}_0, & (t, x, y) &\in (0, T) \times \Omega \times Y, \\
    u_0^i(x, t) &= 0, & (t, x) &\in (0, T) \times (S_0 \cup S_L), \\
    a_i^{\text{eff}} \nabla u_0^i \cdot \nu &= J^c, & (t, x) &\in (0, T) \times \Sigma, \\
    v_0(0, x) &= V^i(x) - V^c(x), & \tilde{g}_0(0, x) &= G_0(x,y) & x \in \Omega, y \in Y.
\end{align*}
\]

Thanks to the linearity of the equation \( \partial_t \tilde{g}_0 = \theta v_0 + a - b \tilde{g}_0 \), averaging in \( y \), yields (2) with the initial condition \( g_0(0, x) = \frac{1}{|\Gamma|} \int_{\Gamma} G_0(x,y) \, d\sigma_y. \)

### 2.3. Well-posedness

In order to show the well-posedness of the microscopic problem (1), we write it as a Cauchy problem for an abstract parabolic equation.
We multiply (1) by a smooth function \( \phi = \begin{cases} \phi^i & \text{in } \Omega^i, \\ \phi^e & \text{in } \Omega^e \end{cases} \), and integrate by parts:

\[
\varepsilon \int_{\Gamma^c} c_m \partial_t v_\varepsilon[\phi] d\sigma + \int_{\Omega^i \cup \Omega^e} a_\varepsilon \nabla u_\varepsilon \cdot \nabla \phi \, dx + \varepsilon \int_{\Gamma^c} I_{\text{ion}}(v_\varepsilon, g_\varepsilon)[\phi] d\sigma = \int_{\Sigma} J^\varepsilon \phi \, d\sigma.
\]

Let us introduce an auxiliary function \( q_\varepsilon \) solving the following problem:

\[
- \text{div} \left( a_\varepsilon \nabla q_\varepsilon \right) = 0, \quad x \in \Omega^i \cup \Omega^e \cup \Gamma^c, \\
\nabla q_\varepsilon \cdot \nu = 0, \quad x \in \Gamma_{m,\varepsilon}, \\
a_\varepsilon \nabla q_\varepsilon \cdot \nu = J^\varepsilon(t, x), \quad x \in \Sigma, \\
q_\varepsilon = 0, \quad x \in (S_0 \cup S_L). \tag{5}
\]

Since the jump of \( q_\varepsilon \) through the Ranvier nodes \( \Gamma^c \) is zero, the change of unknown

\[
\tilde{u}_\varepsilon = u_\varepsilon - q_\varepsilon
\]

allows us to transfer the external excitation \( J^\varepsilon \) from the lateral boundary \( \Sigma \) to the membrane \( \Gamma^c \). Namely, we get the following weak formulation for the new unknown function \( \tilde{u}_\varepsilon \):

\[
\varepsilon \int_{\Gamma^c} c_m \partial_t v_\varepsilon[\phi] d\sigma + \int_{\Omega^i \cup \Omega^e} a_\varepsilon \nabla \tilde{u}_\varepsilon \cdot \nabla \phi \, dx + \varepsilon \int_{\Gamma^c} I_{\text{ion}}(v_\varepsilon, g_\varepsilon)[\phi] d\sigma \\
+ \int_{\Gamma^c} (a_\varepsilon \nabla q_\varepsilon \cdot \nu)[\phi] d\sigma = 0.
\]

Let us define the subspace

\[
H^1_{S_0 \cup S_L}(\Omega^i \cup \Omega^e) := \left\{ \phi \in H^1_{S_0 \cup S_L}(\Omega^i \cup \Omega^e) : \phi|_{S_0 \cup S_L} = 0 \right\},
\]

and introduce the operator \( A_\varepsilon : D(A_\varepsilon) \subset H^{1/2}(\Gamma^c) \to H^{-1/2}(\Gamma^c) \) as follows

\[
(A_\varepsilon v_\varepsilon, [\phi])_{L^2(\Gamma^c)} := \int_{\Omega^i \cup \Omega^e} a_\varepsilon \nabla \tilde{u}_\varepsilon \cdot \nabla \phi \, dx, \quad \forall \phi \in H^1_{S_0 \cup S_L}(\Omega^i \cup \Omega^e), \tag{6}
\]

where \( \tilde{u}_\varepsilon \in H^1(\Omega^i \cup \Omega^e) \), for a given jump \([\tilde{u}_\varepsilon] = v_\varepsilon\), solves the following problem:

\[
- \text{div} \left( a_\varepsilon \nabla \tilde{u}_\varepsilon \right) = 0, \quad x \in \Omega^i \cup \Omega^e, \\
a_\varepsilon \nabla \tilde{u}_\varepsilon \cdot \nu = a_i \nabla \tilde{u}_e \cdot \nu, \quad x \in \Gamma^c, \\
\tilde{u}_i^e - \tilde{u}_e^i = v_\varepsilon, \quad x \in \Gamma^c, \\
a_\varepsilon \nabla \tilde{u}_e \cdot \nu = 0, \quad x \in \Gamma_{m,\varepsilon}, \\
a_\varepsilon \nabla \tilde{u}_e \cdot \nu = 0, \quad x \in \Sigma. \tag{7}
\]

8
\( \vec{u}_\varepsilon = 0, \quad x \in (S_0 \cup S_L). \)

Thus, the problem can be rewritten in the following compact form:

\[
\varepsilon c_m \partial_t v_\varepsilon + A_\varepsilon v_\varepsilon + \varepsilon I_{\text{ion}}(v_\varepsilon, g_\varepsilon) = -a_i \nabla q_\varepsilon \cdot \nu, \quad (8)
\]

\[
\partial_t g_\varepsilon + b g_\varepsilon - \theta v_\varepsilon = a
\]

on \( \Gamma_\varepsilon. \) In order to reduce the problem to a monotone one, we perform the following change of unknowns:

\[
W_\varepsilon = \begin{pmatrix} w_\varepsilon \\ h_\varepsilon \end{pmatrix} = e^{-\lambda t} \begin{pmatrix} v_\varepsilon \\ g_\varepsilon \end{pmatrix}, \quad W_\varepsilon^0 = \begin{pmatrix} V_\varepsilon^0 \\ G_\varepsilon^0 \end{pmatrix}. \quad (9)
\]

with \( \lambda \) real positive. Substituting (9) into (8) yields

\[
\varepsilon \partial_t \begin{pmatrix} w_\varepsilon \\ h_\varepsilon \end{pmatrix} + \begin{pmatrix} \frac{1}{c_m} A_\varepsilon w_\varepsilon + \frac{\varepsilon}{c_m} \left( \frac{e^{2\lambda t}}{3} w_\varepsilon^3 - w_\varepsilon - h_\varepsilon \right) + \varepsilon \lambda w_\varepsilon \\ \varepsilon (b + \lambda) h_\varepsilon - \varepsilon \theta w_\varepsilon \end{pmatrix} = e^{-\lambda t} \begin{pmatrix} -a_i \nabla q_\varepsilon \cdot \nu \\ \varepsilon a \end{pmatrix}, \quad (10)
\]

which can be further rewritten as follows:

\[
\varepsilon \partial_t W_\varepsilon + A_\varepsilon(t, W_\varepsilon) = F_\varepsilon(t), \quad (t, x) \in (0, T) \times \Gamma_\varepsilon,
\]

\[
W_\varepsilon(0, x) = W_\varepsilon^0(x), \quad x \in \Gamma_\varepsilon.
\]

\[
A_\varepsilon(t, W_\varepsilon) := B_\varepsilon^{(1)}(t, W_\varepsilon) + B_\varepsilon^{(2)}(t, W_\varepsilon), \quad (11)
\]

\[
B_\varepsilon^{(1)}(t, W_\varepsilon) := \begin{pmatrix} \frac{1}{c_m} A_\varepsilon w_\varepsilon + \frac{\varepsilon}{c_m} \left( \lambda - \frac{1}{c_m} \right) w_\varepsilon - \frac{\varepsilon}{c_m} h_\varepsilon \\ \varepsilon (b + \lambda) h_\varepsilon - \varepsilon \theta w_\varepsilon \end{pmatrix}, \quad (12)
\]

\[
B_\varepsilon^{(2)}(t, W_\varepsilon) := \begin{pmatrix} \frac{\varepsilon e^{2\lambda t}}{3c_m} w_\varepsilon^3 \\ 0 \end{pmatrix}, \quad F_\varepsilon(t) := e^{-\lambda t} \begin{pmatrix} -a_i \nabla q_\varepsilon \cdot \nu \\ \varepsilon a \end{pmatrix}. \quad (13)
\]

Here the operator \( A_\varepsilon \) is defined in [3].

The existence of a unique solution to problem (10) follows from Theorem 1.4 in [22] and Remark 1.8 in Chapter 2 (see also Theorem 4.1 in [23]). For the reader’s convenience, we formulate the corresponding result below.

**Lemma 2.2.** Let \( V_i, \ i = 1, \ldots, m, \) be reflexive Banach spaces, and \( H \) be a real Hilbert space such that \( V_i \subset H \subset V'_i. \) Let \( A(t) = \sum_{i=1}^m A_i(t), \) and let
\{A_i(t): t \in [0, T]\}, i = 1, \ldots, m, be a family of nonlinear, monotone, and demi-continuous operators from \(V_i\) to \(V_i'\) that satisfy the following conditions:

(i) The function \(t \mapsto A_i(t)u(t) \in V_i'\) is measurable for every measurable function \(u : [0, T] \to V\).

(ii) There exists a seminorm \([u]\) on \(V_i\) such that, for some constants \(\alpha_1 > 0\) and \(\alpha_2 > 0\), we have that

\[ [u] + \alpha_1\|u\|_H \geq \alpha_2\|u\|_{V_i}, \]

and for some \(\varepsilon > 0\) and \(p_i > 1\),

\[ (A_i(t)u, u) \geq \varepsilon [u]^{p_i}, \quad u \in V_i, \; t \in [0, T]. \]

(iii) For some \(C\) and the same \(p_i > 1\) as in (ii),

\[ \|A_i(t)u\|_{V_i'} \leq C(1 + \|u\|_{V_i}^{p_i-1}), \quad u \in V_i, \; t \in [0, T]. \]

Then, for every \(u_0 \in H\) and \(f \in \sum_{i=1}^m L^{q_i}(0, T; V_i')\), \(1/p_i + 1/q_i = 1\), there is a unique absolutely continuous function \(u \in \bigcap_{i=1}^m W^{1,q_i}(0, T; V_i')\) that satisfies

\[
\begin{align*}
&\frac{du}{dt}(t) + A(t)u(t) = f(t), \quad \text{a.e. } t \in (0, T), \\
&u(0) = u_0.
\end{align*}
\]

In order to apply Lemma 2.2 we introduce the necessary functional spaces:

\[
H = L^2(\Gamma_e) \times L^2(\Gamma_e),
\]

\[
\widetilde{H}^{1/2}(\Gamma_e) = \left\{ v = (u^i - u^e)^t \right|_{\Gamma_e} : u^i \in H^1(\Omega_i^l), \; u^f = 0 \text{ on } S_0 \cap S_L, \; l = i, e \right\},
\]

\[
V_1 = \widetilde{H}^{1/2}(\Gamma_e) \times L^2(\Gamma_e), \quad V'_1 = H^{-1/2}(\Gamma_e) \times L^2(\Gamma_e),
\]

\[
V_2 = L^4(\Gamma_e) \times L^2(\Gamma_e), \quad V'_2 = L^{4/3}(\Gamma_e) \times L^2(\Gamma_e).\]

As the operator \(A_1(t, \cdot) : V_1 \to V'_1\) we take \(B^{(1)}_\varepsilon(t, \cdot)\) given by (12); as the operator \(A_2(t, \cdot) : V_2 \to V'_2\) we take \(B^{(2)}_\varepsilon(t, \cdot)\) given by (13). Let us check that the operator \(A_\varepsilon(t, \cdot) = B^{(1)}_\varepsilon + B^{(2)}_\varepsilon\) satisfies the assumptions of Lemma 2.2. The right-hand side \(F_\varepsilon\) satisfies clearly the assumptions of Lemma 2.2.

