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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.

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 [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 [2]. Later a more simple model for nonlinear dynamics in axons was introduced in [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 modeled by coupled systems of a large number of cable equations (cf. [7,8]), but a continuous mathematical model for a fascicle of myelinated axons, to our best knowledge, has not been rigorously derived. An analogous coupling phenomenon is observed in the electrical conductance of cardiac tissues [9], leading to the celebrated *bidomain model*, 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 employed for the asymptotic analysis. Homogenization techniques based on two-scale convergence and unfolding are applied to model syncytial tissues [13–16].

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

The asymptotic analysis of a nerve fascicle with a large number of axons also leads to a bidomain model. It was suggested in [19] that bidomain models provide a unified framework for modeling electrical stimulation of both peripheral nerves, cortical neurons, and syncytical tissues. In [20] 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 ε. By means of two-scale analysis we derive a bidomain model that describes the asymptotic behavior of the transmembrane potential on Ranvier nodes when ε 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 recast the problem to a form allowing us to combine the 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.

Fig. 1. A fascicle of myelinated axons and the periodicity cell Y.

2. Microscopic model

2.1. Problem setup

A nerve fascicle is modeled by the cylinder $\Omega := (0, L) \times \omega \subset \mathbb{R}^3$ with length $L > 0$ and cross-section $\omega \subset \mathbb{R}^2$, being a bounded domain in $\mathbb{R}^2$ with a Lipschitz boundary $\partial\omega$ (see Fig. 1). The lateral boundary of the cylinder is denoted by $\Sigma := [0, L] \times \partial\omega$, with bases $S_0 := \{0\} \times \omega$, $S_L := \{L\} \times \omega$. 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 $Y_i := [-\frac{1}{2}, \frac{1}{2}) \times D_{r_0}$, where D_{r_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 $\Gamma_{mi} := \overline{Y}_i \cap \overline{Y}_m$ the interface between Y_i and Y_m. The interface between the extracellular domain Y_e and a myelin sheath Y_m is $\Gamma_{me} := \overline{Y}_e \cap \overline{Y}_m$. The unmyelinated part of the boundary of Y_i –the Ranvier node– will be denoted by $\Gamma = \overline{Y}_i \cap \overline{Y}_e$ (see Fig. 1). We will assume that Γ does not degenerate, and, for simplicity, that Γ 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 Ω. 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 Fig. 1). The unmyelinated part of the boundary of Ω^i_ε is denoted by Γ_ε. The boundary of the myelin is denoted by Γ^m_ε. Let u_ε denotes the electric potential $u_\varepsilon = u^l_\varepsilon$ in Ω^l_ε, $l = i, e$. We assume that u_ε satisfies homogeneous Neumann boundary conditions on the boundary of the myelin sheath Γ^m_ε, i.e. the myelin sheath is assumed to be a perfect insulator (see [4] for other insulation assumptions). The transmembrane potential $v_\varepsilon = [u_\varepsilon] = u^i_\varepsilon - u^e_\varepsilon$ is the potential jump across the Ranvier nodes Γ_ε. We assume that the conductivity is a piecewise constant function:

$$a_\varepsilon = \begin{cases} a_e & \text{in } \Omega^e_\varepsilon, \\ a_i & \text{in } \Omega^i_\varepsilon, \end{cases}$$

with a_e and a_i real, positive and bounded. On Γ_ε we further assume current continuity, and FitzHugh–Nagumo [3,21] dynamics for the transmembrane potential. Namely, the ionic current is described as

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

where g_ε 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 $\theta, a, b > 0$. The recovery variable is introduced to eliminate the excitability of the model after excitation has occurred (see [3]).

We consider an arbitrary time interval $(0, T)$, with $T > 0$. The electric activity in the bundle Ω is described by the following system of equations for the unknowns v_ε and g_ε:

$$\begin{aligned}
&-\operatorname{div}(a_\varepsilon \nabla u_\varepsilon) = 0, && (t,x) \in (0,T) \times (\Omega_\varepsilon^i \cup \Omega_\varepsilon^e),\\
&a_e \nabla u_\varepsilon^e \cdot \nu = a_i \nabla u_\varepsilon^i \cdot \nu, && (t,x) \in (0,T) \times \Gamma_\varepsilon,\\
&\varepsilon(c_m \partial_t [u_\varepsilon] + I_{ion}([u_\varepsilon], g_\varepsilon)) = -a_i \nabla u_\varepsilon^i \cdot \nu, && (t,x) \in (0,T) \times \Gamma_\varepsilon,\\
&\partial_t g_\varepsilon = \theta[u_\varepsilon] + a - b g_\varepsilon, && (t,x) \in (0,T) \times \Gamma_\varepsilon,\\
&u_\varepsilon = 0, && (t,x) \in (0,T) \times (S_0 \cup S_L),\\
&a_e \nabla u_\varepsilon^e \cdot \nu = J_\varepsilon^e(t,x), && (t,x) \in (0,T) \times \Sigma,\\
&\nabla u_\varepsilon^e \cdot \nu = 0, && (t,x) \in (0,T) \times \Gamma_\varepsilon^m,\\
&[u_\varepsilon](0,x) = V_\varepsilon^0(x), \ g_\varepsilon(0,x) = G_\varepsilon^0(x), && x \in \Gamma_\varepsilon,
\end{aligned} \tag{1}$$

where ν denotes the unit normal on Γ_ε, Γ_ε^m, and Σ, exterior to Ω_ε^i, Ω_ε^m, and Ω, respectively. The function $J_\varepsilon^e(t,x)$ models an external boundary excitation of the nerve fascicle. The membrane capacity per unit area c_m is assumed to be a positive constant. The myelin sheath is assumed to be a perfect insulator implying that the electrical field does not penetrate it: this leads to the homogeneous Neumann boundary condition on Γ_ε^m. That is why the equation in the bulk is posed for $x \in \Omega_\varepsilon^i \cup \Omega_\varepsilon^e$.

System (1), modeling the electrical conduction in nerves, arises from Maxwell equations in the quasi-stationary approximation. A derivation of (1) from the first principles is presented in [22] (see also [23] for a numerical comparison of different models). On the membrane Γ_ε we assume the continuity of fluxes condition and the nonlinear FitzHugh dynamics for the potential jump (action potential) $[u_\varepsilon]$. A similar model has been used for modeling the electric conduction in the cardiac tissue (cf. [11,12,15,16]). While the cardiac tissue models assume that both intracellular and extracellular domains are connected, in the present model the intracellular domain is formed by non-intersecting individual axons.

We study the asymptotic behavior of u_ε, as $\varepsilon \to 0$, and derive a macroscopic model describing the potential u_ε in the fascicle, under the following conditions:

(H1) The initial data is such that[1] $\|V_\varepsilon^0\|_{L^4(\Gamma_\varepsilon)} \le C$. Moreover, we assume that V_ε^0 can be extended to the whole Ω such that, keeping the same notation for the extension, $\|V_\varepsilon^0\|_{H^1(\Omega)} \le C$ and $V_\varepsilon^0 = 0$ on $S_0 \cup S_L$. We also assume that there exists a weak limit $V_\varepsilon^0 \rightharpoonup V^0$ in $H^1(\Omega)$.

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

- for any $\phi \in C(\overline{\Omega})$, it holds that

$$\lim_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} G_\varepsilon^0(x)\phi(x)\, d\sigma = \frac{|\Gamma|}{|Y|} \int_\Omega G^0(x)\phi(x)\, dx;$$

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

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

$$\int_0^T \int_\Sigma |\partial_t J_\varepsilon^e|^2\, d\sigma d\tau \le C.$$

Remark 1. Hypothesis (H2) actually assumes strong two-scale convergence (cf. Proposition 2.5 in [24]). Hypothesis (H2) is satisfied if G_ε^0 is sufficiently regular, e.g., continuous, and independent of ε. Note that (H1) and (H2) are not satisfied for rapidly oscillating initial data.

[1] Throughout, C denotes a generic constant independent of ε, whose value may be different from line to line.

Remark 2. The scaling factor ε in the nonlinear equation for $[u_\varepsilon]$ on Γ_ε leads to a limit bidomain model and a nontrivial coupling of the potentials in the individual axons in the bundle through the extracellular currents. Different scaling factors in the equation on the Ranvier nodes Γ_ε might be considered. In [25,26], the authors address an hierarchy of models for the electrical conduction of biological tissue in linear and nonlinear cases. Namely, for ε^k, $k=-1,0,1$, the homogenization procedure yields different limit problems.

2.2. Main result

The main result of the paper (Theorem 2.1 below) shows that the asymptotic behavior of solutions of the boundary value problem (1) is described by the following effective bidomain model in Ω:

$$\begin{aligned}
&c_m\partial_t v_0 + I_{ion}(v_0,g_0) = a_i^{\text{eff}}\partial^2_{x_1x_1}u_0^i, && (t,x)\in(0,T)\times\Omega,\\
&c_m\partial_t v_0 + I_{ion}(v_0,g_0) = -\text{div}\left(a_e^{\text{eff}}\nabla u_0^e\right), && (t,x)\in(0,T)\times\Omega,\\
&\partial_t g_0 = \theta v_0 + a - b\,g_0, && (t,x)\in(0,T)\times\Omega,\\
&u_0^{i,e}(t,x)=0, && (t,x)\in(0,T)\times(S_0\cup S_L),\\
&a_e^{\text{eff}}\nabla u_0^e\cdot\nu = J^e, && (t,x)\in(0,T)\times\Sigma,\\
&v_0(0,x)=V^0(x),\ \ g_0(0,x)=G^0(x), && x\in\Omega,
\end{aligned} \tag{2}$$

where $v_0 = u_0^i - u_0^e$. The effective scalar coefficient a_i^{eff} is

$$a_i^{\text{eff}} := \frac{|Y_i|}{|\Gamma|}a_i. \tag{3}$$

The effective matrix $a_e^{\text{eff}}\in\mathbb{R}^{3\times3}$ is given by

$$(a_e^{\text{eff}})_{kl} := \frac{1}{|\Gamma|}\int_{Y_e} a_e(\partial_l N_k^e(y)+\delta_{kl})\,dy, \quad k,l=1,2,3, \tag{4}$$

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

$$\begin{aligned}
&-\Delta N_k^e = 0, && y\in Y_e,\\
&\nabla N_k^e\cdot\nu = -\nu_k, && y\in\Gamma\cup\Gamma_m,\\
&N_k^e(y)\ \text{ is }\ Y-\text{periodic}.
\end{aligned}$$

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

(i) For any $\phi(t,x)\in C([0,T]\times\overline{\Omega})$, it holds that

$$\lim_{\varepsilon\to0}\varepsilon\int_0^T\int_{\Gamma_\varepsilon}v_\varepsilon(t,x)\phi(t,x)\,d\sigma_x dt = \frac{|\Gamma|}{|Y|}\int_0^T\int_\Omega v_0(t,x)\phi(t,x)\,dxdt,$$

and for any $t\in[0,T]$ $\lim_{\varepsilon\to0}\varepsilon\int_{\Gamma_\varepsilon}|v_\varepsilon|^2\,d\sigma = \frac{|\Gamma|}{|Y|}\int_\Omega|v_0|^2\,dx$.