**Lemma 2.3.** For every \(t \in [0, T]\), the linear operator \(B^{(1)}_\varepsilon(t, \cdot) : V_1 \to V'_1\) has the following properties:

(i) Monotonicity:

\[
(B^{(1)}_\varepsilon(t, W_1) - B^{(1)}_\varepsilon(t, W_2), W_1 - W_2) \geq 0, \quad \forall \; W_1, W_2 \in V_1.
\]
(ii) Coercivity:

\[ (B_\varepsilon^{(1)}(t, W), W) \geq C_1 \|W\|_{V_1}^2, \quad \forall \ W \in V_1. \]

(iii) Boundedness:

\[ \|B_\varepsilon^{(1)}(t, W)\|_{V_1'} \leq C_2 \|W\|_{V_1}, \quad \forall \ W \in V_1. \]

Proof. (i) The monotonicity of the operator \( B_\varepsilon^{(1)} \) follows from its linearity and coercivity properties (as shown below).

(ii) By (12), for any \( W_\varepsilon \in \dot{H}^{1/2}(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon) \), we have

\[
(B_\varepsilon^{(1)}(t, W_\varepsilon), W_\varepsilon) = \frac{1}{c_m} \int_{\Omega^\varepsilon \cup \Omega_\varepsilon^c} a_t |\nabla \tilde{w}_\varepsilon|^2 \, dx + \varepsilon \left( \frac{1}{c_m} \right) \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 \, d\sigma 
- \varepsilon \left( \frac{\theta + \frac{1}{c_m}}{c_m} \right) \int_{\Gamma_\varepsilon} h_\varepsilon w_\varepsilon \, d\sigma + \varepsilon(b + \lambda) \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 \, d\sigma.
\]

Here \( \tilde{w}_\varepsilon = e^{-\lambda t} u_\varepsilon \) solves (7) with the jump on \( \Gamma_\varepsilon \) that equals to \( e^{-\lambda t} v_\varepsilon \). Using the trace inequality and choosing \( \lambda \) sufficiently large and independent of \( \varepsilon \), we obtain

\[
(B_\varepsilon^{(1)}(t, W_\varepsilon), W_\varepsilon) \geq C_1^\varepsilon \|w_\varepsilon\|_{\dot{H}^{1/2}(\Gamma_\varepsilon)}^2 + C_2^\varepsilon \|h_\varepsilon\|_{L^2(\Gamma_\varepsilon)}^2 = C^\varepsilon \|W_\varepsilon\|_{V_1}^2.
\]

Here \( C_1^\varepsilon, C_2^\varepsilon, \) and \( C^\varepsilon \) are positive constants.

(iii) Let us estimate the norm of \( B_\varepsilon^{(1)}(t, W) \). For any \( W_\varepsilon \in V_1 \) and a test function \( \Phi = (|\varphi|, \psi)^T \in V_1 \), by (11), we have

\[
(B_\varepsilon^{(1)}(t, W_\varepsilon), \Phi)_{L^2(\Gamma_\varepsilon)^2} = \frac{1}{c_m} \int_{\Omega^\varepsilon \cup \Omega_\varepsilon^c} a_t \nabla \tilde{w}_\varepsilon \cdot \nabla \varphi \, dx + \varepsilon \left( \frac{1}{c_m} \right) \int_{\Gamma_\varepsilon} |w_\varepsilon| |\varphi| \, d\sigma 
- \varepsilon \left( \frac{\theta + \frac{1}{c_m}}{c_m} \right) \int_{\Gamma_\varepsilon} h_\varepsilon |\varphi| \, d\sigma + \varepsilon(b + \lambda) \int_{\Gamma_\varepsilon} h_\varepsilon \psi |\varphi| \, d\sigma - \varepsilon \theta \int_{\Gamma_\varepsilon} w_\varepsilon \psi |\varphi| \, d\sigma.
\]

Here \( \varphi \) solves a stationary problem (7) with a given jump \( |\varphi| \) on \( \Gamma_\varepsilon \). Clearly, \( \|\nabla \tilde{w}_\varepsilon\|_{L^2(\Omega^\varepsilon \cup \Omega_\varepsilon^c)} \leq C \|w_\varepsilon\|_{\dot{H}^{1/2}(\Gamma_\varepsilon)} \). The test function \( \varphi \) is estimated in a standard way in terms of \( |||\varphi|||_{\dot{H}^{1/2}(\Gamma_\varepsilon)} \). Then, by the Cauchy-Schwartz inequality, one retrieves

\[
(B_\varepsilon^{(1)}(t, W_\varepsilon), \Phi)_{L^2(\Gamma_\varepsilon)^2} \leq C_1 |||w_\varepsilon|||_{\dot{H}^{1/2}(\Gamma_\varepsilon)} |||\varphi|||_{\dot{H}^{1/2}(\Gamma_\varepsilon)} + C_2 (|||w_\varepsilon|||_{\dot{H}^{1/2}(\Gamma_\varepsilon)} + \|h_\varepsilon\|_{\dot{H}^{1/2}(\Gamma_\varepsilon)}) \|[\Phi]\|_{V_1'},
\]

which proves the estimate from above for \( \|B_\varepsilon^{(1)}(t, W)\|_{V_1'} \). \qed
Lemma 2.4. For every $t \in [0, T]$, the operator $B^{(2)}_\varepsilon(t, \cdot) : V_2 \to V'_2$ has the following properties:

(i) Monotonicity:

$$(B^{(2)}_\varepsilon(t, W_1) - B^{(2)}_\varepsilon(t, W_2), W_1 - W_2) \geq 0, \quad \forall W_1, W_2 \in V_2.$$ 

(ii) Coercivity: $\| \cdot \|_{L^4(\Gamma_\varepsilon)}$ defines a seminorm on $V_2$ such that, for some constants $\alpha_1 > 0$ and $\alpha_2 > 0$, we have

$$\| W \|_{L^4(\Gamma_\varepsilon)} + \alpha_1 \| W \|_H \geq \alpha_2 \| W \|_{V_2},$$

and

$$(B^{(2)}_\varepsilon(t, W), W) \geq C_1 \| W \|_{V_2}^4, \quad \forall W \in V_1.$$ 

(iii) Boundedness:

$$\| B^{(2)}_\varepsilon(t, W) \|_{V'_2} \leq C_2 \| W \|_{L^4(\Gamma_\varepsilon)}^3, \quad \forall W \in V_2.$$ 

Proof. (i) The monotonicity of $B^{(2)}_\varepsilon$ follows from the monotonicity of the cubic function $f(u) = u^3$.

(ii) By definition (13), it holds that

$$(B^{(2)}_\varepsilon(t, W_\varepsilon), W_\varepsilon) = \frac{\varepsilon e^{2\lambda t}}{3c_m} \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 \, d\sigma,$$

which proves (ii).

(iii) The boundedness follows from (13):

$$\| B^{(2)}_\varepsilon(t, W_\varepsilon) \|_{V'_2} = \varepsilon \left[ \int_{\Gamma_\varepsilon} \left( \frac{e^{2\lambda t}}{3c_m} (w_\varepsilon)^3 \right)^{\frac{4}{3}} \, d\sigma \right]^{\frac{3}{4}} = \frac{\varepsilon e^{2\lambda t}}{3c_m} \| w_\varepsilon \|_{L^4(\Gamma_\varepsilon)}^3 \leq C^\varepsilon \| W_\varepsilon \|_{V_2}^3,$$

where $C^\varepsilon$ is a positive constant. \hfill \Box

2.4. A priori estimates

The next lemma provides the estimates for $(z_\varepsilon, h_\varepsilon) = e^{-\lambda t}(u_\varepsilon, g_\varepsilon)$, where $[z_\varepsilon] = w_\varepsilon$, at time $t = 0$. 

Lemma 2.5. Under hypotheses (H1)–(H3), at time \( t = 0 \) the following estimates hold

\[
\int_{\Omega_i \cup \Omega_e^i} a \varepsilon |\nabla z \varepsilon|^2 \, dx \bigg|_{t=0} + \int_{\Sigma} |z \varepsilon|^2 \, d\sigma \bigg|_{t=0} \leq C. \tag{14}
\]

**Proof.** One can see that the operator \( A \varepsilon \) given by (11) can be defined by means of the minimization problem

\[
(A \varepsilon w \varepsilon, w \varepsilon) = \min_{[\phi \varepsilon] = w \varepsilon} \int_{\Omega_i \cup \Omega_e^i} a \varepsilon |\nabla \phi \varepsilon|^2 \, dx,
\]

where the minimum is taken over the functions \( \phi \varepsilon \in H^1(\Omega_i \cup \Omega_e^i) \) with the given jump \( [\phi \varepsilon] = w \varepsilon \) on \( \Gamma \varepsilon \). Since \( V_0^\varepsilon = V_i^\varepsilon - V_e^\varepsilon \) on \( \Gamma \varepsilon \), by (H1) we have that

\[
\int_{\Omega_i \cup \Omega_e^i} a \varepsilon |\nabla z \varepsilon|^2 \, dx \bigg|_{t=0} = (A \varepsilon w \varepsilon, w \varepsilon) \bigg|_{t=0} \leq \int_{\Omega_i^t} a \varepsilon |\nabla V_i^\varepsilon|^2 \, dx + \int_{\Omega_e^t} a \varepsilon |\nabla V_e^\varepsilon|^2 \, dx \leq C.
\]

The last estimate together with the trace inequality and (17) completes the proof. \( \square \)

Now we prove the a priori estimates for the solution of solution of (10) for \( t \in [0,T] \).

**Lemma 2.6** (A priori estimates). Let \( W_\varepsilon = (w_\varepsilon, h_\varepsilon) \) be a solution of (10). Then, for \( t \in [0,T] \), the following estimates hold:

(i) \( \varepsilon \int_{\Gamma \varepsilon} |w_\varepsilon|^4 \, d\sigma + \varepsilon \int_{0}^{t} \int_{\Gamma \varepsilon} |\partial_\tau w_\varepsilon|^2 \, d\sigma d\tau \leq C. \)

(ii) \( \varepsilon \int_{\Gamma \varepsilon} |h_\varepsilon|^2 \, d\sigma + \varepsilon \int_{0}^{t} \int_{\Gamma \varepsilon} |\partial_\tau h_\varepsilon|^2 \, d\sigma d\tau \leq C. \)

(iii) Let \( z_\varepsilon = e^{-\lambda t} u_\varepsilon \) with the jump \( [z_\varepsilon] = w_\varepsilon \) on \( \Gamma \varepsilon \). Then, one has that

\[
\int_{\Omega_i \cup \Omega_e^i} (|z_\varepsilon|^2 + |\nabla z_\varepsilon|^2) \, dx \leq C,
\]

for a constant \( C \) independent of \( \varepsilon \), but depending on \( T \), and the norms of initial functions \( \|G_\varepsilon\|^L^2(\Gamma \varepsilon), \|V_0^\varepsilon\|^L^4(\Gamma \varepsilon), \|V_l^\varepsilon\|^H^1(\Omega \varepsilon) \).