(ii) For any $\phi(t,x)\in C([0,T]\times\overline{\Omega})$,

$$\lim_{\varepsilon\to0}\varepsilon\int_0^T\int_{\Gamma_\varepsilon}g_\varepsilon(t,x)\phi(t,x)\,d\sigma_x dt = \frac{|\Gamma|}{|Y|}\int_0^T\int_\Omega g_0(t,x)\phi(t,x)\,dxdt,$$

and for any $t\in[0,T]$ $\lim_{\varepsilon\to0}\varepsilon\int_{\Gamma_\varepsilon}|g_\varepsilon|^2\,d\sigma = \frac{|\Gamma|}{|Y|}\int_\Omega|g_0|^2\,dx$.

(iii) $\lim_{\varepsilon\to0}\int_0^T\int_{\Omega_\varepsilon^{i,e}}\left|u_\varepsilon^{i,e}-u_0^{i,e}\right|^2 dxdt = 0.$

Remark 3. If v_0 is continuous, the convergences (i), (ii) imply strong convergence of v_ε. 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 that

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

Remark 4. This result can be generalized to the case of a varying cross section, as in [5]. In such a case, the solution N_1^i of the cell problem (A.5) is no longer constant, and the corresponding effective coefficient is given by

$$a_i^{\text{eff}} = \frac{1}{|\Gamma|} \int_{Y_i} a_i(\partial_1 N_1^i + 1) dy.$$

Remark 5. Hypothesis (H2) can be generalized to the case of an oscillating initial function G_ε^0. Namely, assume that there exists $G^0(x,y) \in L^2(\Omega \times \Gamma)$, Y-periodic in y such that

- for any $\phi(x,y) \in C(\overline{\Omega} \times Y)$, Y-periodic in y,

$$\lim_{\varepsilon\to 0} \varepsilon \int_{\Gamma_\varepsilon} G_\varepsilon^0(x)\phi\left(x, \frac{x}{\varepsilon}\right) d\sigma_x = \frac{1}{|Y|} \int_\Omega \int_\Gamma G^0(x,y)\phi(x,y)\, d\sigma_y dx;$$

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

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

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

Thanks to the linearity of the equation $\partial_t \widetilde{g}_0 = \theta v_0 + a - b\,\widetilde{g}_0$, 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 $\phi = \begin{cases} \phi^i \text{ in } \Omega_\varepsilon^i \\ \phi^e \text{ in } \Omega_\varepsilon^e \end{cases}$, $\phi^{i,e} = 0$ on $S_0 \cup S_L$, and integrate by parts:

$$\varepsilon \int_{\Gamma_\varepsilon} c_m \partial_t v_\varepsilon [\phi]\, d\sigma + \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon \nabla u_\varepsilon \cdot \nabla \phi \, dx + \varepsilon \int_{\Gamma_\varepsilon} I_{ion}(v_\varepsilon, g_\varepsilon)[\phi]\, d\sigma = \int_\Sigma J_\varepsilon^e \phi \, d\sigma.$$

Let us introduce an auxiliary function q_ε solving the following problem:

$$-\text{div}\,(a_\varepsilon \nabla q_\varepsilon) = 0, \qquad x \in \Omega_\varepsilon^i \cup \Omega_\varepsilon^e \cup \Gamma_\varepsilon,$$

$$\begin{aligned}
&\nabla q_\varepsilon \cdot \nu = 0, && x \in \Gamma_{m,\varepsilon}, \\
&a_e \nabla q_\varepsilon \cdot \nu = J^e_\varepsilon(t,x), && x \in \Sigma, \\
&q_\varepsilon = 0, && x \in (S_0 \cup S_L).
\end{aligned} \tag{5}$$

Since the jump of q_ε through the Ranvier nodes Γ_ε is zero, the change of unknown

$$\widetilde{u}_\varepsilon = u_\varepsilon - q_\varepsilon$$

allows us to transfer the external excitation J^e_ε from the lateral boundary Σ to the membrane Γ_ε. Namely, we get the following weak formulation for the new unknown function $\widetilde{u}_\varepsilon$:

$$\varepsilon \int_{\Gamma_\varepsilon} c_m \partial_t v_\varepsilon [\phi]\, d\sigma + \int_{\Omega^i_\varepsilon \cup \Omega^e_\varepsilon} a_\varepsilon \nabla \widetilde{u}_\varepsilon \cdot \nabla \phi \, dx + \varepsilon \int_{\Gamma_\varepsilon} I_{ion}(v_\varepsilon, g_\varepsilon)[\phi]\, d\sigma + \int_{\Gamma_\varepsilon} (a_i \nabla q_\varepsilon \cdot \nu)[\phi]\, d\sigma = 0.$$

Let us define the subspace

$$H^1_{S_0 \cup S_L}(\Omega^i_\varepsilon \cup \Omega^e_\varepsilon) := \left\{ \phi \in H^1(\Omega^i_\varepsilon \cup \Omega^e_\varepsilon) \ : \ \phi\big|_{S_0 \cap S_L} = 0 \right\},$$

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

$$(A_\varepsilon v_\varepsilon, [\phi])_{L^2(\Gamma_\varepsilon)} := \int_{\Omega^i_\varepsilon \cup \Omega^e_\varepsilon} a_\varepsilon \nabla \widetilde{u}_\varepsilon \cdot \nabla \phi \, dx, \quad \forall\, \phi \in H^1_{S_0 \cup S_L}(\Omega^i_\varepsilon \cup \Omega^e_\varepsilon), \tag{6}$$

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

$$\begin{aligned}
&-\operatorname{div}(a_\varepsilon \nabla \widetilde{u}_\varepsilon) = 0, && x \in \Omega^i_\varepsilon \cup \Omega^e_\varepsilon, \\
&a_e \nabla \widetilde{u}^e_\varepsilon \cdot \nu = a_i \nabla \widetilde{u}^i_\varepsilon \cdot \nu, && x \in \Gamma_\varepsilon, \\
&\widetilde{u}^i_\varepsilon - \widetilde{u}^e_\varepsilon = v_\varepsilon, && x \in \Gamma_\varepsilon, \\
&a_\varepsilon \nabla \widetilde{u}_\varepsilon \cdot \nu = 0, && x \in \Gamma_{m,\varepsilon}, \\
&a_e \nabla \widetilde{u}_\varepsilon \cdot \nu = 0, && x \in \Sigma, \\
&\widetilde{u}_\varepsilon = 0, && x \in (S_0 \cup S_L).
\end{aligned} \tag{7}$$

Thus, problem (1) can be rewritten in the following compact form:

$$\begin{aligned}
&\varepsilon c_m \partial_t v_\varepsilon + A_\varepsilon v_\varepsilon + \varepsilon I_{ion}(v_\varepsilon, g_\varepsilon) = -a_i \nabla q_\varepsilon \cdot \nu, \\
&\partial_t g_\varepsilon + b g_\varepsilon - \theta v_\varepsilon = a
\end{aligned} \tag{8}$$

on Γ_ε. In order to reduce the problem to a monotone one, we perform the following change of unknowns:

$$W_\varepsilon = \begin{pmatrix} w_\varepsilon \\ h_\varepsilon \end{pmatrix} = e^{-\lambda t} \begin{pmatrix} v_\varepsilon \\ g_\varepsilon \end{pmatrix}, \quad W^0_\varepsilon = \begin{pmatrix} V^0_\varepsilon \\ G^0_\varepsilon \end{pmatrix}. \tag{9}$$

with λ real positive. Substituting (9) into (8) yields

$$\varepsilon \partial_t \begin{pmatrix} w_\varepsilon \\ h_\varepsilon \end{pmatrix} + \begin{pmatrix} \dfrac{1}{c_m} A_\varepsilon w_\varepsilon + \dfrac{\varepsilon}{c_m}\left(\dfrac{e^{2\lambda t}}{3} w^3_\varepsilon - w_\varepsilon - h_\varepsilon \right) + \varepsilon \lambda w_\varepsilon \\ \varepsilon(b+\lambda) h_\varepsilon - \varepsilon \theta w_\varepsilon \end{pmatrix} = e^{-\lambda t} \begin{pmatrix} -\dfrac{a_i}{c_m} \nabla q_\varepsilon \cdot \nu \\ \varepsilon a \end{pmatrix},$$

which can be further rewritten as follows:

$$\varepsilon \partial_t W_\varepsilon + \mathbb{A}_\varepsilon(t, W_\varepsilon) = F_\varepsilon(t), \quad (t,x) \in (0,T) \times \Gamma_\varepsilon, \tag{10}$$

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

with

$$\mathbb{A}_\varepsilon(t, W_\varepsilon) := B_\varepsilon^{(1)}(t, W_\varepsilon) + B_\varepsilon^{(2)}(t, W_\varepsilon), \tag{11}$$

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

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

Here the operator A_ε is defined in (6).

The existence of a unique solution to problem (10) follows from Theorem 1.4 in [27] and Remark 1.8 in Chapter 2 (see also Theorem 4.1 in [28]). For the reader's convenience, we formulate the corresponding result below.