**Proof.** We will work with the equation in vector form (10) and derive the a priori estimates for the pair \( (w_\varepsilon, h_\varepsilon) \). Let \( z_\varepsilon \) be the solution of the stationary problem with the jump \( w_\varepsilon \):

\[
- \text{div} (a \varepsilon \nabla z_\varepsilon) = 0, \quad x \in \Omega_i^t \cup \Omega_e^t,
\]
Using the Young inequality with a parameter in (16) and (17), yields

\[ a_e \nabla z_e^\varepsilon \cdot \nu = a_i \nabla z_i^\varepsilon \cdot \nu, \quad x \in \Gamma_e, \]
\[ z_e^1 - z_e^\varepsilon = w_e, \quad x \in \Gamma_e, \]
\[ a_e \nabla z_e \cdot \nu = 0, \quad x \in \Gamma_m, \varepsilon, \]
\[ a_e \nabla z_e \cdot \nu = \frac{e^{-\lambda t}}{c_m} J_e^c, \quad x \in \Sigma, \]
\[ z_e = 0, \quad x \in (S_0 \cup S_L). \]

We multiply (10) by \( W \) and integrate over \( \Gamma_e \):

\[
\frac{\varepsilon}{2} \partial_t \int_{\Gamma_e} |w_e|^2 d\sigma + \frac{1}{c_m} \int_{\Omega_0 \cup \Omega_e} a_e \nabla z_e \cdot \nabla z_e dx + \frac{\varepsilon}{c_m} \int_{\Gamma_e} \frac{e^{2\lambda t}}{3} w_e^4 d\sigma \\
+ \varepsilon \left( \lambda - \frac{1}{c_m} \right) \int_{\Gamma_e} |w_e|^2 d\sigma - \varepsilon \left( \theta + \frac{1}{c_m} \right) \int_{\Gamma_e} h_e w_e d\sigma + \frac{\varepsilon}{2} \partial_t \int_{\Gamma_e} |h_e|^2 d\sigma \tag{16} \\
+ \varepsilon (\lambda + b) \int_{\Gamma_e} |h_e|^2 d\sigma = \frac{e^{-\lambda t}}{c_m} \int_{\Sigma} J_e^c z_e d\sigma + \varepsilon \frac{e^{-\lambda t}}{e} \int_{\Gamma_e} h_e d\sigma.
\]

It is known [24] that there exists an extension operator \( P_e \) from \( \Omega_e \) to \( \Omega \) such that \( \| \nabla P_e z_e^\varepsilon \|_{L^2(\Omega)} \leq C \| \nabla z_e^\varepsilon \|_{L^2(\Omega_e)} \) with a constant \( C \) independent of \( \varepsilon \). This result combined with the Friedrichs inequality \( (z_e = 0 \text{ on } S_0 \cup S_L) \) implies that

\[ \| P_e z_e^\varepsilon \|_{H^1(\Omega)} \leq C \| \nabla z_e^\varepsilon \|_{L^2(\Omega_e)}. \tag{17} \]

By the trace inequality, the \( L^2(\Sigma) \)-norm of \( z_e \) is then bounded by \( \| \nabla z_e^\varepsilon \|_{L^2(\Omega_e)} \). Using the Young inequality with a parameter in (16) and (17), yields

\[
\partial_t \left( \varepsilon \int_{\Gamma_e} |w_e|^2 d\sigma + \varepsilon \int_{\Gamma_e} |h_e|^2 d\sigma \right) + \int_{\Omega_0 \cup \Omega_e} |\nabla z_e| d\sigma + \varepsilon \int_{\Gamma_e} |w_e|^2 d\sigma \\
+ \left( \varepsilon \int_{\Gamma_e} |w_e|^2 d\sigma + \varepsilon \int_{\Gamma_e} |h_e|^2 d\sigma \right) \leq C \int_{\Sigma} |J_e^c|^2 d\sigma. \tag{18}
\]

Applying the Grönwall inequality in (18), we obtain the following estimate:

\[ \varepsilon \int_{\Gamma_e} |w_e|^2 d\sigma + \varepsilon \int_{\Gamma_e} |h_e|^2 d\sigma \leq C. \tag{19} \]

Integrating (18) with respect to \( t \) gives

\[
\int_0^t \int_{\Omega_0 \cup \Omega_e} \nabla z_e^\varepsilon \cdot \nabla z_e^\varepsilon dx + \varepsilon \int_0^t |w_e|^2 d\sigma \leq C \left( \int_0^t |J_e^c|^2 d\sigma + \varepsilon \int_{\Gamma_e} |\nabla z_e^\varepsilon|^2 d\sigma + \varepsilon \int_{\Gamma_e} |G_{z_e^\varepsilon}| d\sigma \right). \tag{20}
\]

Next, we derive the estimates for \( \partial_t W_e \). To this end, we multiply (10) by \( \partial_t W_e \):
and integrate over $(0, t) \times \Gamma_\varepsilon$:

\[
\begin{align*}
\frac{\varepsilon}{2} & \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau w_\varepsilon|^2 d\sigma d\tau + \frac{\varepsilon}{2} \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau h_\varepsilon|^2 d\sigma d\tau \\
+ & \frac{1}{2c_m} \int_{\Omega_i \cup \Omega_e} a_\varepsilon |\nabla z_\varepsilon|^2 dx - \frac{1}{2c_m} \int_{\Omega_i \cup \Omega_e} a_\varepsilon |\nabla z_\varepsilon|^2 dx \bigg|_{t=0} \\
+ & \frac{\varepsilon}{12c_m} e^{2\lambda t} \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 d\sigma - \frac{\varepsilon}{12c_m} \int_{\Gamma_\varepsilon} |V_\varepsilon^0|^4 d\sigma \\
+ & \frac{\varepsilon}{2} (\lambda - \frac{1}{c_m}) \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 d\sigma - \frac{\varepsilon}{2} (\lambda - \frac{1}{c_m}) \int_{\Gamma_\varepsilon} |V_\varepsilon^0|^2 d\sigma \\
+ & \frac{\varepsilon}{2} (\lambda + b) \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 d\sigma - \frac{\varepsilon}{2} (\lambda + b) \int_{\Gamma_\varepsilon} |G_\varepsilon^0|^2 d\sigma \\
& \leq 2\lambda \varepsilon \int_0^t e^{2\lambda \tau} \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 d\sigma d\tau \\
& + 2\theta^2 \varepsilon \int_0^t \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 d\sigma d\tau + \frac{2\varepsilon}{c_m^2} \int_0^t \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 d\sigma d\tau \\
& + \frac{e^{-\lambda t}}{c_m} \int_{\Omega_i} J_\varepsilon^z z_\varepsilon d\sigma - \frac{1}{c_m} \int_{\Omega_i} J_\varepsilon^z z_\varepsilon d\sigma \bigg|_{t=0} \\
& + \lambda \int_0^t e^{-\lambda \tau} \int_{\Omega_i} J_\varepsilon^z z_\varepsilon d\sigma d\tau - \int_0^t e^{-\lambda \tau} \int_{\Omega_i} \partial_\tau J_\varepsilon^z z_\varepsilon d\sigma d\tau \\
& + \varepsilon a e^{-\lambda t} \int_{\Gamma_\varepsilon} h_\varepsilon d\sigma - \varepsilon a \int_{\Gamma_\varepsilon} G_\varepsilon^0 d\sigma + \varepsilon a \lambda \int_0^t e^{-\lambda \tau} \int_{\Gamma_\varepsilon} h_\varepsilon d\sigma d\tau.
\end{align*}
\]

Combining (19), (20), and (14) we get

\[
\varepsilon \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau w_\varepsilon|^2 d\sigma d\tau + \varepsilon \int_{\Omega_i \cup \Omega_e} |\nabla z_\varepsilon|^2 dx + \varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 dx \leq C.
\]

Thanks to the homogeneous Dirichlet boundary condition on the bases $S_0 \cup S_L$, the $L^2$-norm of $z_\varepsilon$ is estimated in terms on the $\nabla z_\varepsilon$. Namely,

\[
\int_{\Omega_i} |z_\varepsilon|^2 dx \leq C \int_{\Omega_i} |\partial_{x_1} z_\varepsilon|^2 dx, \\
\int_{\Omega_e} |z_\varepsilon|^2 dx \leq C \int_{\Omega_e} |\nabla z_\varepsilon|^2 dx.
\]

The proof of Lemma 2.6 is finally complete. \(\square\)

3. Derivation of the macroscopic problem

3.1. Formal asymptotic expansions

So as to provide an insight on how the effective coefficients and the corresponding cell problems in (2) appear, we apply the formal asymptotic expansion
method to the stationary problem $A_x v_\varepsilon = \varepsilon g$. Specifically, we write

$$-\text{div} (a_\varepsilon \nabla u_\varepsilon) = 0, \quad x \in \Omega_i^e \cup \Omega_e^e,$$

$$a_\varepsilon \nabla u_\varepsilon \cdot \nu = a_i \nabla u_i^e \cdot \nu = \varepsilon g(x), \quad x \in \Gamma_{\varepsilon},$$

$$u_i^\varepsilon - u_e^\varepsilon = v_\varepsilon, \quad x \in \Gamma_{\varepsilon},$$

$$a_\varepsilon \nabla u \cdot \nu = 0, \quad x \in \Gamma_{m} \cup \Sigma,$$

$$u_\varepsilon = 0, \quad x \in (S_0 \cup S_L).$$

Here $g = g(x)$ is some smooth function. Take

$$u_i^\varepsilon(x) \sim u_i^0(x,y) + \varepsilon u_1^1(x,y) + \varepsilon^2 u_2^1(x,y) + \ldots, \quad y = \frac{x}{\varepsilon},$$

where $x \in \Omega_i^l$ and $y \in Y_l$, $l \in \{i,e\}$. Then we get

$$\text{div}(a_l \nabla u_\varepsilon^l) \sim \frac{1}{\varepsilon^2} \text{div}_y (a_l \nabla_y u_0^l) + \frac{1}{\varepsilon} (\text{div}_y (a_l \nabla_x u_0^l) + \text{div}_y (a_l \nabla_y u_1^l) + \text{div}_y (a_l \nabla_y u_2^l)) + \text{div}_x (a_l \nabla_y u_0^l) + \text{div}_x (a_l \nabla_y u_1^l) + \text{div}_x (a_l \nabla_y u_2^l) + \varepsilon (\text{div}_x (a_l \nabla_x u_1^l) + \text{div}_x (a_l \nabla_y u_2^l)) + \varepsilon^2 \text{div}_x (a_l \nabla_x u_2^l).$$

Taking the terms of order $\varepsilon^{-2}$ in the volume and the ones of order $\varepsilon^{-1}$ on the boundary, we obtain the following problem for $u_0^l$:

$$-\text{div}_y (a_l \nabla_y u_0^l) = 0, \quad y \in Y_l,$$

$$a_l \nabla_y u_0^l = 0 \quad y \in \Gamma \cup \Gamma^m,$$

$u_i^0$ is 1-periodic in $y_1$, and $u_i^0$ is $Y$-periodic.