Lemma 2.2. *Let V_i, $i = 1, \dots, m$, 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 $\{A_i(t);\ t \in [0,T]\}$, $i = 1, \dots, m$, 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 $\overline{c} > 0$ and $p_i > 1$,

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

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

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

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 $u \in \cap_{i=1}^m W^{1,q_i}([0,T];V_i')$ that satisfies

$$\begin{aligned} &u \in L^\infty([0,T];H),\ u \in \cap_{i=1}^m L^{p_i}([0,T];V_i), \\ &\frac{du}{dt}(t) + A(t)u(t) = f(t), \quad a.e.\ t \in (0,T), \\ &u(0) = u_0. \end{aligned}$$

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

$$\begin{aligned} &H = L^2(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon), \\ &\widetilde{H}^{1/2}(\Gamma_\varepsilon) = \left\{ v = (u^i - u^e)\Big|_{\Gamma_\varepsilon} \ :\ u^l \in H^1(\Omega_\varepsilon^l),\ u^l = 0 \text{ on } S_0 \cap S_L, l = i, e \right\}, \\ &V_1 = \widetilde{H}^{1/2}(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon), \quad V_1' = H^{-1/2}(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon), \\ &V_2 = L^4(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon), \quad V_2' = L^{4/3}(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon). \end{aligned}$$

As the operator $A_1(t,\cdot) : V_1 \to V_1'$ we take $B_\varepsilon^{(1)}(t,\cdot)$ given by (12); as the operator $A_2(t,\cdot) : V_2 \to V_2'$ we take $B_\varepsilon^{(2)}(t,\cdot)$ given by (13). Let us check that the operator $\mathbb{A}_\varepsilon(t,\cdot) = B_\varepsilon^{(1)} + B_\varepsilon^{(2)}$ satisfies the assumptions of Lemma 2.2 with $p_1 = 2$ and $p_2 = 4$. The right-hand side F_ε satisfies clearly the assumptions of Lemma 2.2.

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

(i) Monotonicity:

$$(B_\varepsilon^{(1)}(t,W_1) - B_\varepsilon^{(1)}(t,W_2), W_1 - W_2) \geq 0, \quad \forall\, W_1, W_2 \in V_1.$$

(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 $W_\varepsilon \in \widetilde{H}^{1/2}(\Gamma_\varepsilon) \times L^2(\Gamma_\varepsilon)$, we have that

$$\begin{aligned}(B_\varepsilon^{(1)}(t,W_\varepsilon), W_\varepsilon) = &\frac{1}{c_m}\int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon |\nabla \widetilde{w}_\varepsilon|^2\, dx + \varepsilon\left(\lambda - \frac{1}{c_m}\right)\int_{\Gamma_\varepsilon} |w_\varepsilon|^2\, d\sigma \\ &- \varepsilon\left(\theta + \frac{1}{c_m}\right)\int_{\Gamma_\varepsilon} h_\varepsilon w_\varepsilon\, d\sigma + \varepsilon(b+\lambda)\int_{\Gamma_\varepsilon} |h_\varepsilon|^2\, d\sigma.\end{aligned}$$

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

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

Here $C_1^\varepsilon, C_2^\varepsilon$, and C^ε 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 find that

$$\begin{aligned}(B_\varepsilon^{(1)}(t,W_\varepsilon), \Phi)_{L^2(\Gamma_\varepsilon)^2} = &\frac{1}{c_m}\int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon \nabla \widetilde{w}_\varepsilon \cdot \nabla \varphi\, dx + \varepsilon\left(\lambda - \frac{1}{c_m}\right)\int_{\Gamma_\varepsilon} w_\varepsilon [\varphi] d\sigma \\ &- \frac{\varepsilon}{c_m}\int_{\Gamma_\varepsilon} h_\varepsilon [\varphi] d\sigma + \varepsilon(b+\lambda)\int_{\Gamma_\varepsilon} h_\varepsilon \psi d\sigma - \varepsilon\theta \int_{\Gamma_\varepsilon} w_\varepsilon \psi d\sigma.\end{aligned}$$

There, φ solves a stationary problem (7) with a given jump $[\varphi]$ on Γ_ε. Clearly, $\|\nabla \widetilde{w}_\varepsilon\|_{L^2(\Omega_\varepsilon^i \cup \Omega_\varepsilon^e)} \leq C\|w_\varepsilon\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)}$. The test function φ is estimated in a standard way in terms of $\|[\varphi]\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)}$. Then, by the Cauchy–Schwarz inequality, one retrieves

$$\begin{aligned}(B_\varepsilon^{(1)}(t,W_\varepsilon), \Phi)_{L^2(\Gamma_\varepsilon)^2} \leq &\, C_1 \|w_\varepsilon\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)} \|[\varphi]\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)} \\ &+ C_2(\|w_\varepsilon\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)} + \|h_\varepsilon\|_{\widetilde{H}^{1/2}(\Gamma_\varepsilon)})\|[\Phi]\|_{V_1},\end{aligned}$$

which proves the estimate from above for $\|B_\varepsilon^{(1)}(t,W)\|_{V_1'}$. □

Lemma 2.4. *For every $t \in [0,T]$, the operator $B_\varepsilon^{(2)}(t,\cdot) : V_2 \to V_2'$ has the following properties:*

(i) Monotonicity:

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

(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

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

(iii) Boundedness:

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

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

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

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

which proves (ii).

(iii) The boundedness follows from (13):

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

where C^ε is a positive constant. □

Obviously, the function $t \mapsto \mathbb{A}_\varepsilon(t,W)$ satisfies the measurability assumption of Lemma 2.2, and the demi-continuity property follows from the estimates in Lemmas 2.3 and 2.4.

3. Proof of Theorem 2.1

3.1. A priori estimates

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

Lemma 3.1. *Under hypotheses (H1)–(H3), at time $t=0$ the following estimate holds*

$$\int_{\Omega_\varepsilon^i\cup\Omega_\varepsilon^e} a_\varepsilon|\nabla z_\varepsilon|^2\,dx\Big|_{t=0} + \int_\Sigma |z_\varepsilon|^2\,d\sigma\Big|_{t=0} \le C. \tag{14}$$

Proof. One can see that the operator A_ε given by (6) can be defined by means of the minimization problem

$$(A_\varepsilon w_\varepsilon, w_\varepsilon) = \min_{[\phi_\varepsilon]=w_\varepsilon}\int_{\Omega_\varepsilon^i\cup\Omega_\varepsilon^e} a_\varepsilon|\nabla\phi_\varepsilon|^2\,dx,$$

where the minimum is taken over the functions $\phi_\varepsilon \in H^1(\Omega_\varepsilon^i\cup\Omega_\varepsilon^e)$ with the given jump $[\phi_\varepsilon]=w_\varepsilon$ on Γ_ε. Consider the test function

$$\phi_\varepsilon = \begin{cases} V_\varepsilon^0 \text{ in } \Omega_\varepsilon^i \\ 0 \text{ in } \Omega_\varepsilon^e \end{cases}.$$

Then, thanks to (H1) it holds that

$$\int_{\Omega_\varepsilon^i\cup\Omega_\varepsilon^e} a_\varepsilon|\nabla z_\varepsilon|^2\,dx\Big|_{t=0} = (A_\varepsilon w_\varepsilon, w_\varepsilon)\Big|_{t=0} = \int_{\Omega_\varepsilon^i} a_i|\nabla V_\varepsilon^0|^2\,dx \le C.$$

The proof of the lemma is completed by using an extension operator from Ω_ε^e to Ω (see (17) below) together with the trace inequality. □

We now prove the a priori estimates for the solutions of (10).

Lemma 3.2 (*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) $\varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 \, d\sigma + \varepsilon \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau w_\varepsilon|^2 \, d\sigma \, d\tau \le C$.
(ii) $\varepsilon \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 \, d\sigma + \varepsilon \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau h_\varepsilon|^2 \, d\sigma \, d\tau \le C$.
(iii) Let $z_\varepsilon = e^{-\lambda t} u_\varepsilon$ with the jump $[z_\varepsilon] = w_\varepsilon$ on Γ_ε. Then, one has that

$$\int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} (|z_\varepsilon|^2 + |\nabla z_\varepsilon|^2) \, dx \le C,$$

for a constant C independent of ε and t, but depending on T and the norms of initial functions $\|G_\varepsilon^0\|_{L^2(\Gamma_\varepsilon)}$, $\|V_\varepsilon^0\|_{L^4(\Gamma_\varepsilon)}$, $\|V_\varepsilon^l\|_{H^1(\Omega)}$.

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_ε be the solution of the stationary problem with the jump w_ε:

$$\begin{aligned}
&-\operatorname{div}(a_\varepsilon \nabla z_\varepsilon) = 0, && x \in \Omega_\varepsilon^i \cup \Omega_\varepsilon^e,\\
&a_e \nabla z_\varepsilon^e \cdot \nu = a_i \nabla z_\varepsilon^i \cdot \nu, && x \in \Gamma_\varepsilon,\\
&z_\varepsilon^i - z_\varepsilon^e = w_\varepsilon, && x \in \Gamma_\varepsilon,\\
&a_\varepsilon \nabla z_\varepsilon \cdot \nu = 0, && x \in \Gamma_{m,\varepsilon},\\
&a_e \nabla z_\varepsilon \cdot \nu = \frac{e^{-\lambda t}}{c_m} J_\varepsilon^e, && x \in \Sigma,\\
&z_\varepsilon = 0, && x \in (S_0 \cup S_L).
\end{aligned} \tag{15}$$

We multiply (10) by W_ε and integrate over Γ_ε:

$$\begin{aligned}
&\frac{\varepsilon}{2} \partial_t \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 \, d\sigma + \frac{1}{c_m} \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon \nabla z_\varepsilon \cdot \nabla z_\varepsilon \, dx + \frac{\varepsilon}{c_m} \int_{\Gamma_\varepsilon} \frac{e^{2\lambda t}}{3} w_\varepsilon^4 \, d\sigma \\
&+ \varepsilon \left(\lambda - \frac{1}{c_m} \right) \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 \, d\sigma - \varepsilon \left(\theta + \frac{1}{c_m} \right) \int_{\Gamma_\varepsilon} h_\varepsilon w_\varepsilon \, d\sigma + \frac{\varepsilon}{2} \partial_t \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 \, d\sigma \\
&+ \varepsilon(\lambda + b) \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 \, d\sigma = \frac{e^{-\lambda t}}{c_m} \int_\Sigma J_\varepsilon^e z_\varepsilon \, d\sigma + \varepsilon a e^{-\lambda t} \int_{\Gamma_\varepsilon} h_\varepsilon d\sigma.
\end{aligned} \tag{16}$$