The solution (defined up to an additive constant) does not depend on the fast variable $y$:

$$u_0^l(x,y) = u_0^l(x), \quad l = i, e. \quad (23)$$

For the next step, we take the terms of order $\varepsilon^{-1}$ in the volume and those of order 1 on the boundary:

$$-\text{div}_y (a_l \nabla_y u_1^l) = 0, \quad y \in Y_l,$$

$$a_l \nabla_y u_1^l \cdot \nu = -a_l \nabla_x u_0^l \cdot \nu, \quad y \in \Gamma \cup \Gamma^m, \quad (24)$$

$u_1^i$ is 1-periodic in $y_1$, and $u_1^e$ is $Y$-periodic.
The solvability condition reads $- \int_{\Gamma} a_l \nabla_x u_0^l \cdot \nu = 0$, which is fulfilled thanks to (23). By seeking a solution of (24) in the form $u_1^l(x,y) = N_l^i(y) \cdot \nabla_x u_0^l(x)$, we obtain

$$a_l \nabla_y u_1^l(x,y) \cdot \nu = a_l \partial_{y_j} N_l^i(y) \nu_j \partial_x u_0^l(x),$$

where we assume summation over the repeated indexes. The boundary condition in (24) yields a boundary condition for $N_i$ on $\Gamma \cup \Gamma_m$:

$$(\partial_{y_j} N_l^i(y) + \delta_{i,j}) \nu_j = 0.$$  

Then, the functions $N_k^i$, $k = 1, 2, 3$, solve the cell problems:

$$-\Delta N_k^i = 0, \quad y \in Y_i, \quad \nabla N_k^i \cdot \nu = -\nu_k, \quad y \in \Gamma \cup \Gamma_m,$$

$$y \mapsto N_k^i(y) \text{ is } Y - \text{periodic};$$  

(25)

For the functions $N_k^i$, due to the periodicity in only one variable $y_1$, one can see that $N_k^i(y) = -y_k$ for $k \neq 1$, that yields $\partial_{i\neq k} N_k^i = 0$. The first component $N_1^i$ solves the problem

$$-\Delta N_1^i = 0, \quad y \in Y_i, \quad \nabla N_1^i \cdot \nu = -\nu_1, \quad y \in \Gamma \cup \Gamma_m,$$

$$y \mapsto N_1^i(y) \text{ is } 1 - \text{periodic};$$  

(26)

Finally, taking the terms of order 1 in the volume and the ones of order $\epsilon^1$ on the boundary, we obtain the following problem for $u_2^i$:

$$-\text{div}_y(a_l \nabla_y u_2^i) = \text{div}_x(a_l \nabla_x u_0^l) + \text{div}_x(a_l \nabla_y u_1^l) + \text{div}_y(a_l \nabla_x u_1^l), \quad y \in Y_i,$$

$$a_l \nabla_y u_2^i \cdot \nu^l = -a_l \nabla_x u_1^l \cdot \nu^l + g(x), \quad y \in \Gamma,$$

$$a_l \nabla_y u_2^i \cdot \nu = 0, \quad y \in \Gamma_m,$$

$u_2^i$ is 1-periodic in $y_1$

and $u_2^i$ is $Y$-periodic.

Here $\nu^l$ is the exterior unit normal, and $\nu^c = -\nu^l$ on $\Gamma$. The solvability condition reads

$$\int_{Y_1} (\text{div}_x(a_l \nabla_x u_0^l) + \text{div}_x(a_l \nabla_y u_1^l) + \text{div}_y(a_l \nabla_x u_1^l)) \, dy - \int_{\Gamma} a_l \nabla_x u_2^i \cdot \nu^l \, ds = 0.$$  

Integrating by parts in the third term of the volume integral, substituting the expression $u_1^l(x,y) = N_l^i(y) \partial_x u_0^l(x)$, and taking into account that $N_k^i(y) = -y_k$
and \( \int_{Y_i} \partial_{\neq 1} N_i^l dy = 0 \), we obtain

\[
-\partial_{kj} u_0^e(x) \int_{Y_e} a_e (\partial_j N_k^e(y) + \delta_{kj}) dy = |\Gamma| g(x),
\]

\[
|Y_i| a_i \partial_{11} u_0^i(x) = |\Gamma| g(x).
\]

Introducing the effective coefficient

\[
(a_{\text{eff}})_{kl} = \frac{1}{|\Gamma|} \int_{Y_e} a_e (\partial_l N_k^e(y) + \delta_{kl}) dy, \quad k, l = 1, 2, 3,
\]

and adding the boundary conditions on \( S_0 \cup S_L \) and \( \Sigma \), we arrive at

\[
\frac{|Y_i|}{|\Gamma|} a_i \partial_{11} u_0^i = -a_{\text{eff}} \Delta u_0^e = g(x), \quad x \in \Omega,
\]

\[
u \cdot a_{\text{eff}} \nabla u_0^e = 0, \quad x \in \Sigma.
\]

### 3.2. Derivation of the macroscopic problem

Since the axons inside the bundle are disconnected, a priori estimates provided by Lemma 2.6 do not imply the strong convergence of the transmembrane potential \( v_\epsilon \) on \( \Gamma_\epsilon \). In turn, this makes passing to the limit in the nonlinear term \( I_{\text{ion}} \) problematic. We choose to combine the two-scale convergence machinery with the method of monotone operators due to G. Minty [25]. For reader’s convenience we provide a brief description of the method for a simple case in Appendix A, while its adaptation for problem (1) is presented in Section 3. For passage to the limit, as \( \epsilon \to 0 \), we will use the two-scale convergence [26]. We refer to [21] for two-scale convergence on periodic surfaces (namely, on \( \Gamma_\epsilon \)).

**Definition 3.1.** We say that a sequence \( \{ u_0^l(t, x) \} \) two-scale converges to the function \( u_0^l(t, x, y) \) in \( L^2(0, T; L^2(\Omega^l)) \), \( l = i, e \), as \( \epsilon \to 0 \), and write

\[
u^l(t, x, y) = u^l(t, x, y),
\]

if

(i) \( \int_0^T \int_{\Omega^l} \left| u_\epsilon^l \right|^2 dx \, dt < C \).

(ii) For any \( \phi(t, x) \in C(0, T; L^2(\Omega^l)) \), \( \psi(y) \in L^2(Y_l) \) we have

\[
\lim_{\epsilon \to 0} \int_0^T \int_{\Omega^l} u_\epsilon^l(t, x) \phi(t, x) \psi \left( \frac{x}{\epsilon} \right) dx \, dt
\]


\[
\frac{1}{|Y|} \int_0^T \int_0^t \int_0^\gamma u_0(t,x,y)\phi(t,x)\psi(y) \, dy \, dx \, dt,
\]

for some function \(u_0 \in L^2(0,T; L^2(\Omega \times Y))\).

**Definition 3.2.** A sequence \(\{v_\varepsilon(t,x)\}\) converges two-scale to the function \(v_0(t,x,y)\) in \(L^2(0,T; L^2(\Gamma_\varepsilon))\), as \(\varepsilon \to 0\), if

(i) \(\varepsilon \int_0^T \int_{\Gamma_\varepsilon} v_\varepsilon^2 \, d\sigma \, dt < C\).

(ii) For any \(\phi(t,x) \in C([0,T]\cap C(\overline{\Omega})), \psi(y) \in C(\Gamma)\) we have that

\[
\lim_{\varepsilon \to 0} \varepsilon \int_0^T \int_{\Gamma_\varepsilon} v_\varepsilon(t,x)\phi(t,x)\psi\left(\frac{x}{\varepsilon}\right) \, d\sigma_x \, dt = \frac{1}{|Y|} \int_0^T \int_\Omega \int_{\Gamma} v_0(t,x,y)\phi(t,x)\psi(y) \, d\sigma_y \, dx \, dt
\]

for some function \(v_0 \in L^2(0,T; L^2(\Omega \times \Gamma))\).

(iii) We say that \(\{v_\varepsilon\}\) converges \(t\)-pointwise two-scale in \(L^2(\Gamma_\varepsilon)\) if, for any \(t \in [0,T]\), and for any \(\phi(x) \in C(\overline{\Omega}), \psi(y) \in C(\Gamma)\) we have

\[
\lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} v_\varepsilon(t,x)\phi(x)\psi\left(\frac{x}{\varepsilon}\right) \, d\sigma_x = \frac{1}{|Y|} \int_0^T \int_\Omega \int_{\Gamma} v_0(t,x,y)\phi(x)\psi(y) \, d\sigma_y \, dx
\]

for some function \(v_0 \in L^2(0,T; L^2(\Omega \times \Gamma))\).

**Lemma 3.3.** Let \(W_\varepsilon\) be a solution of \([10]\), and let \(z_\varepsilon\) be a solution of problem \([15]\). Then there exist functions \(z_0^l \in L^2(0,T; L^2(\Omega)), l = i,e, \) such that \(\partial_{x_1} z_0^l, \partial_{x_2} z_0^l \in L^2(0,T; L^2(\Omega))\) (\(j = 1,2,3\)), \(w_0 = z_0^i - z_0^e \in L^4(0,T; L^4(\Omega))\), and up to a subsequence, as \(\varepsilon \to 0\), the following two-scale convergence holds:

(i) \(\chi^i\left(\frac{x}{\varepsilon}\right)z_\varepsilon^i(t,x) \xrightarrow{\ast} \chi^i(y)z_0^i(t,x)\) in \(L^2(0,T; L^2(\Omega_\varepsilon))\), \(l = i,e\).

(ii) \(\chi^i\left(\frac{x}{\varepsilon}\right)\nabla z_\varepsilon^i(t,x) \xrightarrow{\ast} \chi^i(y)\left[e_1 \partial_{x_1} z_0^i(t,x) + \nabla_y z_1^i(t,x,y)\right], \) where \(z_1^i(t,x,y) \in L^2((0,T) \times \Omega; H^1(Y_i))\) is \(1\)-periodic in \(y_1\).

(iii) \(\chi^e\left(\frac{x}{\varepsilon}\right)\nabla z_\varepsilon^e(t,x) \xrightarrow{\ast} \chi^e(y)\left[\nabla z_0^e(t,x) + \nabla_y z_1^e(t,x,y)\right], \) where \(z_1^e(t,x,y) \in L^2((0,T) \times \Omega; H^1(Y_e))\) is \(Y\)-periodic in \(y\).
(iv) $w_\varepsilon \xrightarrow{\varepsilon} w_0(t,x)$ $t$-pointwise in $L^2(\Gamma_\varepsilon)$, and $w_0 = (z_0^i - z_0^i)$. Moreover, 
$\partial_t w_\varepsilon \xrightarrow{\varepsilon} \partial_t w_0$ in $L^2(0,T;L^2(\Gamma_\varepsilon))$.

(v) $h_\varepsilon \xrightarrow{\varepsilon} \tilde{h}_0(t,x,y)$ $t$-pointwise in $L^2(\Gamma_\varepsilon)$, and $\partial_t h_\varepsilon \xrightarrow{\varepsilon} \partial_t \tilde{h}_0$ in $L^2(0,T;L^2(\Gamma_\varepsilon))$.

Proof. From a priori estimates the two-scale convergence of $z_\varepsilon^i$ and $\nabla z_\varepsilon^i$ is proved applying standard arguments (see [26]). When it comes to $z_\varepsilon^i$ and its gradient, the main difficulty stems from the fact that $\Omega_\varepsilon^i$ consists of many disconnected components.

Since $z_\varepsilon^i$ is bounded uniformly in $\varepsilon$ (cf. Lemma 2.6) in $L^2((0,T) \times \Omega_\varepsilon^i)$, there exists a subsequence—still denoted by $\{z_\varepsilon^i\}$—such that $\chi^i(\frac{x}{\varepsilon})z_\varepsilon^i(t,x)$ converging two-scale to some $\chi^i(y)z_0^i(t,x,y)$ in $L^2(0,T;L^2(\Omega \times Y))$. Similarly, due to (20), up to a subsequence, $\chi^i(\frac{x}{\varepsilon})\nabla z_\varepsilon^i(t,x)$ converges two-scale to $\chi^i(y)p^i(t,x,y)$.

Let us show that $z_0^i = z_0^i(t,x)$. Take a smooth test function $\Phi(t,x,\frac{x}{\varepsilon}) = \varphi(t,x)\psi\left(\frac{x}{\varepsilon}\right)$, where $\varphi \in C([0,T];C^\infty_0(\Omega))$, and $\psi \in (C^\infty(Y_i))^3$ is 1-periodic in $y_1$ and such that $\psi = 0$ on $\Gamma_{mi} \cup \Gamma$.

$$\varepsilon \int_0^T \int_{\Omega_\varepsilon^i} \nabla z_\varepsilon^i(t,x) \cdot \varphi(t,x)\psi\left(\frac{x}{\varepsilon}\right) dxdt = -\varepsilon \int_0^T \int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\nabla \varphi(t,x) \cdot \psi\left(\frac{x}{\varepsilon}\right) dxdt$$
$$- \int_0^T \int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\varphi(t,x)\nabla_y \psi\left(\frac{x}{\varepsilon}\right) dxdt.$$

Passing to the limit, we derive

$$\frac{1}{|Y_i|} \int_0^T \int_{\Omega} \int_{Y_i} z_0^i(t,x,y)\varphi(t,x)\nabla_y \psi(y) dy dxdt = 0,$$

which implies that $\partial_y z_0^i(t,x,y) = 0$, $i = 1,2,3$. Thus, $z_0^i = z_0^i(t,x)$.