It is known [29] that there exists an extension operator P_ε from Ω_ε^e to Ω such that $\|\nabla P_\varepsilon z_\varepsilon^e\|_{L^2(\Omega)} \le C \|\nabla z_\varepsilon^e\|_{L^2(\Omega_\varepsilon^e)}$ with a constant C independent of ε. This result combined with the Friedrichs inequality ($z_\varepsilon = 0$ on $S_0 \cup S_L$) implies that

$$\|P_\varepsilon z_\varepsilon^e\|_{H^1(\Omega)} \le C \|\nabla z_\varepsilon^e\|_{L^2(\Omega_\varepsilon^e)}. \tag{17}$$

By the trace inequality, the $L^2(\Sigma)$-norm of z_ε is then bounded by $\|\nabla z_\varepsilon^e\|_{L^2(\Omega_\varepsilon^e)}$. Using Young's inequality with a parameter in (16) and (17), one retrieves

$$\begin{aligned}
&\partial_t \left(\varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 d\sigma + \varepsilon \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 d\sigma \right) + \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} |\nabla z_\varepsilon|^2 \, dx + \varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 d\sigma \\
&+ \left(\varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 d\sigma + \varepsilon \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 d\sigma \right) \le C \int_\Sigma |J_\varepsilon^e|^2 \, d\sigma.
\end{aligned} \tag{18}$$

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

$$\varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 d\sigma + \varepsilon \int_{\Gamma_\varepsilon} |h_\varepsilon|^2 d\sigma \le C. \tag{19}$$

Integrating (18) with respect to t gives

$$\int_0^t \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} |\nabla z_\varepsilon|^2 \, dx + \varepsilon \int_0^t \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 d\sigma \\ \le C \left(\int_0^t \int_\Sigma |J_\varepsilon^e|^2 d\sigma d\tau + \varepsilon \int_{\Gamma_\varepsilon} |V_\varepsilon^0|^2 \, d\sigma + \varepsilon \int_{\Gamma_\varepsilon} |G_\varepsilon^0|^2 \, d\sigma \right). \tag{20}$$

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

$$\begin{aligned} &\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_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon |\nabla z_\varepsilon|^2 \, dx - \frac{1}{2c_m} \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon |\nabla z_\varepsilon|^2 \, dx \Big|_{t=0} \\ &+ \frac{\varepsilon}{12 c_m} e^{2\lambda t} \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 \, d\sigma - \frac{\varepsilon}{12 c_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 \\ &\le 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_\Sigma J_\varepsilon^e z_\varepsilon \, d\sigma - \frac{1}{c_m} \int_\Sigma J_\varepsilon^e z_\varepsilon \, d\sigma \Big|_{t=0} \\ &+ \frac{\lambda}{c_m} \int_0^t e^{-\lambda\tau} \int_\Sigma J_\varepsilon^e z_\varepsilon \, d\sigma d\tau - \int_0^t \frac{e^{-\lambda\tau}}{c_m} \int_\Sigma \partial_\tau J_\varepsilon^e 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{aligned} \tag{21}$$

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

$$\varepsilon \int_0^t \int_{\Gamma_\varepsilon} |\partial_\tau w_\varepsilon|^2 \, d\sigma d\tau + \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} |\nabla z_\varepsilon|^2 \, dx + \varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^4 \, d\sigma \le C.$$

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

$$\int_{\Omega_\varepsilon^i} |z_\varepsilon^i|^2 \, dx \le C \int_{\Omega_\varepsilon^i} |\partial_{x_1} z_\varepsilon^i|^2 \, dx,$$

$$\int_{\Omega_\varepsilon^e} |z_\varepsilon^e|^2 \, dx \le C \int_{\Omega_\varepsilon^e} |\nabla z_\varepsilon^e|^2 \, dx.$$

The proof of Lemma 3.2 is finally complete. □

3.2. Derivation of the macroscopic model

Since the axons inside the bundle are disconnected, a priori estimates provided by Lemma 3.2 do not imply the strong convergence of the transmembrane potential v_ε on Γ_ε. In turn, this makes passing to the limit in the nonlinear term I_{ion} problematic. We choose to combine the two-scale convergence machinery with the method of monotone operators due to G. Minty [30]. 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 below. For passage to the limit, as $\varepsilon \to 0$, we will use the two-scale convergence [31]. We refer to [24] for two-scale convergence on periodic surfaces (namely, on Γ_ε).

Definition 3.3. We say that a sequence $\{u^l_\varepsilon(t,x)\}$ two-scale converges to the function $u^l_0(t,x,y)$ in $L^2(0,T;L^2(\Omega^l_\varepsilon))$, $l=i,e$, as $\varepsilon \to 0$, and write

$$u^l_\varepsilon(t,x) \overset{2}{\rightharpoonup} u^l_0(t,x,y),$$

if

(i) $\int_0^T \int_{\Omega^l_\varepsilon} |u_\varepsilon|^2 dx\, dt < C$.
(ii) For any $\phi(t,x) \in C(0,T;L^2(\Omega))$, $\psi(y) \in L^2(Y_l)$, one has that

$$\lim_{\varepsilon\to 0} \int_0^T \int_{\Omega^l_\varepsilon} u^l_\varepsilon(t,x)\phi(t,x)\psi\left(\frac{x}{\varepsilon}\right) dx\, dt = \frac{1}{|Y|}\int_0^T \int_\Omega \int_{Y^l} u^l_0(t,x,y)\phi(t,x)\psi(y)\, dy\, dx\, dt,$$

for some function $u^l_0 \in L^2(0,T;L^2(\Omega\times Y))$.

Definition 3.4. 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 $\phi(t,x) \in C([0,T];C(\overline{\Omega}))$, $\psi(y) \in C(\Gamma)$ 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

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

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

Lemma 3.5. *Let W_ε be a solution of (10), and let z_ε be a solution of problem (15). Then there exist functions $z^l_0 \in L^2(0,T;L^2(\Omega))$, $l=i,e$, such that $\partial_{x_1} z^i_0, \partial_{x_j} z^e_0 \in L^2(0,T;L^2(\Omega))$ ($j=1,2,3$), $w_0 = z^i_0 - z^e_0 \in L^4(0,T;L^4(\Omega))$, and up to a subsequence, as $\varepsilon \to 0$, the following two-scale convergence holds:*

(i) $\chi^l\left(\frac{x}{\varepsilon}\right) z^l_\varepsilon(t,x) \overset{2}{\rightharpoonup} \chi^l(y) z^l_0(t,x)$ *in* $L^2(0,T;L^2(\Omega^l_\varepsilon))$, $l=i,e$.
(ii) $\chi^i\left(\frac{x}{\varepsilon}\right) \nabla z^i_\varepsilon(t,x) \overset{2}{\rightharpoonup} \chi^i(y)\left[\mathbf{e}_1 \partial_{x_1} z^i_0(t,x) + \nabla_y z^i_1(t,x,y)\right]$, *where* $z^i_1(t,x,y) \in L^2((0,T)\times\Omega;H^1(Y_i))$ *is 1-periodic in* y_1.
(iii) $\chi^e\left(\frac{x}{\varepsilon}\right) \nabla z^e_\varepsilon(t,x) \overset{2}{\rightharpoonup} \chi^e(y)\left[\nabla z^e_0(t,x) + \nabla_y z^e_1(t,x,y)\right]$, *where* $z^e_1(t,x,y) \in L^2((0,T)\times\Omega;H^1(Y_e))$ *is Y-periodic in y.*
(iv) $w_\varepsilon \overset{2}{\rightharpoonup} w_0(t,x)$ *t-pointwise in* $L^2(\Gamma_\varepsilon)$, *and* $w_0 = (z^i_0 - z^e_0)$.
Moreover, $\partial_t w_\varepsilon \overset{2}{\rightharpoonup} \partial_t w_0$ *in* $L^2(0,T;L^2(\Gamma_\varepsilon))$.

(v) $h_\varepsilon \stackrel{2}{\rightharpoonup} \widetilde{h}_0(t,x,y)$ *t–pointwise in* $L^2(\Gamma_\varepsilon)$, *and* $\partial_t h_\varepsilon \stackrel{2}{\rightharpoonup} \partial_t\widetilde{h}_0$ *in* $L^2(0,T;L^2(\Gamma_\varepsilon))$.

Proof. From a priori estimates the two-scale convergence of z_ε^e and ∇z_ε^e is proved applying standard arguments (see [31]). When it comes to z_ε^i and its gradient, the main difficulty stems from the fact that Ω_ε^i consists of many disconnected components.

Since z_ε^i is bounded uniformly in ε (cf. Lemma 3.2) 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, $\chi^i\left(\frac{x}{\varepsilon}\right)\nabla z_\varepsilon^i(t,x)$ 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 $\Phi\left(t,x,\frac{x}{\varepsilon}\right) = \varphi(t,x)\psi\left(\frac{x}{\varepsilon}\right)$, where $\varphi \in C([0,T];C_0^\infty(\Omega))$, and $\psi \in (C^\infty(Y_i))^3$ is 1-periodic in y_1 and such that $\psi = 0$ on $\Gamma_{mi}\cup\Gamma$.

$$
\begin{aligned}
&\varepsilon\int_0^T\int_{\Omega_\varepsilon^i}\nabla z_\varepsilon^i(t,x)\cdot\varphi(t,x)\psi\left(\frac{x}{\varepsilon}\right)dxdt\\
&= -\varepsilon\int_0^T\int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\nabla\varphi(t,x)\cdot\psi\left(\frac{x}{\varepsilon}\right)dxdt\\
&-\int_0^T\int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\varphi(t,x)\mathrm{div}_y\psi\left(\frac{x}{\varepsilon}\right)dxdt.
\end{aligned}
$$

Passing to the limit, we derive

$$
\frac{1}{|Y|}\int_0^T\int_\Omega\int_{Y_i} z_0^i(t,x,y)\varphi(t,x)\mathrm{div}_y\psi(y)\,dydxdt = 0,
$$