Next we prove that $\partial_x z_0^i \in L^2((0,T) \times \Omega)$. Let us take a test function $\Phi(t,x,\frac{x}{\varepsilon}) = \varphi(t,x)e_1 + \varphi(t,x)\nabla_y N_1^i\left(\frac{x}{\varepsilon}\right)$ such that

$$\Delta_y N_1^i = 0, \quad Y_i,$$
$$\nabla N_1^i \cdot \nu = -\nu_1, \quad \Gamma \cup \Gamma_{mi},$$

(27) $N_1^i$ is 1-periodic in $y_1$.

Integrating by parts yields

$$\int_0^T \int_{\Omega_\varepsilon^i} \nabla z_\varepsilon^i(t,x) \cdot \Phi(t,x,\frac{x}{\varepsilon}) dxdt$$
$$= - \int_0^T \int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\left(e_1 + \nabla_y N_1^i\left(\frac{x}{\varepsilon}\right)\right) \cdot \nabla \varphi(t,x) dxdt,$$
and passing to the limit, as \( \varepsilon \to 0 \), we obtain

\[
\frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{Y_i} p^i(t, x, y) \cdot \varphi(t, x) \left( e_1 + \nabla_y N^i_1(y) \right) \, dy \, dx \, dt
= - \frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{Y_i} z^i_0(t, x) \nabla \varphi(t, x) \cdot \left( e_1 + \nabla_y N^i_1(y) \right) \, dy \, dx \, dt.
\]

(28)

Let us observe that \( \int_{Y_i} \partial_{y_k} N^i_1(y) \, dy = 0 \) for \( k \neq 1 \). Indeed, for \( k \neq 1 \), \( y_k \) can be taken as a test function in (27):

\[
0 = - \int_{Y_i} \Delta N^i_1(y) y_k \, dy = \int_{Y_i} \partial_{y_k} N^i_1(y) \, dy.
\]

Furthermore, it holds that

\[
\int_{Y_i} \left( \delta_{1k} + \partial_{y_k} N^i_1(y) \right) \, dy = \delta_{1k} |\Gamma| \frac{a^{\text{eff}}}{a_i}.
\]

Consequently, it is straightforward to check that

\[
a^{\text{eff}} = \frac{1}{|\Gamma|} \int_{Y_i} a_i \left( 1 + \partial_{y_i} N^i_1(y) \right) \, dy = \frac{1}{|\Gamma|} \int_{Y_i} a_i \left( 1 + \partial_{y_i} N^i_1(y) \right)^2 \, dy > 0.
\]

(29)

We turn back to (28). Due to (29), we have the estimate

\[
\left| \int_0^T \int_{\Omega} z^i_0(t, x) \partial_{x_i} \varphi(t, x) \, dx \, dt \right|
= \left| \frac{a_i}{(a^{\text{eff}})_{11}} \int_0^T \int_{\Omega} \int_{Y_i} p^i(t, x, y) \cdot \varphi(t, x) \left( e_1 + \nabla_y N^i_1(y) \right) \, dy \, dx \, dt \right|
\leq C \| \varphi \|_{L^2((0,T) \times \Omega)}.
\]

Next, we show that \( p^i(t, x, y) = e_1 \partial_{x_i} z^i_0(t, x) + \nabla_y z^i_1(t, x, y) \) for some \( z^i_1 \) periodic in \( y_1 \). Take a smooth test function \( \varphi(t, x) \psi(y) \) such that \( \text{div}_y \psi = 0 \) in \( Y_i \), \( \psi \cdot \nu = 0 \) on \( \Gamma_{mi} \cup \Gamma \), and periodic in \( y_1 \).

\[
\int_0^T \int_{\Omega} \nabla z^i_\varepsilon \cdot \varphi(t, x) \psi \left( \frac{x}{\varepsilon} \right) \, dx \, dt = - \int_0^T \int_{\Omega} z^i_\varepsilon \nabla \varphi(t, x) \cdot \psi \left( \frac{x}{\varepsilon} \right) \, dx \, dt.
\]

Passing to the limit, as \( \varepsilon \to 0 \) we obtain

\[
\frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{Y_i} p^i \cdot \varphi(t, x) \psi(y) \, dy \, dx \, dt = - \frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{Y_i} z^i_0 \nabla \varphi(t, x) \cdot \psi(y) \, dy \, dx \, dt.
\]
Since $\int_{Y_i} \psi_k(y) \, dy = 0$ for $k \neq 1,$
\[
\int_0^T \int_{Y_i} p^i(t, x, y) \cdot \phi(t, x) \psi(y) \, dy \, dx \, dt = \int_0^T \int_{Y_i} \partial_{x_1} z_0^i(t, x) \varphi(t, x) \psi_1(y) \, dy \, dx \, dt,
\]
and thus
\[
\int_0^T \int_{Y_i} (p^i(x, y) - e_1 \partial_{x_1} z_0^i(t, x)) \varphi(t, x) \cdot \psi(y) \, dy \, dx \, dt = 0.
\]
Since $\psi$ is solenoidal, there exists $z_1^i(t, x, y) \in L^2((0, T) \times \Omega; H^1(Y_i))$, 1-periodic in $y_1$, such that
\[
p^i(t, x, y) = e_1 \partial_{x_1} z_0^i(t, x) + \nabla_y z_1^i(t, x, y).
\]
Next we prove that the jump $w_\varepsilon$ converges two-scale in $L^2(0, T; L^2(\Gamma))$ to $z_1^i - z_0^i$. To this end, for $\psi \in H^{1/2}(\Gamma)$, we consider test functions $\tilde{\psi}^l, l = i, e$, solving
\[
\Delta \tilde{\psi}^l = \frac{1}{|Y_l|} \int_{\Gamma} \psi \, d\sigma, \quad y \in Y_l,
\]
\[
\nabla \tilde{\psi}^l \cdot \nu^l = \psi, \quad y \in \Gamma; \quad \nabla \tilde{\psi}^l \cdot \nu^l = 0, \quad y \in \Gamma_{ml},
\]
$\tilde{\psi}^l$ is $Y$-periodic.

Integration by parts yields
\[
\varepsilon \int_{\Gamma_{x}} \int_0^T w_\varepsilon \varphi(t, x) \psi\left(\frac{x}{\varepsilon}\right) \, dx \, dt
\]
\[
= \varepsilon \int_0^T \int_{\Omega_{x}} \nabla z_\varepsilon^i \cdot \varphi(t, x) \nabla_y \tilde{\psi}^i\left(\frac{x}{\varepsilon}\right) \, dx \, dt
\]
\[
+ \varepsilon \int_0^T \int_{\Omega_{x}} z_\varepsilon^i \nabla \varphi(t, x) \cdot \nabla_y \tilde{\psi}^i\left(\frac{x}{\varepsilon}\right) \, dx \, dt
\]
\[
+ \frac{1}{|Y_l|} \int_0^T \int_{\Omega_{x}} z_\varepsilon^i \varphi(t, x) \int_\Gamma \psi \, d\sigma \, dx \, dt
\]
\[
- \varepsilon \int_0^T \int_{\Omega_{x}} \nabla z_\varepsilon^e \cdot \varphi(t, x) \nabla_y \tilde{\psi}^e\left(\frac{x}{\varepsilon}\right) \, dx \, dt
\]
\[
- \varepsilon \int_0^T \int_{\Omega_{x}} z_\varepsilon^e \nabla \varphi(t, x) \cdot \nabla_y \tilde{\psi}^e\left(\frac{x}{\varepsilon}\right) \, dx \, dt
\]
\[
- \frac{1}{|Y_l|} \int_0^T \int_{\Omega_{x}} z_\varepsilon^e \varphi(t, x) \int_\Gamma \psi \, d\sigma \, dx \, dt.
\]
Passing to the limit, as $\varepsilon \to 0$, we get
\[
\left\{\frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{\Gamma} w_0(t, x, y) \varphi(t, x) \psi(y) \, d\sigma \, dx \, dt
\right.\]
\[
= \left\{\frac{1}{|Y|} \int_0^T \int_{\Omega} \int_{\Gamma} (z_0^i - z_0^e) \varphi(t, x) \psi(y) \, d\sigma \, dx \, dt,\right\}
\]
that proves the two-scale convergence of \( w_\varepsilon \) to the difference \( w_0 = z_0^\varepsilon - z_{0e}^\varepsilon \).

Note that the uniform bound of \( w_\varepsilon \) in \( L^4((0,T) \times \Gamma_\varepsilon) \)—by Lemma 2.6(i)—implies \( w_0 \in L^4((0,T) \times \Omega) \). Indeed, for smooth \( \varphi(t,x) \), we have that

$$
|\Gamma| \int_0^T \int_\Omega w_0(t,x) \varphi(t,x) \, dx \, dt = \lim_{\varepsilon \to 0} |Y| \int_0^T \int_{\Gamma_\varepsilon} w_\varepsilon(t,x) \varphi(t,x) \, d\sigma \, dt
$$

$$
\leq |Y| \lim_{\varepsilon \to 0} \left( \varepsilon \int_0^T \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 \, d\sigma \, dt \right)^{\frac{1}{4}} \left( \varepsilon \int_0^T \int_{\Gamma_\varepsilon} |\varphi(t,x)|^{4/3} \, d\sigma \, dt \right)^{\frac{3}{4}}
$$

$$
\leq C \lim_{\varepsilon \to 0} \left( \varepsilon \int_0^T \int_{\Gamma_\varepsilon} |\varphi(t,x)|^{4/3} \, d\sigma \, dt \right)^{\frac{3}{4}}.
$$

By density of smooth functions in \( L^4((0,T) \times \Omega) \), \( \|w_0\|_{L^4((0,T) \times \Omega)} \leq C \).

Thanks to the uniform in \( \varepsilon \) estimate (20), \((v)\), \((vi)\), and \((vii)\) hold. \( \square \)

**Lemma 3.4.** Let the initial functions \( V_0^\varepsilon \) satisfy hypothesis (H1). Then, one has that

$$
\varepsilon \int_{\Gamma_\varepsilon} |V_0^\varepsilon|^2 \, d\sigma = \frac{|\Gamma|}{|Y|} \int_\Omega |V^i - V^0|^2 \, dx.
$$

**Proof.** Approximating \( V^0 = V^i - V^\varepsilon \) by smooth functions \( V_0^\delta \) in \( H^1(\Omega) \), we find

$$
\varepsilon \int_{\Gamma_\varepsilon} |V_0^\varepsilon|^2 \, d\sigma = \varepsilon \int_{\Gamma_\varepsilon} |V_0^\varepsilon - V_0^\delta|^2 \, d\sigma
$$

$$
+ 2\varepsilon \int_{\Gamma_\varepsilon} (V_0^\varepsilon - V_0^\delta) V_0^\delta \, d\sigma + \varepsilon \int_{\Gamma_\varepsilon} |V_0^\delta|^2 \, d\sigma. \tag{30}
$$

Applying the trace inequality in the rescaled periodicity cell \( \varepsilon Y \), adding up over all the cells in \( \Omega \), and using assumption (H1) leads to

$$
\varepsilon \int_{\Gamma_\varepsilon} |V_0^\varepsilon - V_0^\delta|^2 \, d\sigma \leq C\varepsilon^2 \int_\Omega |\nabla (V_0^\varepsilon - V_0^\delta)|^2 \, dx + C \int_\Omega |V_0^\varepsilon - V_0^\delta|^2 \, dx
$$

$$
\leq C\varepsilon^2 \int_\Omega |\nabla (V_0^\varepsilon - V_0^\delta)|^2 \, dx + C \int_\Omega |V_0^\varepsilon - V_0^\delta|^2 \, dx
$$

$$
+ C \int_\Omega |V_0^\delta - V^0|^2 \, dx \to 0, \quad \varepsilon, \delta \to 0.
$$

Then, since \( V_0^\delta \) is smooth, it converges strongly two-scale, and passing to the
limit as $\varepsilon \to 0$ in [30] we obtain
\[
\lim_{\delta \to 0} \limsup_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} |V_\varepsilon^0|^2 \, d\sigma = \frac{|\Gamma|}{|Y|} \int_{\Omega} |V|^2 \, dx,
\]
as stated.