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

Next we prove that $\partial_{x_1}z_0^i \in L^2((0,T)\times\Omega)$. Let us take a test function $\Phi\left(t,x,\frac{x}{\varepsilon}\right) = \varphi(t,x)\mathbf{e}_1 + \varphi(t,x)\nabla_y N_1^i\left(\frac{x}{\varepsilon}\right)$ such that

$$
\begin{aligned}
&\Delta_y N_1^i = 0, \quad Y_i,\\
&\nabla N_1^i\cdot\nu = -\nu_1, \quad \Gamma\cup\Gamma_{mi},\\
&N_1^i \text{ is 1-periodic in } y_1.
\end{aligned}
\tag{22}
$$

Integrating by parts yields

$$
\begin{aligned}
&\int_0^T\int_{\Omega_\varepsilon^i}\nabla z_\varepsilon^i(t,x)\cdot\Phi\left(t,x,\frac{x}{\varepsilon}\right)dxdt\\
&= -\int_0^T\int_{\Omega_\varepsilon^i} z_\varepsilon^i(t,x)\left(\mathbf{e}_1+\nabla_y N_1^i\left(\frac{x}{\varepsilon}\right)\right)\cdot\nabla\varphi(t,x)\,dxdt,
\end{aligned}
$$

and passing to the limit, as $\varepsilon\to 0$, we obtain

$$
\begin{aligned}
&\frac{1}{|Y|}\int_0^T\int_\Omega\int_{Y_i} p^i(t,x,y)\cdot\varphi(t,x)\left(\mathbf{e}_1+\nabla_y N_1^i(y)\right)dydxdt\\
&= -\frac{1}{|Y|}\int_0^T\int_\Omega\int_{Y_i} z_0^i(t,x)\nabla\varphi(t,x)\cdot\left(\mathbf{e}_1+\nabla_y N_1^i(y)\right)dydxdt.
\end{aligned}
\tag{23}
$$

Let us observe that $\int_{Y_i}\partial_{y_k}N_1^i(y)\,dy = 0$ for $k\neq 1$. Indeed, for $k\neq 1$, y_k can be taken as a test function in (22):

$$
0 = -\int_{Y_i}\Delta N_1^i(y)y_k\,dy = \int_{Y_i}\partial_{y_k}N_1^i(y)\,dy.
$$

Furthermore, it holds that

$$
\int_{Y_i}\left(\delta_{1k}+\partial_{y_k}N_1^i(y)\right)dy = \delta_{1k}|\Gamma|\frac{a_i^{\mathrm{eff}}}{a_i}.
$$

Consequently, it is straightforward to check that

$$a_i^{\text{eff}} = \frac{1}{|\Gamma|}\int_{Y_i} a_i \left(1 + \partial_{y_1} N_1^i(y)\right)\, dy = \frac{1}{|\Gamma|}\int_{Y_i} a_i \left(1 + \partial_{y_1} N_1^i(y)\right)^2\, dy > 0. \tag{24}$$

We turn back to (23). Due to (24), we have the estimate

$$\begin{aligned}
&\left|\int_0^T\int_\Omega z_0^i(t,x)\partial_{x_1}\varphi(t,x)\, dxdt\right| \\
&= \left|\frac{a_i}{(a_i^{\text{eff}})_{11}}\int_0^T\int_\Omega\int_{Y_i} p^i(t,x,y)\cdot\varphi(t,x)\left(\mathbf{e}_1 + \nabla_y N_1^i(y)\right)\, dydxdt\right| \\
&\leq C\|\varphi\|_{L^2((0,T)\times\Omega)}.
\end{aligned}$$

Next, we show that $p^i(t,x,y) = \mathbf{e}_1\partial_{x_1} z_0^i(t,x) + \nabla_y z_1^i(t,x,y)$ for some z_1^i periodic in y_1. Take a smooth test function $\varphi(t,x)\psi(y)$ such that $\operatorname{div}_y\psi = 0$ in Y_i, $\psi\cdot\nu = 0$ on $\Gamma_{mi}\cup\Gamma$, and periodic in y_1.

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

Passing to the limit, as $\varepsilon\to 0$ we obtain

$$\frac{1}{|Y|}\int_0^T\int_\Omega\int_{Y_i} p^i\cdot\varphi(t,x)\psi(y)\, dydxdt = -\frac{1}{|Y|}\int_0^T\int_\Omega\int_{Y_i} z_0^i\nabla\varphi(t,x)\cdot\psi(y)\, dydxdt.$$

Since $\int_{Y_i}\psi_k(y)\, dy = 0$ for $k\neq 1$,

$$\int_0^T\int_\Omega\int_{Y_i} p^i(t,x,y)\cdot\varphi(t,x)\psi(y)\, dydxdt = \int_0^T\int_\Omega\int_{Y_i}\partial_{x_1} z_0^i(t,x)\varphi(t,x)\psi_1(y)\, dydxdt,$$

and thus

$$\int_0^T\int_\Omega\int_{Y_i}\left(p^i(x,y) - \mathbf{e}_1\partial_{x_1} z_0^i(t,x)\right)\varphi(t,x)\cdot\psi(y)\, dydxdt = 0.$$

Since ψ 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

$$p^i(t,x,y) = \mathbf{e}_1\partial_{x_1} z_0^i(t,x) + \nabla_y z_1^i(t,x,y).$$

Next we prove that the jump w_ε converges two-scale in $L^2(0,T;L^2(\Gamma_\varepsilon))$ to $z_0^i - z_0^e$. To this end, for $\psi\in H^{1/2}(\Gamma)$, we consider test functions $\widetilde{\psi}^l$, $l = i,e$, solving

$$\begin{aligned}
&\Delta\widetilde{\psi}^l = \frac{1}{|Y_l|}\int_\Gamma\psi\, d\sigma, \quad y\in Y_l, \\
&\nabla\widetilde{\psi}^l\cdot\nu^l = \psi, \quad y\in\Gamma; \quad \nabla\widetilde{\psi}^l\cdot\nu^l = 0, \quad y\in\Gamma_{ml}, \\
&\widetilde{\psi}^l \text{ is } Y-\text{periodic}.
\end{aligned}$$

Integration by parts yields

$$\begin{aligned}
&\varepsilon\int_0^T\int_{\Gamma_\varepsilon} w_\varepsilon\,\varphi(t,x)\psi\left(\frac{x}{\varepsilon}\right)\, dxdt \\
&= \varepsilon\int_0^T\int_{\Omega_\varepsilon^i}\nabla z_\varepsilon^i\cdot\varphi(t,x)\nabla_y\widetilde{\psi}^i\left(\frac{x}{\varepsilon}\right)\, dxdt + \varepsilon\int_0^T\int_{\Omega_\varepsilon^i} z_\varepsilon^i\,\nabla\varphi(t,x)\cdot\nabla_y\widetilde{\psi}^i\left(\frac{x}{\varepsilon}\right)\, dxdt
\end{aligned}$$

$$
\begin{aligned}
&+\frac{1}{|Y_i|}\int_0^T\int_{\Omega_\varepsilon^i} z_\varepsilon^i\varphi(t,x)\int_\Gamma \psi(y)\,d\sigma dxdt\\
&-\varepsilon\int_0^T\int_{\Omega_\varepsilon^e}\nabla z_\varepsilon^e\cdot\varphi(t,x)\nabla_y\widetilde{\psi}^e\left(\frac{x}{\varepsilon}\right)dxdt-\varepsilon\int_0^T\int_{\Omega_\varepsilon^e} z_\varepsilon^e\nabla\varphi(t,x)\cdot\nabla_y\widetilde{\psi}^e\left(\frac{x}{\varepsilon}\right)dxdt\\
&-\frac{1}{|Y_e|}\int_0^T\int_{\Omega_\varepsilon^e} z_\varepsilon^e\varphi(t,x)\int_\Gamma\psi(y)\,d\sigma dxdt.
\end{aligned}
$$

Passing to the limit, as $\varepsilon \to 0$, we get

$$
\begin{aligned}
&\frac{1}{|Y|}\int_0^T\int_\Omega\int_\Gamma w_0(t,x,y)\varphi(t,x)\psi(y)\,d\sigma dxdt\\
&=\frac{1}{|Y|}\int_0^T\int_\Omega\int_\Gamma (z_0^i-z_0^e)\varphi(t,x)\psi(y)\,d\sigma dxdt,
\end{aligned}
$$

that proves the two-scale convergence of w_ε to the difference $w_0 = z_0^i - z_0^e$.

Note that the uniform bound of w_ε in $L^4((0,T)\times\Gamma_\varepsilon)$ – by Lemma 3.2(i) – implies $w_0 \in L^4((0,T)\times\Omega)$. Indeed, for smooth $\varphi(t,x)$, we have that

$$
\begin{aligned}
&|\Gamma|\int_0^T\int_\Omega w_0(t,x)\varphi(t,x)\,dxdt=\lim_{\varepsilon\to0}\varepsilon|Y|\int_0^T\int_{\Gamma_\varepsilon} w_\varepsilon(t,x)\varphi(t,x)\,d\sigma dt\\
&\le |Y|\lim_{\varepsilon\to0}\left(\varepsilon\int_0^T\int_{\Gamma_\varepsilon}|w_\varepsilon|^4\,d\sigma dt\right)^{\frac14}\left(\varepsilon\int_0^T\int_{\Gamma_\varepsilon}|\varphi(t,x)|^{4/3}\,d\sigma dt\right)^{\frac34}\\
&\le C\lim_{\varepsilon\to0}\left(\varepsilon\int_0^T\int_{\Gamma_\varepsilon}|\varphi(t,x)|^{\frac43}\,d\sigma_x dt\right)^{\frac34}\\
&= C\left(\frac{|\Gamma|}{|Y|}\int_0^T\int_\Omega\int_\Gamma|\varphi(t,x)|^{\frac43}\,dxdt\right)^{\frac34}.
\end{aligned}
$$

By density of smooth functions in $L^{\frac43}((0,T)\times\Omega)$, $\|w_0\|_{L^4((0,T)\times\Omega)} \le C$. Thanks to the uniform in ε estimates (i), (ii) in Lemma 3.2, (iv) and (v) hold. Indeed, for any $t\in[0,T]$ and any $\varphi(t,x)\in C^1([0,T]\times\overline{\Omega})$, $\psi(y)\in C(\Gamma)$, such that $\varphi(0,x)=0$

$$
\begin{aligned}
&\varepsilon\int_{\Gamma_\varepsilon} w_\varepsilon(t,x)\varphi(t,x)\psi\Big(\frac{x}{\varepsilon}\Big)d\sigma\\
&=\varepsilon\int_0^t\int_{\Gamma_\varepsilon}(w_\varepsilon(\tau,x)\partial_\tau\varphi(\tau,x)+\partial_\tau w_\varepsilon(\tau,x)\varphi(\tau,x))\psi\Big(\frac{x}{\varepsilon}\Big)d\sigma\\
&\to\frac{1}{|Y|}\int_0^t\int_\Omega\int_\Gamma(w_0(\tau,x)\partial_\tau\varphi(\tau,x)+\partial_\tau w_0(\tau,x)\varphi(\tau,x))\psi(y)d\sigma_y dxd\tau\\
&=\frac{1}{|Y|}\int_\Omega\int_\Gamma w_0(t,x)\varphi(t,x)\psi(y)d\sigma_y dx,\quad \varepsilon\to0.\quad\square\quad\square
\end{aligned}
$$

Lemma 3.6. *Let the initial functions V_ε^0 satisfy hypothesis (H1). Then $V_\varepsilon^0 \overset{2}{\rightharpoonup} V^0$ in $L^2(\Gamma_\varepsilon)$, and*

$$
\limsup_{\varepsilon\to0}\varepsilon\int_{\Gamma_\varepsilon}|V_\varepsilon^0|^2\,d\sigma=\frac{|\Gamma|}{|Y|}\int_\Omega|V^0|^2\,dx.
$$

Proof. The weak two-scale convergence follows from Proposition 2.6 in [24]. Approximating V^0 by smooth functions V_δ^0 in $H^1(\Omega)$, we find

$$
\varepsilon\int_{\Gamma_\varepsilon}|V_\varepsilon^0|^2\,d\sigma=\varepsilon\int_{\Gamma_\varepsilon}|V_\varepsilon^0-V_\delta^0|^2\,d\sigma+2\varepsilon\int_{\Gamma_\varepsilon}(V_\varepsilon^0-V_\delta^0)V_\delta^0\,d\sigma+\varepsilon\int_{\Gamma_\varepsilon}|V_\delta^0|^2\,d\sigma. \tag{25}
$$

Applying the trace inequality in the rescaled periodicity cell εY, adding up over all the cells in Ω, and using assumption (H1) leads to

$$\begin{aligned}
&\varepsilon \int_{\Gamma_\varepsilon} |V_\varepsilon^0 - V_\delta^0|^2 \, d\sigma \le C\varepsilon^2 \int_\Omega |\nabla(V_\varepsilon^0 - V_\delta^0)|^2 \, dx + C \int_\Omega |V_\varepsilon^0 - V_\delta^0|^2 \, dx \\
&\le C\varepsilon^2 \int_\Omega |\nabla(V_\varepsilon^0 - V_\delta^0)|^2 \, dx + C \int_\Omega |V_\varepsilon^0 - V^0|^2 \, dx \\
&+ C \int_\Omega |V_\delta^0 - V^0|^2 \, dx \quad \to \quad 0, \quad \varepsilon, \delta \to 0.
\end{aligned}$$

Then, since V_δ^0 is smooth, it converges strongly two-scale, and passing to the limit as $\varepsilon \to 0$ in (25) we obtain

$$\lim_{\delta\to 0} \limsup_{\varepsilon \to 0} \varepsilon \int_{\Gamma_\varepsilon} |V_\varepsilon^0|^2 \, d\sigma = \frac{|\Gamma|}{|Y|} \int_\Omega |V^0|^2 \, dx,$$

as stated. □

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

$$M_\varepsilon := \begin{pmatrix} [\mu_\varepsilon] \\ \rho \end{pmatrix}, \quad \text{where } \rho = \rho(t,x), \text{ and}$$

$$\mu_\varepsilon(x) := \begin{cases} \mu_0^e(t,x) + \varepsilon \mu_1^e\left(t, x, \frac{x}{\varepsilon}\right), & x \in \Omega_\varepsilon^e \\ \mu_0^i(t,x) + \varepsilon \mu_1^i\left(t, x, \frac{x}{\varepsilon}\right), & x \in \Omega_\varepsilon^i. \end{cases}$$

The monotonicity property of the operator $\mathbb{A}_\varepsilon(t,\cdot)$ entails

$$\int_0^t \int_{\Gamma_\varepsilon} (\mathbb{A}_\varepsilon(\tau, W_\varepsilon) - \mathbb{A}_\varepsilon(\tau, M_\varepsilon)) \cdot (W_\varepsilon - M_\varepsilon) \, d\sigma d\tau \ge 0. \tag{26}$$

By the definition of A_ε (6),

$$(A_\varepsilon([\mu_\varepsilon] - w_\varepsilon), ([\mu_\varepsilon] - w_\varepsilon))_{L^2(\Gamma_\varepsilon)} \le \int_{\Omega_\varepsilon^i \cup \Omega_\varepsilon^e} a_\varepsilon \nabla(\mu_\varepsilon - z_\varepsilon) \cdot \nabla(\mu_\varepsilon - z_\varepsilon) \, dx,$$

where z_ε solves (15). It follows then from (26), (10), and the definition of the operator $\mathbb{A}_\varepsilon(t,\cdot)$ that

$$\begin{aligned}
&\varepsilon \int_0^t \int_{\Gamma_\varepsilon} \partial_\tau w_\varepsilon([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau + \varepsilon \int_0^t \int_{\Gamma_\varepsilon} \partial_\tau h_\varepsilon(\rho - h_\varepsilon) \, d\sigma d\tau \\
&+ \frac{1}{c_m} \int_0^t \int_{\Omega_\varepsilon^e \cup \Omega_\varepsilon^i} a_\varepsilon \nabla \mu_\varepsilon \cdot \nabla(\mu_\varepsilon - z_\varepsilon) \, dx d\tau + \varepsilon(\lambda - \frac{1}{c_m}) \int_0^t \int_{\Gamma_\varepsilon} [\mu_\varepsilon]([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau \\
&- \frac{\varepsilon}{c_m} \int_0^t \int_{\Gamma_\varepsilon} \rho([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau + \varepsilon(b + \lambda) \int_0^t \int_{\Gamma_\varepsilon} \rho(\rho - h_\varepsilon) \, d\sigma d\tau \\
&- \varepsilon\theta \int_0^t \int_{\Gamma_\varepsilon} [\mu_\varepsilon](\rho - h_\varepsilon) \, d\sigma d\tau + \varepsilon \frac{1}{3c_m} \int_0^t e^{2\lambda\tau} \int_{\Gamma_\varepsilon} [\mu_\varepsilon]^3([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau \\
&+ \int_0^t \int_{\Gamma_\varepsilon} \frac{e^{-\lambda\tau}}{c_m} (a_i \nabla q_\varepsilon \cdot \nu)([\mu_\varepsilon] - w_\varepsilon) \, d\sigma d\tau - \varepsilon a \int_0^t \int_{\Gamma_\varepsilon} e^{-\lambda\tau}(\rho - h_\varepsilon) \, d\sigma d\tau \ge 0.
\end{aligned} \tag{27}$$

Consider the first two terms in (27), 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, [24]) and Lemma 3.6 renders

$$\begin{aligned}
&\limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} w_\varepsilon \partial_\tau w_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega w_0 \partial_\tau w_0 \, dx d\tau\Big] \\
&= \limsup_{\varepsilon\to 0}\Big[\frac{\varepsilon}{2}\int_{\Gamma_\varepsilon} w_\varepsilon^2 \, d\sigma\Big|_{\tau=t} - \frac{|\Gamma|}{2|Y|}\int_\Omega w_0^2\, dx\Big] \\
&+ \lim_{\varepsilon\to 0}\Big[-\frac{\varepsilon}{2}\int_{\Gamma_\varepsilon} (V_\varepsilon^0)^2 \, d\sigma + \frac{|\Gamma|}{2|Y|}\int_\Omega (V^0)^2\, dx\Big] \geq 0.
\end{aligned}$$

Similarly, for the integral of $h_\varepsilon \partial_\tau h_\varepsilon$, denoting the mean value of the two-scale limit $\widetilde{h}_0(t,x,y)$ in y by $h_0(t,x) = \frac{1}{|\Gamma|}\int_\Gamma \widetilde{h}_0(t,x,y)\, dy$, we get

$$\begin{aligned}
&\limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} h_\varepsilon \partial_\tau h_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega h_0 \partial_\tau h_0 \, dx d\tau\Big] \\
&= \limsup_{\varepsilon\to 0}\Big[\frac{\varepsilon}{2}\int_{\Gamma_\varepsilon} h_\varepsilon^2 \, d\sigma\Big|_{\tau=t} - \frac{|\Gamma|}{2|Y|}\int_\Omega h_0^2\, dx\Big|_{\tau=t}\Big] \\
&+ \lim_{\varepsilon\to 0}\Big[-\frac{\varepsilon}{2}\int_{\Gamma_\varepsilon} (G_\varepsilon^0)^2 \, d\sigma + \frac{|\Gamma|}{2|Y|}\int_\Omega (G^0)^2\, dx\Big] \geq 0.
\end{aligned}$$

For smooth $\mu_0^l(t,x)$ and $\mu_1^l(t,x,y)$, $l=i,e$, we use Lemma 3.5 to pass to the limit in the third term:

$$\begin{aligned}
&\frac{1}{c_m}\int_0^t \int_{\Omega_\varepsilon^e \cup \Omega_\varepsilon^i} a_\varepsilon \nabla \mu_\varepsilon \cdot \nabla(\mu_\varepsilon - z_\varepsilon)\, dx d\tau \\
&\to \frac{1}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_i} a_i(\nabla \mu_0^i + \nabla_y \mu_1^i)\cdot(\nabla \mu_0^i + \nabla_y \mu_1^i - \partial_1 z_0^i \mathbf{e}_1 - \nabla_y z_1^i) dx dy d\tau \\
&+ \frac{1}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_e} a_e(\nabla \mu_0^e + \nabla_y \mu_1^e)\cdot(\nabla \mu_0^e + \nabla_y \mu_1^e - \nabla z_0^e - \nabla_y z_1^e) dx dy d\tau.
\end{aligned}$$