We proceed with the Minty method for passing to the limit in the microscopic problem. Consider arbitrary functions $\mu_0^i(t,x) \in C^\infty(0,T] \times \Omega)$ and $\mu_1^i(t,x,y) \in C^\infty([0,T] \times \Omega \times Y)$, $Y$-periodic in $y$, and such that $\mu_0^i = \mu_1^i = 0$ when $x \in S_0 \cap S_L$.

Take the test function
\[
M_\varepsilon := \left( \frac{[\mu_\varepsilon]}{\rho} \right), \quad \text{where } \rho = \rho(t,x), \quad \text{and}
\]
\[
\mu_\varepsilon(x) := \begin{cases} 
\mu_0^i(t,x) + \varepsilon \mu_1^i(t,x,\frac{x}{\varepsilon}), & x \in \Omega_\varepsilon \\
\mu_0^i(t,x) + \varepsilon \mu_1^i(t,x,\frac{x}{\varepsilon}), & x \in \Omega_\varepsilon^c.
\end{cases}
\]
The monotonicity property of the operator $A_\varepsilon(t,\cdot)$ entails
\[
\int_0^t \int_{\Gamma_\varepsilon} (A_\varepsilon(\tau,W_\varepsilon) - A_\varepsilon(\tau,M_\varepsilon)) \cdot (W_\varepsilon - M_\varepsilon) \, d\sigma d\tau \geq 0.
\]

It follows from [10] and the definition of the operator $A_\varepsilon(t,\cdot)$ that
\[
\varepsilon \int_0^t \int_{\Gamma_\varepsilon} \partial_\tau w_\varepsilon([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau + \varepsilon \int_0^t \int_{\Gamma_\varepsilon} \partial_\tau h_\varepsilon(\rho - h_\varepsilon) \, d\sigma d\tau
\]
\[
+ \frac{1}{c_m} \int_0^t \int_{\Gamma_\varepsilon} A_\varepsilon[\mu_\varepsilon](\mu_\varepsilon - w_\varepsilon) \, d\sigma d\tau + \varepsilon(\lambda - \frac{1}{c_m}) \int_0^t \int_{\Gamma_\varepsilon} [\mu_\varepsilon]\mu_\varepsilon \, d\sigma d\tau
\]
\[
- \frac{\varepsilon}{c_m} \int_0^t \int_{\Gamma_\varepsilon} \rho([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau + \varepsilon(\lambda + \lambda) \int_0^t \int_{\Gamma_\varepsilon} \rho(\rho - h_\varepsilon) \, d\sigma d\tau \quad (31)
\]
\[
- \varepsilon \theta \int_0^t \int_{\Gamma_\varepsilon} [\mu_\varepsilon](\rho - h_\varepsilon) \, d\sigma d\tau + \frac{1}{3c_m} \int_0^t \int_{\Gamma_\varepsilon} e^{2\lambda \tau} \int_{\Gamma_\varepsilon} [\mu_\varepsilon]^3(\mu_\varepsilon - w_\varepsilon) \, d\sigma d\tau
\]
\[
+ \int_0^t \int_{\Gamma_\varepsilon} \frac{e^{-\lambda \tau}}{c_m}(a_i \nabla q_k \cdot \nu)([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau - \varepsilon \lambda \int_0^t \int_{\Gamma_\varepsilon} e^{-\lambda \tau}(\rho - h_\varepsilon) \, d\sigma d\tau \geq 0.
\]

Consider the first two terms in (31), specifically integrals $\varepsilon \int_0^t \int_{\Gamma_\varepsilon} w_\varepsilon \partial_\tau w_\varepsilon \, d\sigma d\tau$ and $\varepsilon \int_0^t \int_{\Gamma_\varepsilon} h_\varepsilon \partial_\tau h_\varepsilon \, d\sigma d\tau$. Integrating by parts with respect to time, passing to the limit as $\varepsilon \to 0$, and using the lower semi-continuity of $L^2$-norm with respect to two-scale convergence (Proposition 2.5, [21] and Lemma 3.4) renders
\[
\limsup_{\varepsilon \to 0} \left[ \varepsilon \int_0^t \int_{\Gamma_\varepsilon} w_\varepsilon \partial_\tau w_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|} \int_0^t \int_{\Omega} w_0 \partial_\tau w_0 \, dx d\tau \right]
\]
\[
= \lim_{\varepsilon \to 0} \sup \left[ \frac{\varepsilon}{2} \int_{\Gamma^e} w_0^2 \, d\sigma \right]_{t} \left. \right|_{t=\tau} - \frac{|\Gamma|}{2|Y|} \int_{\Omega} w_0^2 \, dx
\]
\[
+ \lim_{\varepsilon \to 0} \left[ - \frac{\varepsilon}{2} \int_{\Gamma^e} (V^0_2)^2 \, d\sigma + \frac{|\Gamma|}{2|Y|} \int_{\Omega} (V^0)^2 \, dx \right] \geq 0.
\]

Similarly, for the integral of \( h_0 \partial_t h_c \), denoting the mean value of the two-scale limit \( h_0(t, x, y) \) by \( \frac{1}{|\Omega|} \int_{\Omega} h_0(t, x, y) \, dy \), we get

\[
\lim_{\varepsilon \to 0} \sup \left[ \frac{\varepsilon}{2} \int_{\Gamma^e} h_0 \, d\sigma \right]_{t} \left. \right|_{t=\tau} - \frac{|\Gamma|}{2|Y|} \int_{\Omega} h_0 \, dx \, d\tau
\]
\[
= \lim_{\varepsilon \to 0} \sup \left[ \frac{\varepsilon}{2} \int_{\Gamma^e} h_0^2 \, d\sigma \right]_{t} \left. \right|_{t=\tau} - \frac{|\Gamma|}{2|Y|} \int_{\Omega} h_0^2 \, dx \, d\tau
\]
\[
+ \lim_{\varepsilon \to 0} \left[ - \frac{\varepsilon}{2} \int_{\Gamma^e} (G^0_2)^2 \, d\sigma + \frac{|\Gamma|}{2|Y|} \int_{\Omega} (G^0)^2 \, dx \right] \geq 0.
\]

For smooth \( \mu_i(t, x) \) and \( \mu_j(t, x, y) \), \( i, j, e \), we use Lemma 3.3 to pass to the limit in the third term:

\[
\frac{1}{c_m} \int_{\Omega} \int_{Y_e} A_{\varepsilon}[\mu_e](\mu_e - w_e) \, d\sigma \, d\tau
\]
\[
\rightarrow \frac{1}{c_m |Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \frac{\partial_t \mu_i^0 + \nabla_y \mu_i^1}{|Y|} \cdot \frac{\partial_t \mu_j^0 + \nabla_y \mu_j^1}{|Y|} \cdot \partial_t z_i^0 e_1 - \nabla_y z_i^1) \, d\tau \, d\sigma \, d\tau
\]
\[
+ \frac{1}{c_m |Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \frac{\partial_t \mu_i^0 + \nabla_y \mu_i^1}{|Y|} \cdot \frac{\partial_t \mu_j^0 + \nabla_y \mu_j^1}{|Y|} \cdot \partial_t z_i^0 e_1 - \nabla_y z_i^1) \, d\tau \, d\sigma \, d\tau.
\]

Taking the limit in (3.1) as \( \varepsilon \to 0 \) (along a subsequence) we obtain

\[
\lim_{\varepsilon \to 0} \sup \left[ \frac{\varepsilon}{2} \int_{\Gamma^e} w_0 \partial_t \partial_x \, d\sigma \right]_{t} \left. \right|_{t=\tau} - \frac{|\Gamma|}{2|Y|} \int_{\Omega} w_0 \partial_t \partial_x \, d\sigma \, d\tau
\]
\[
+ \lim_{\varepsilon \to 0} \sup \left[ \frac{\varepsilon}{2} \int_{\Gamma^e} h_0 \, d\sigma \right]_{t} \left. \right|_{t=\tau} - \frac{|\Gamma|}{2|Y|} \int_{\Omega} h_0 \, dx \, d\tau
\]
\[
\leq \frac{|\Gamma|}{|Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \partial_t w_0(\mu_0 - w_0) \, d\sigma \, d\tau \, d\tau + \frac{|\Gamma|}{|Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \partial_t h_0(\rho - h_0) \, dx \, d\tau
\]
\[
+ \frac{1}{c_m |Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \frac{\partial_t \mu_0^0 + \nabla_y \mu_0^1}{|Y|} \cdot \frac{\partial_t \mu_j^0 + \nabla_y \mu_j^1}{|Y|} \cdot \partial_t z_i^0 e_1 - \nabla_y z_i^1) \, d\tau \, d\sigma \, d\tau
\]
\[
+ \frac{1}{c_m |Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \frac{\partial_t \mu_0^0 + \nabla_y \mu_0^1}{|Y|} \cdot \frac{\partial_t \mu_j^0 + \nabla_y \mu_j^1}{|Y|} \cdot \partial_t z_i^0 e_1 - \nabla_y z_i^1) \, d\tau \, d\sigma \, d\tau
\]
\[
+ (\lambda - \frac{1}{c_m}) |\Gamma| \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \frac{\rho(\mu_0 - w_0) \, d\sigma \, d\tau \, d\tau
\]
\[
- \frac{|\Gamma|}{|Y|} \int_{\Omega} \int_{Y_e} \int_{0}^{t} \int_{\Gamma^e} \rho(\rho - h_0) \, d\sigma \, d\tau
\]

(32)
Then, for smooth test functions \( \psi \)
transform the integrand in second line of (32) to the form

\[
- \frac{1}{Y} \int_0^t \int_\Omega [\mu_0(\rho - h_0) \, dx \, d\tau] + \frac{1}{3c_m Y} \int_0^t \int_\Omega \int_0^1 e^{2\lambda \tau} [\mu_0]^3 (|\mu_0| - w_0) \, dx \, d\tau
- \int_0^t \int_\Sigma e^{-\lambda \tau} J^c (\mu^i - z^i_0) \, d\sigma \, d\tau - a \frac{\Gamma}{Y} \int_0^t \int_\Omega e^{-\lambda \tau} (\rho - h_0) \, d\sigma \, d\tau,
\]

where \([\mu_0] = \mu_0^i - \mu_0^c\). Consider the spaces

\[
H_t = \{ z^i \in L^2(\Omega) : \partial_x z^i \in L^2(\Omega), z^i = 0 \text{ on } S_0 \cup S_L \}, \\
H_e = \{ z^e \in L^2(\Omega) : \nabla z^e \in L^2(\Omega)^3, z^e = 0 \text{ on } S_0 \cup S_L \},
\]

with the standard \(H^1\)-norm in \(H_e\), and

\[
\|z\|_H = \left( \int_\Omega |z|^2 \, dx \right)^{\frac{1}{2}} + \left( \int_\Omega |\partial_x z|^2 \, dx \right)^{\frac{1}{2}}.
\]

By density of smooth functions, inequality (32) still holds for test functions \( \mu_1^i \in L^2((0, T) \times \Omega; H^1(Y_l)) \), and \( \mu_0^i \in L^2(0, T; H_t) \) such that \([\mu_0] \in L^2((0, T) \times \Omega)\).