Taking the limit in (27) as $\varepsilon \to 0$ (along a subsequence) we obtain

$$\begin{aligned}
&\limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} w_\varepsilon \partial_\tau w_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega w_0 \partial_\tau w_0 \, dx d\tau\Big] \\
&+ \limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} h_\varepsilon \partial_\tau h_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega h_0 \partial_\tau h_0 \, dx d\tau\Big] \\
&\leq \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega \partial_\tau w_0([\mu_0] - w_0)\, dx d\tau + \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega \partial_\tau h_0(\rho - h_0)\, dx d\tau \\
&+ \frac{1}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_i} a_i(\nabla \mu_0^i + \nabla_y \mu_1^i)\cdot(\nabla \mu_0^i + \nabla_y \mu_1^i - \partial_1 z_0^i \mathbf{e}_1 - \nabla_y z_1^i) dx dy d\tau \\
&+ \frac{1}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_e} a_e(\nabla \mu_0^e + \nabla_y \mu_1^e)\cdot(\nabla \mu_0^e + \nabla_y \mu_1^e - \nabla z_0^e - \nabla_y z_1^e) dx dy d\tau \\
&+ (\lambda - \frac{1}{c_m})\frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega [\mu_0]([\mu_0] - w_0)\, dx d\tau \qquad (28) \\
&- \frac{|\Gamma|}{|Y| c_m}\int_0^t \int_\Omega \rho([\mu_0] - w_0)\, dx d\tau + (b+\lambda)\frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega \rho(\rho - h_0)\, dx d\tau \\
&- \theta\frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega [\mu_0](\rho - h_0)\, dx d\tau + \frac{1|\Gamma|}{3c_m|Y|}\int_0^t \int_\Omega e^{2\lambda\tau}[\mu_0]^3([\mu_0] - w_0)\, dx d\tau \\
&- \int_0^t \int_\Sigma \frac{e^{-\lambda\tau}}{c_m} J^e(\mu_0^e - z_0^e)\, d\sigma d\tau - a\frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega e^{-\lambda\tau}(\rho - h_0)\, d\sigma d\tau,
\end{aligned}$$

where $[\mu_0] = \mu_0^i - \mu_0^e$. Consider the spaces

$$H_i = \{z^i \in L^2(\Omega) : \ \partial_{x_1} z^i \in L^2(\Omega), \ z^i = 0 \text{ on } S_0 \cup S_L\},$$
$$H_e = \{z^e \in L^2(\Omega) : \ \nabla z^e \in L^2(\Omega)^3, \ z^e = 0 \text{ on } S_0 \cup S_L\},$$

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

$$\|z\|_{H_i} = \left(\int_\Omega |z|^4 \, dx\right)^{\frac{1}{4}} + \left(\int_\Omega |\partial_{x_1} z|^2 \, dx\right)^{\frac{1}{2}}.$$

By density of smooth functions, inequality (28) still holds for test functions $\mu_1^l \in L^2((0,T) \times \Omega; H^1(Y_l))$, and $\mu_0^l \in L^2(0,T; H_l)$ such that $[\mu_0] \in L^4((0,T) \times \Omega)$.

Modifying the test function μ_1^i by setting $\mu_1^i(x,y) = \widetilde{\mu}_1^i(x,y) - \nabla_{x'}\mu_0^i \cdot y'$ we transform the integrand in the fourth line of (28) to the form

$$a_i(\partial_{x_1}\mu_0^i \mathbf{e}_1 + \nabla_y \widetilde{\mu}_1^i) \cdot (\partial_{x_1}\mu_0^i \mathbf{e}_1 + \nabla_y \widetilde{\mu}_1^i - \partial_{x_1} z_0^i \mathbf{e}_1 - \nabla_y z_1^i).$$

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

$$\begin{aligned}
\mu_0^l(t,x) &= z_0^l(t,x) + \delta\psi^l(t,x), \quad l = i, e, \\
\mu_1^e(t,x,y) &= z_1^e(t,x,y) + \delta\,\Psi^e(t,x,y), \\
\widetilde{\mu}_1^i(t,x,y) &= z_1^i(t,x,y) + \delta\,\Psi^i(t,x,y), \\
\rho(t,x) &= h_0(t,x) + \delta\varphi(t,x),
\end{aligned}$$

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

$$\begin{aligned}
&\limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} w_\varepsilon \partial_\tau w_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega w_0 \partial_\tau w_0 \, dx d\tau\Big] \\
&+ \limsup_{\varepsilon\to 0}\Big[\varepsilon \int_0^t \int_{\Gamma_\varepsilon} h_\varepsilon \partial_\tau h_\varepsilon \, d\sigma d\tau - \frac{|\Gamma|}{|Y|}\int_0^t \int_\Omega h_0 \partial_\tau h_0 \, dx d\tau\Big] \\
&\le \frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega \partial_\tau w_0 [\psi] \, dx d\tau + \frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega \partial_\tau h_0 \, \varphi \, dx d\tau \\
&+ \frac{\delta}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_i} a_i(\partial_{x_1}(z_0^i + \delta\psi^i)\mathbf{e}_1 + \nabla_y(z_1^i + \delta\,\Psi^i)) \cdot (\partial_{x_1}\psi^i \mathbf{e}_1 + \nabla_y \Psi^i) dx dy d\tau \\
&+ \frac{\delta}{c_m|Y|}\int_0^t \int_\Omega \int_{Y_e} a_e(\nabla(z_0^e + \delta\psi^e) + \nabla_y(z_1^e + \delta\,\Psi^e)) \cdot (\nabla\psi^e + \nabla_y \Psi^e) dx dy d\tau \\
&+ (\lambda - \frac{1}{c_m})\frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega (w_0 + \delta[\psi])[\psi] \, dx d\tau \\
&- \frac{\delta|\Gamma|}{|Y|c_m}\int_0^t \int_\Omega (h_0 + \delta\varphi)[\psi] \, dx d\tau + (b + \lambda)\frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega (h_0 + \delta\varphi)\varphi \, dx d\tau \\
&- \theta\frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega (w_0 + \delta[\psi])\varphi \, dx d\tau + \frac{|\Gamma|}{3c_m|Y|}\delta\int_0^t \int_\Omega e^{2\lambda\tau}(w_0 + \delta[\psi])^3[\psi] \, dx d\tau \\
&- \frac{\delta}{c_m}\int_0^t \int_\Sigma e^{-\lambda\tau} J^e \psi^e \, d\sigma d\tau - a\frac{\delta|\Gamma|}{|Y|}\int_0^t \int_\Omega e^{-\lambda\tau}\varphi \, d\sigma d\tau.
\end{aligned} \tag{29}$$

Since the left-hand side of (29) is non-negative and δ is arbitrary, we obtain

$$\limsup_{\varepsilon\to 0}\Big[\varepsilon \int_{\Gamma_\varepsilon} |w_\varepsilon|^2 \, d\sigma - \frac{|\Gamma|}{|Y|}\int_\Omega |w_0|^2 \, dx\Big] = 0,$$

$$\limsup_{\varepsilon\to 0}\Big[\varepsilon\int_{\Gamma_\varepsilon}|h_\varepsilon|^2\,d\sigma-\frac{|\Gamma|}{|Y|}\int_\Omega |h_0|^2\,dx\Big]=0.$$

Note that the last convergence implies that the two-scale limit $\widetilde{h}_0$ does not depend on y. Indeed, by Proposition 2.5 in [24], one has the estimate

$$\limsup_{\varepsilon\to 0}\varepsilon\int_{\Gamma_\varepsilon}|h_\varepsilon|^2\,d\sigma\geq\frac{1}{|Y|}\int_\Omega\int_\Gamma\big|\widetilde{h}_0\big|^2\,d\sigma_y dx\geq\frac{|\Gamma|}{|Y|}\int_\Omega|h_0|^2\,dx.$$

Thus, one can see that

$$\frac{1}{|\Gamma|}\int_\Omega\int_\Gamma\big|\widetilde{h}_0\big|^2\,d\sigma_y dx=\int_\Omega\Big(\frac{1}{|\Gamma|}\int_\Gamma\widetilde{h}_0\,d\sigma_y\Big)^2\,dx.$$

Moreover, it is clear that

$$\begin{aligned}\frac{1}{|\Gamma|}\int_\Omega\int_\Gamma\big|\widetilde{h}_0\big|^2\,d\sigma_y dx&=\frac{1}{|\Gamma|}\int_\Omega\int_\Gamma\big|\widetilde{h}_0-h_0\big|^2\,d\sigma_y dx\\&+\frac{2}{|\Gamma|}\int_\Omega\int_\Gamma(\widetilde{h}_0-h_0)h_0\,d\sigma_y dx\\&+\frac{1}{|\Gamma|}\int_\Omega\int_\Gamma|h_0|^2\,d\sigma_y dx=\int_\Omega|h_0|^2\,dx,\end{aligned}$$

which yields

$$\frac{1}{|\Gamma|}\int_\Omega\int_\Gamma\big|\widetilde{h}_0-h_0\big|^2\,d\sigma_y dx=0\quad\Rightarrow\quad\widetilde{h}_0=h_0(t,x).$$

Now, dividing (29) by $\delta\neq 0$ and passing to the limit as $\delta\to+0$ and $\delta\to-0$, we derive

$$\begin{aligned}&\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega\partial_\tau w_0[\psi]\,dxd\tau+\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega\partial_\tau h_0\,\varphi\,dxd\tau\\&+\frac{1}{c_m|Y|}\int_0^t\int_\Omega\int_{Y_i}a_i(\partial_{x_1}z_0^i\mathbf{e}_1+\nabla_y z_1^i)\cdot(\partial_{x_1}\psi^i\mathbf{e}_1+\nabla_y\Psi^i)dydxd\tau\\&+\frac{1}{c_m|Y|}\int_0^t\int_\Omega\int_{Y_e}a_e(\nabla z_0^e+\nabla_y z_1^e)\cdot(\nabla\psi^e+\nabla_y\Psi^e)\,dydxd\tau\\&+(\lambda-\frac{1}{c_m})\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega w_0[\psi]\,dxd\tau-\frac{|\Gamma|}{|Y|c_m}\int_0^t\int_\Omega h_0[\psi]\,dxd\tau\\&+(b+\lambda)\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega h_0\varphi\,dxd\tau-\theta\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega w_0\varphi\,dxd\tau\\&+\frac{|\Gamma|}{3c_m|Y|}\int_0^t\int_\Omega e^{2\lambda\tau}w_0^3[\psi]\,dxd\tau-\int_0^t\int_\Sigma\frac{e^{-\lambda\tau}}{c_m}J^e\psi^e\,d\sigma d\tau\\&-a\frac{|\Gamma|}{|Y|}\int_0^t\int_\Omega e^{-\lambda\tau}\varphi\,dxd\tau=0.\end{aligned}$$