Modifying the test function \( \mu_1^i \) by setting \( \mu_1^i(x, y) = \overline{\mu}_1^i(x, y) - \nabla x \mu_0^i \cdot y \) we transform the integrand in second line of (32) to the form

\[
a_i(\partial_x \mu_0^i e_1 + \nabla_y \overline{\mu}_1^i) \cdot (\partial_x \mu_0^e e_1 + \nabla_y \overline{\mu}_1^e - \partial_x z_0^e e_1 - \nabla_y z_1^e).
\]

Then, for smooth test functions \( \psi^i(t, x), \varphi(t, x) \) vanishing at \( x = 0, L \), and \( \Psi^i(t, x, y) \) periodic in \( y \) and equal to zero when \( x = 0, L, l = i, e \), we can set

\[
\begin{align*}
\mu_0^i(t, x) &= z_0^i(t, x) + \delta \psi^i(t, x), \quad l = i, e, \\
\mu_1^i(t, x, y) &= z_1^i(t, x, y) + \delta \Psi^i(t, x, y), \\
\overline{\mu}_1^i(t, x, y) &= z_1^i(t, x, y) + \delta \Psi^i(t, x, y), \\
\rho(t, x) &= h_0(t, x) + \delta \varphi(t, x),
\end{align*}
\]

where \( \delta \) is a small auxiliary parameter. Setting \( [\psi] = \psi^i - \psi^e \), we have that

\[
\begin{align*}
&\limsup_{\varepsilon \to 0} \left[ \varepsilon \int_0^t \int_{Y_l} w_e \partial_x w_e \, d\sigma \, d\tau - \frac{\Gamma}{|Y|} \int_0^t \int_\Omega w_0 \partial_x w_0 \, dx \, d\tau \right] \\
+ \limsup_{\varepsilon \to 0} \left[ \varepsilon \int_0^t \int_{Y_e} h_e \partial_x h_e \, d\sigma \, d\tau - \frac{\Gamma}{|Y|} \int_0^t \int_\Omega h_0 \partial_x h_0 \, dx \, d\tau \right] \\
\leq \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{Y_l} \partial_x w_0 [\psi] \, d\sigma \, d\tau + \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{Y_e} \partial_x h_0 \varphi \, d\sigma \, d\tau \\
+ \frac{\delta}{c_m |Y|} \int_0^t \int_{Y_l} \int_{Y_l} a_e (\partial_{x_1} (z_0^i + \delta \psi^i) e_1 + \nabla_y (z_1^i + \delta \Psi^i)) \cdot (\partial_{x_1} (\psi^i e_1 + \nabla_y \Psi^i) dxdy \, d\tau \\
+ \frac{\delta}{c_m |Y|} \int_0^t \int_{Y_e} \int_{Y_l} a_e (\nabla (z_0^e + \delta \psi^e) + \nabla_y (z_1^e + \delta \Psi^e)) \cdot (\nabla \psi^e + \nabla_y \Psi^e) dxdy \, d\tau
\end{align*}
\]
\[ + (\lambda - \frac{1}{c_m}) \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{\Omega} \left( \omega_0 + \delta [\psi] \right) dxd\tau \]

\[ - \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{\Omega} \left( h_0 + \delta \varphi \right) dxd\tau + (b + \lambda) \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{\Omega} \left( h_0 + \delta \varphi \right) dxd\tau \]

\[ - \theta \frac{\delta |\Gamma|}{|Y|} \int_0^t \int_{\Omega} \left( \omega_0 + \delta [\psi] \right) \varphi dxd\tau + \frac{|\Gamma|}{3c_m|Y|} \delta \int_0^t \int_{\Omega} e^{2\lambda \tau} \left( \omega_0 + \delta [\psi] \right)^2 [\psi] dxd\tau \]

\[ - \frac{\delta}{c_m} \int_0^t \int_{\Sigma} e^{-\lambda \tau} J^\epsilon \psi \sigma d\sigma d\tau + \frac{a}{|\Gamma|} \int_0^t \int_{\Omega} e^{-\lambda \tau} \varphi d\sigma d\tau. \]

Since the left-hand side of (33) is non-negative and \( \delta \) is arbitrary, we obtain

\[
\limsup_{\epsilon \to 0} \left[ \epsilon \int_{\Gamma_\epsilon} |w_\epsilon|^2 d\sigma - \frac{|\Gamma|}{|Y|} \int_{\Omega} \omega_0^2 \right] = 0,
\]

\[
\limsup_{\epsilon \to 0} \left[ \epsilon \int_{\Gamma_\epsilon} |h_\epsilon|^2 d\sigma - \frac{|\Gamma|}{|Y|} \int_{\Omega} h_0^2 \right] = 0.
\]

Note that the last convergence implies that the two-scale limit \( \tilde{h}_0 \) does not depend on \( y \). Indeed, by Proposition 2.5 in [21], one has the estimate

\[
\limsup_{\epsilon \to 0} \epsilon \int_{\Gamma_\epsilon} |h_\epsilon|^2 d\sigma \geq \frac{1}{|\Gamma|} \int_{\Gamma} |\tilde{h}_0|^2 d\sigma_y d\sigma_x \geq \frac{|\Gamma|}{|Y|} \int_{\Omega} h_0^2 dx.
\]

Thus, one can see that

\[
\frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |\tilde{h}_0|^2 d\sigma_y dx = \int_{\Omega} \left( \frac{1}{|\Gamma|} \int_{\Gamma} \tilde{h}_0 d\sigma_y \right)^2 dx.
\]

Moreover, it is clear that

\[
\frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |\tilde{h}_0|^2 d\sigma_y dx = \frac{1}{|\Gamma|} \int_{\Gamma} \int_{\Gamma} |\tilde{h}_0 - h_0|^2 d\sigma_y dx
\]

\[+ \frac{2}{|\Gamma|} \int_{\Omega} \int_{\Gamma} (\tilde{h}_0 - h_0) h_0 d\sigma_y dx
\]

\[+ \frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |h_0|^2 d\sigma_y dx = \int_{\Omega} h_0^2 dx,
\]

which yields

\[
\frac{1}{|\Gamma|} \int_{\Omega} \int_{\Gamma} |\tilde{h}_0 - h_0|^2 d\sigma_y dx = 0 \Rightarrow \tilde{h}_0 = h_0(t, x).
\]

Now, dividing (33) by \( \delta \neq 0 \) and passing to the limit as \( \delta \to +0 \) and \( \delta \to -0 \), we derive

\[
\frac{|\Gamma|}{|Y|} \int_0^t \int_{\Omega} \partial_\tau \omega_0 [\psi] dxd\tau + \frac{|\Gamma|}{|Y|} \int_0^t \int_{\Omega} \partial_\tau h_0 [\psi] dxd\tau
\]
Lemma 3.3. Indeed, for any smooth test function $\psi$, we have

$$+ \frac{1}{c_m} \int_0^t \int_{Y_i} a_i(\partial_{x_i} z_0^i \mathbf{e}_1 + \nabla_y z_0^i) \cdot (\partial_{x_i} \psi \mathbf{e}_1 + \nabla_y \psi^i) dy dx d\tau$$

$$+ \frac{1}{c_m} \int_0^t \int_{Y_i} a_t(\nabla z_0^i + \nabla_y z_0^i) \cdot (\nabla \psi^c + \nabla_y \Psi^c) dy dx d\tau$$

$$+ (\lambda - \frac{1}{c_m}) \frac{|\Gamma|}{|Y|} \int_0^t \int_{Y_0} w_0[\psi] d\tau dx - \frac{|\Gamma|}{|Y|} c_m \int_0^t \int_{Y_0} h_0[\psi] d\tau dx$$

Taking $\psi^i = \psi^c = \varphi = 0$, we obtain $z_0^c(t, x, y) = N^c(y) \cdot \nabla z_0^c(t, x)$, $z_0^i(t, x, y) = N_1^c(y) \partial_{x_i} z_0^c(t, x)$, where $N_0^c, N_1^c$ solve the cell problems (25) and (26), respectively. Note that in the case when $Y_i$ is a cylinder—constant cross-section—, $N_1^c(y)$ is constant. Recalling the definition of the effective coefficients $(a_{\text{eff}}^{ik})_{kl}$ [4], and taking $\Psi^c = 0$, we obtain

$$\int_0^t \int_{Y_0} \partial_t w_0[\psi] d\tau dx + \int_0^t \int_{Y_0} \partial_t h_0 \varphi d\tau dx$$

$$+ \frac{1}{c_m} \int_0^t \int_{Y_0} a_{\text{eff}}^{ik} \partial_{x_i} z_0^c \partial_{x_k} \psi^c d\tau + \frac{1}{c_m} \int_0^t \int_{Y_0} a_{\text{eff}}^{ik} \nabla z_0^c \cdot \nabla \psi^c d\tau$$

$$+ (\lambda - \frac{1}{c_m}) \frac{|\Gamma|}{|Y|} \int_0^t \int_{Y_0} w_0[\psi] d\tau dx - \frac{|\Gamma|}{|Y|} c_m \int_0^t \int_{Y_0} h_0[\psi] d\tau dx$$

$$+ (b + \lambda) \int_0^t \int_{Y_0} h_0 \varphi d\tau dx - \theta \int_0^t \int_{Y_0} w_0 \varphi d\tau dx$$

$$+ \frac{1}{3c_m} \int_0^t \int_{Y_0} e^{2\lambda t} w_0^3[\psi] d\tau dx$$

$$= \frac{|\Gamma|}{c_m |Y|} \int_0^t \int_{\Sigma} e^{-\lambda t} J^e \psi^c d\sigma d\tau + \alpha \int_0^t \int_{\Omega} e^{-\lambda t} \varphi d\sigma d\tau.$$

Performing the change of unknowns $u_0^i = e^{\lambda t} z_0^i$, $v_0 = e^{\lambda t} w_0$, $g_0 = e^{\lambda t} h_0$, we obtain (2). Note that the initial condition $v_0(0, x) = V^i - V^c$ is obtained using Lemma 3.3. Indeed, for any smooth test function $\psi(t, x)$ such that $\psi(T, x) = 0$, we have

$$\int_\Omega z_0^c(0, x) \psi dx = \int_0^T \int_\Omega \left( z_0^c \partial_t \psi + \partial_t z_0^c \psi \right) dx dt$$

$$\xrightarrow{\varepsilon \to 0} \int_0^T \int_\Omega \left( z_0^c \partial_t \psi + \partial_t z_0^c \psi \right) dx dt = \int_\Omega V^i \psi dx.$$
The proof of Theorem 2.1 is completed.

4. Well-posedness of the limit problem

In order to prove the well-posedness of the homogenized problem given by its weak formulation (34), we rewrite it in matrix form as an abstract parabolic equation. We introduce \( q_0 \) solving the auxiliary problem in \( \Omega \):

\[
- \text{div}(a_{\text{eff}} \nabla q_0) - a^i_{\text{eff}} \partial_{x_i} q_0 = 0, \quad x \in \Omega, \\
a_{\text{eff}} \nabla q_0 \cdot \nu = \frac{|Y|}{|\Gamma|} J^e, \quad x \in \Sigma, \\
q_0 = 0, \quad x \in S_0 \cup S_L. 
\]

Here, the effective coefficient \( a^i_{\text{eff}} = |Y_i| a_i / |\Gamma| \). Multiplication (35) by a smooth test function \( \psi^e \) such that \( \psi^e = 0 \) on \( S_0 \cup S_L \) leads to

\[
\frac{|Y|}{|\Gamma|} \int_\Sigma J^e \psi^e d\sigma = \int_\Omega a^i_{\text{eff}} \nabla q_0 \cdot \nabla \psi^e d\sigma + \int_\Omega a^i_{\text{eff}} \partial_{x_i} q_0 \partial_{x_i} \psi^e d\sigma. 
\]

Substituting (36) into (34), and introducing \( \tilde{z}^i_0 = z^i_0 - q_0 e^{-\lambda t} \), \( i, e \), we have the following weak formulation:

\[
\int_0^t \int_\Omega \partial_\tau w_0[\psi] \, dx \, d\tau + \int_0^t \int_\Omega \partial_\tau h_0 \varphi \, dx \, d\tau \\
+ \frac{1}{c_m} \int_0^t \int_\Omega a^i_{\text{eff}} \partial_{x_i} \tilde{z}^i_0 \partial_{x_i} \psi^i d\sigma d\tau + \frac{1}{c_m} \int_0^t \int_\Omega a^e_{\text{eff}} \nabla \tilde{z}^e_0 \cdot \nabla \psi^e d\sigma d\tau \\
+ \left( \lambda - \frac{1}{c_m} \right) \int_0^t \int_\Omega w_0[\psi] \, dx \, d\tau - \frac{1}{c_m} \int_0^t \int_\Omega h_0[\psi] \, dx \, d\tau \\
+ (b + \lambda) \int_0^t \int_\Omega h_0 \varphi \, dx \, d\tau - \theta \int_0^t \int_\Omega w_0 \varphi \, dx \, d\tau \\
+ \frac{1}{3c_m} \int_0^t \int_\Omega e^{2\lambda t} w^3_0[\psi] \, dx \, d\tau \\
= a \int_0^t \int_\Omega e^{-\lambda t} \varphi \, d\sigma d\tau + \int_0^t \int_\Omega e^{-\lambda t} a^i_{\text{eff}} \partial^2_{x_i x_i} q_0 [\psi] \, dx \, d\tau. 
\]

We seek to rewrite the weak formulation (37) in matrix form as an abstract parabolic equation. To this end, we first introduce the following functional spaces:

\[
H_0 = L^2(\Omega) \times L^2(\Omega), \\
H_i = \{ z^i \in L^2(\Omega) : \partial_{x_i} z^i \in L^2(\Omega), \, z^i = 0 \, \text{on} \, S_0 \cup S_L \}, \\
H_e = \{ z^e \in L^2(\Omega) : \nabla z^e \in L^2(\Omega)^3, \, z^e = 0 \, \text{on} \, S_0 \cup S_L \}, \\
X_0 = \{ w = z^i - z^e : \, z^i \in H_i, \, z^e \in H_e \}. 
\]
The norm in $H_i$ is given by
\[ \|z\|^2_{H_i} = \int_\Omega |z|^2 \, dx + \int_\Omega |\partial_{x_1}z|^2 \, dx. \]

For the one associated to $H_e$, we adopt the standard $H^1$-norm. For each element $w_0 \in X_0$, we associate a unique pair $(\tilde{z}_i^0, \tilde{z}_e^0) \in H_i \times H_e$ solving the following problem
\[ -a_{\text{eff}} \partial_{x_1}^2 \tilde{z}_i^0 = \text{div}(a_{\text{eff}} \nabla \tilde{z}_e^0), \quad x \in \Omega, \]
\[ \tilde{z}_i^0 - \tilde{z}_e^0 = w_0, \quad x \in \Omega, \]
\[ a_{\text{eff}} \nabla \tilde{z}_e^0 \cdot \nu = 0, \quad x \in \Sigma, \]
\[ \tilde{z}_i^0 = \tilde{z}_e^0 = 0, \quad x \in S_0 \cup S_L. \]

The pair $(\tilde{z}_i^0, \tilde{z}_e^0)$ can be determined by solving the minimization problem
\[ \|w_0\|^2_{W_0} := \inf \left\{ \int_\Omega a_{\text{eff}} |\partial_{x_1}z_i^0|^2 \, dx + \int_\Omega a_{\text{eff}} \nabla z_i^0 \cdot \nabla z_e^0 \, dx \mid z_i^0 \in W_i, \ z_e^0 \in W_e \right\}. \]

Note that $W_0$ is a Hilbert space with a scalar product given by
\[ (z_1^i, z_2^i)_{L^2(\Omega)} := \int_\Omega a_{\text{eff}} \partial_{x_1}^2 z_i^0 \partial_{x_1} z_i^0 \, dx + \int_\Omega a_{\text{eff}} \nabla z_i^0 \cdot \nabla z_e^0 \, dx, \]
where $(z_1^i, z_2^i)$ and $(z_1^e, z_2^e)$ solve (38) for $w_1, w_2$ given. Now (37) is written in the form
\[ \partial_t \begin{pmatrix} w_0 \\ h_0 \end{pmatrix} + \frac{1}{c_m} A_{\text{eff}} w_0 + \frac{1}{c_m} \left( \frac{2\lambda t}{3} w_0^3 - w_0 - h_0 \right) + \lambda w_0 = e^{-\lambda t} \begin{pmatrix} a_{\text{eff}} \partial_{x_1}^2 q_0 \\ a \end{pmatrix}, \]
where the operator $A_{\text{eff}}$ defined on smooth functions $w_0$ by
\[ (A_{\text{eff}} w_0, [\psi])_{L^2(\Omega)} := \int_\Omega a_{\text{eff}} \partial_{x_1} z_i^0 \partial_{x_1} \chi^i \, dx + \int_\Omega a_{\text{eff}} \nabla z_i^0 \cdot \nabla \psi^e \, dx, \]
and $(\tilde{z}_i^0, \tilde{z}_e^0)$ solve (38). In operator form one writes
\[ \partial_t W_0 + A_0(t, W_0) = F_0(t), \quad (t, x) \in (0, T) \times \Omega, \]
\[ W_0(0, x) = W_0^0(x), \quad x \in \Omega. \]

Therein, we have the following operators
\[ A_0(t, W_0) := B_0^{(1)}(t, W_0) + B_0^{(2)}(t, W_0), \]
\[ B_0^{(1)}(t, W_0) := \left( \frac{1}{c_m} A_{\text{eff}} w_0 + (\lambda - \frac{1}{c_m}) w_0 - \frac{1}{c_m} h_0 \right), \]
\[ B_0^{(2)}(t, W_0) := \left( \frac{e^{2\lambda t}}{3c_m} w_0^3 \right), \]
\[ F_0(t) := e^{-\lambda t} \left( \frac{a_{\text{eff}} \partial_x^2 q_0}{a} \right). \]

Introducing the spaces
\[
H_0 = L^2(\Omega) \times L^2(\Omega), \quad V_1 = X_0 \times L^2(\Omega), \quad V'_1 = X'_0 \times L^2(\Omega),
\]
\[
V_2 = L^4(\Omega) \times L^2(\Omega), \quad V'_2 = L^{4/3}(\Omega) \times L^2(\Omega),
\]
we can prove the existence of a unique solution \( W_0 \in L^\infty((0, T); H_0) \cap L^2((0, T); V_1) \cap L^4((0, T); V_2) \) to problem (39). It follows, as in Section 2.3 from Theorem 1.4 in [22] and Remark 1.8 in Chapter 2.

**Appendix A. Monotonicity method**

The passage to the limit in the microscopic problem requires us to adapt the method of monotone operators due to G. Minty [25]. The application of the method to problem (1) is given in Section 3. The proof is quite technical, and in order to extract the main idea of the method we provide its brief description for a model case when the monotone operator is independent of \( \varepsilon \). In [26], it is shown how to combine the method of monotone operators and the two-scale convergence for a stationary problem.

Let \( A \) be a nonlinear continuous monotone operator in a Hilbert space \( H \). The scalar product in \( H \) will be denoted by \( (u, v) \). We consider a parabolic problem
\[
\partial_t u_\varepsilon + A(u_\varepsilon) = f_\varepsilon, \quad \text{(A.1)}
\]
\[
\left. u_\varepsilon \right|_{t=0} = V_\varepsilon^0.
\]
Assume that we know that \( u_\varepsilon \) converges weakly to \( u_0 \), \( \partial_t u_\varepsilon \) converges weakly to \( \partial_t u_0 \), and \( f_\varepsilon, V_\varepsilon^0 \) converge strongly in \( H \) to \( f \) and \( V^0 \), respectively, as \( \varepsilon \to 0 \). We aim to show that \( u_0 \) satisfies the limit equation \( \partial_t u_0 + A(u_0) = f \). Note that, because of the weak convergence, we cannot pass to the limit in the nonlinear term \( A(u_\varepsilon) \) directly.

By monotonicity, for any \( w_1, w_2 \in D(A) \), one has
\[
(A(w_1) - A(w_2), w_1 - w_2) \geq 0.
\]
Taking \( w_1 = u_\varepsilon, w_2 = u_0 + \delta \varphi, \) with \( \delta \in \mathbb{R} \) and \( \varphi \in C^1([0,T]; D(A)) \), and using \( (A.1) \), we get

\[
0 \leq \int_0^t (A(u_\varepsilon) - A(u_0 + \delta \varphi), u_\varepsilon - (u_0 + \delta \varphi))d\tau.
\]

\[
= \int_0^t (f_\varepsilon, u_\varepsilon - (u_0 + \delta \varphi))d\tau - \int_0^t (\partial_\tau u_\varepsilon, u_\varepsilon)d\tau + \int_0^t (\partial_\tau u_\varepsilon, (u_0 + \delta \varphi))d\tau.
\]

\[
(A.2)
\]

Integrating by parts, we get

\[
\int_0^t (\partial_\tau u_\varepsilon, u_\varepsilon)d\tau = \frac{1}{2} \int_0^t \frac{d}{d\tau} \|u_\varepsilon\|^2_H d\tau = \frac{1}{2} \|u_\varepsilon(t, \cdot)\|^2_H - \frac{1}{2} \|V^0\|^2_H.
\]

Then inequality \( (A.2) \) transforms into

\[
\frac{1}{2} \|u_\varepsilon(t, \cdot)\|^2_H - \frac{1}{2} \|u_0(t, \cdot)\|^2_H \leq \frac{1}{2} \|V^0\|^2_H + \frac{1}{2} \|V^0\|^2_H
\]

\[
\leq \int_0^t (f_\varepsilon, u_\varepsilon - (u_0 + \delta \varphi))d\tau - \int_0^t (\partial_\tau u_0, u_0)d\tau
\]

\[
+ \int_0^t (\partial_\tau u_\varepsilon, (u_0 + \delta \varphi))d\tau - \int_0^t (A(u_0 + \delta \varphi), u_\varepsilon - (u_0 + \delta \varphi))d\tau.
\]

\[
(A.3)
\]

Passage to the limit, as \( \varepsilon \to 0 \), in \( (A.3) \) yields

\[
0 \leq \frac{1}{2} \limsup_{\varepsilon \to 0} \left( \|u_\varepsilon(t, \cdot)\|^2_H - \|u_0(t, \cdot)\|^2_H \right)
\]

\[
\leq \delta \int_0^t (-f + \partial_\tau u_0 + A(u_0 + \delta \varphi), \varphi)d\tau.
\]

Since the left-hand side is positive and \( \delta \) is arbitrary, that delivers the strong convergence of \( u_\varepsilon \)

\[
\limsup_{\varepsilon \to 0} \left( \|u_\varepsilon(t, \cdot)\|^2_H - \|u_0(t, \cdot)\|^2_H \right) = 0.
\]

Furthermore, one can show that

\[
\int_0^t (\partial_\tau u_0 + A(u_0 + \delta \varphi) - f, \delta \varphi)d\tau \geq 0.
\]

\[
(A.4)
\]

Dividing \( (A.4) \) first by \( \delta > 0 \) and passing to the limit, as \( \delta \to 0 \), we obtain

\[
\int_0^t (\partial_\tau u_0 + A(u_0) - f, \varphi)d\tau \geq 0.
\]
Then, dividing (A.4) by $\delta < 0$ and passing to the limit, as $\delta \to 0$, we have the opposite inequality
\[
\int_0^t (\partial_\tau u_0 + A(u_0) - f, \varphi) d\tau \leq 0.
\]
Thus,
\[
\int_0^t (\partial_\tau u_0 + A(u_0) - f, \varphi) d\tau = 0.
\]
The last equality holds for an arbitrary $\varphi \in C^1(0, T; D(A))$, so $\partial_\tau u_0 + A(u_0) = f$.

This method is used for problem (10), where both the domain and the operator $A$ depend on $\varepsilon$, and the test functions have a more complicated two-scale structure.

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