Taking $\psi^i=\psi^e=\varphi=0$, we obtain $z_1^e(t,x,y)=N^e(y)\cdot\nabla z_0^e(t,x)$, $z_1^i(t,x,y)=N_1^i(y)\partial_{x_1}z_0^i(t,x)$, where N_k^e, N_1^i solve the cell problems (A.4) and (A.5), respectively. Note that in the case when Y_i is a cylinder – constant cross-section –, $N_1^i(y)$ is constant. Recalling the definition of the effective coefficients $(a_e^{\text{eff}})_{kl}$ (4), and taking $\Psi^l=0$, we obtain

$$\begin{aligned}&\int_0^t\int_\Omega\partial_\tau w_0[\psi]\,dxd\tau+\int_0^t\int_\Omega\partial_\tau h_0\,\varphi\,dxd\tau\\&+\frac{1}{c_m}\int_0^t\int_\Omega a_i^{\text{eff}}\partial_{x_1}z_0^i\,\partial_{x_1}\psi^i dxd\tau+\frac{1}{c_m}\int_0^t\int_\Omega a_e^{\text{eff}}\nabla z_0^e\cdot\nabla\psi^e\,dxd\tau\\&+(\lambda-\frac{1}{c_m})\int_0^t\int_\Omega w_0[\psi]\,dxd\tau-\frac{1}{c_m}\int_0^t\int_\Omega h_0[\psi]\,dxd\tau\end{aligned}\qquad(30)$$

$$
\begin{aligned}
&+(b+\lambda)\int_0^t\int_\Omega h_0\varphi\,dxd\tau-\theta\int_0^t\int_\Omega w_0\varphi\,dxd\tau\\
&+\frac{1}{3c_m}\int_0^t\int_\Omega e^{2\lambda\tau}w_0^3[\psi]\,dxd\tau\\
&=\frac{|Y|}{c_m|\Gamma|}\int_0^t\int_\Sigma e^{-\lambda\tau}J^e\psi^e\,d\sigma d\tau+a\int_0^t\int_\Omega e^{-\lambda\tau}\varphi\,d\sigma d\tau.
\end{aligned}
$$

Performing the change of unknowns $u_0^l = e^{\lambda\tau}z_0^l$, $v_0 = e^{\lambda\tau}w_0$, $g_0 = e^{\lambda\tau}h_0$, and taking the test functions $e^{-\lambda\tau}\varphi$ and $e^{-\lambda\tau}\psi$ in place of φ and ψ in (30), we obtain a weak formulation of (2):

$$
\begin{aligned}
&\int_0^t\int_\Omega \partial_\tau v_0[\psi]\,dxd\tau\\
&+\frac{1}{c_m}\int_0^t\int_\Omega a_i^{\mathrm{eff}}\partial_{x_1}u_0^i\,\partial_{x_1}\psi^i dxd\tau+\frac{1}{c_m}\int_0^t\int_\Omega a_e^{\mathrm{eff}}\nabla u_0^e\cdot\nabla\psi^e\,dxd\tau\\
&+\frac{1}{c_m}\int_0^t\int_\Omega\big(\frac{1}{3}v_0^3-v_0-g_0\big)[\psi]\,dxd\tau\\
&+\int_0^t\int_\Omega\big(\partial_\tau g_0+bg_0-\theta v_0-a\big)\,\varphi\,dxd\tau\\
&=\frac{|Y|}{c_m|\Gamma|}\int_0^t\int_\Sigma J^e\psi^e\,d\sigma d\tau.
\end{aligned}
$$

Note that in view of the well-posedness of the limit problem proved in the next section, the convergence takes place for the whole sequence. The proof of Theorem 2.1 is completed.

4. Well-posedness of the macroscopic problem

In order to prove the well-posedness of the homogenized problem given by its weak formulation (30), we rewrite it in matrix form as an abstract parabolic equation. We introduce q_0 solving the auxiliary problem in Ω:

$$
\begin{aligned}
-\operatorname{div}(a_e^{\mathrm{eff}}\nabla q_0)-a_i^{\mathrm{eff}}\partial^2_{x_1x_1}q_0&=0, && x\in\Omega,\\
a_e^{\mathrm{eff}}\nabla q_0\cdot\nu&=\frac{|Y|}{|\Gamma|}J^e, && x\in\Sigma,\\
q_0&=0, && x\in S_0\cup S_L.
\end{aligned}
\tag{31}
$$

Here, the effective coefficient $a_i^{\mathrm{eff}} = |Y_i|a_i/|\Gamma|$. Multiplication (31) by a smooth test function ψ^e such that $\psi^e = 0$ on $S_0\cup S_L$ leads to

$$
\frac{|Y|}{|\Gamma|}\int_\Sigma J^e\psi^e\,d\sigma=\int_\Omega a_e^{\mathrm{eff}}\nabla q_0\cdot\nabla\psi^e\,dx+\int_\Omega a_i^{\mathrm{eff}}\partial_{x_1}q_0\partial_{x_1}\psi^e\,dx. \tag{32}
$$

Substituting (32) into (30), and introducing $\widetilde{z}_0^l = z_0^l - q_0e^{-\lambda t}$, $l = i, e$, we have the following weak formulation:

$$
\begin{aligned}
&\int_0^t\int_\Omega\partial_\tau w_0[\psi]\,dxd\tau+\int_0^t\int_\Omega\partial_\tau h_0\,\varphi\,dxd\tau\\
&+\frac{1}{c_m}\int_0^t\int_\Omega a_i^{\mathrm{eff}}\partial_{x_1}\widetilde{z}_0^i\,\partial_{x_1}\psi^i dxd\tau+\frac{1}{c_m}\int_0^t\int_\Omega a_e^{\mathrm{eff}}\nabla\widetilde{z}_0^e\cdot\nabla\psi^e\,dxd\tau\\
&+\Big(\lambda-\frac{1}{c_m}\Big)\int_0^t\int_\Omega w_0[\psi]\,dxd\tau-\frac{1}{c_m}\int_0^t\int_\Omega h_0[\psi]\,dxd\tau\\
&+(b+\lambda)\int_0^t\int_\Omega h_0\varphi\,dxd\tau-\theta\int_0^t\int_\Omega w_0\varphi\,dxd\tau
\end{aligned}
\tag{33}
$$

$$
\begin{aligned}
&+\frac{1}{3c_m}\int_0^t\int_\Omega e^{2\lambda\tau}w_0^3[\psi]\,dxd\tau\\
&=a\int_0^t\int_\Omega e^{-\lambda\tau}\varphi\,d\sigma d\tau+\int_0^t\int_\Omega e^{-\lambda\tau}a_i^{\text{eff}}\partial^2_{x_1x_1}q_0\,[\psi]\,dxd\tau.
\end{aligned}
$$

We seek to rewrite the weak formulation (33) in matrix form as an abstract parabolic equation. To this end, we first introduce the following functional spaces:

$$
\begin{aligned}
&H_0=L^2(\Omega)\times L^2(\Omega),\\
&H_i=\{z^i\in L^2(\Omega):\ \partial_{x_1}z^i\in L^2(\Omega),\ z^i=0\text{ on }S_0\cup S_L\},\\
&H_e=\{z^e\in L^2(\Omega):\ \nabla z^e\in L^2(\Omega)^3,\ z^e=0\text{ on }S_0\cup S_L\},\\
&X_0=\{w=z^i-z^e:\ z^i\in H_i,\ z^e\in H_e\}.
\end{aligned}
$$

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 $(\widetilde{z}_0^i,\widetilde{z}_0^e)\in H_i\times H_e$ solving the following problem

$$
\begin{aligned}
-a_i^{\text{eff}}\partial^2_{x_1x_1}\widetilde{z}_0^i&=\operatorname{div}(a_e^{\text{eff}}\nabla\widetilde{z}_0^e), && x\in\Omega,\\
\widetilde{z}_0^i-\widetilde{z}_0^e&=w_0, && x\in\Omega,\\
a_e^{\text{eff}}\nabla\widetilde{z}_0^e\cdot\nu&=0, && x\in\Sigma,\\
\widetilde{z}_0^i=\widetilde{z}_0^e&=0, && x\in S_0\cup S_L.
\end{aligned}
\tag{34}
$$

The pair $(\widetilde{z}_0^i,\widetilde{z}_0^e)$ can be determined by solving the minimization problem

$$
\|w_0\|^2_{W_0}:=\inf\Big\{\int_\Omega a_i^{\text{eff}}|\partial_{x_1}\widetilde{z}_0^i|^2\,dx+\int_\Omega a_e^{\text{eff}}\nabla\widetilde{z}_0^e\cdot\nabla\widetilde{z}_0^e\,dx\;\Big|\;\widetilde{z}_0^i\in W_i,\,\widetilde{z}_0^e\in W_e\Big\}.
$$

Note that W_0 is a Hilbert space with a scalar product given by

$$
(w_1,w_2)_{W_0}=\int_\Omega a_i^{\text{eff}}\partial_{x_1}z_1^i\,\partial_{x_1}z_2^i\,dx+\int_\Omega a_e^{\text{eff}}\nabla z_1^e\cdot\nabla z_2^e\,dx,
$$

where (z_1^i,z_1^e) and (z_2^i,z_2^e) solve (34) for w_1,w_2 given. Now (33) is written in the form

$$
\partial_t\begin{pmatrix}w_0\\h_0\end{pmatrix}+\begin{pmatrix}\frac{1}{c_m}A_{\text{eff}}w_0+\frac{1}{c_m}\left(\frac{e^{2\lambda t}}{3}w_0^3-w_0-h_0\right)+\lambda w_0\\(b+\lambda)h_0-\theta w_0\end{pmatrix}=e^{-\lambda t}\begin{pmatrix}a_i^{\text{eff}}\partial^2_{x_1x_1}q_0\\a\end{pmatrix},
$$

where the operator A_{eff} defined on smooth functions w_0 by

$$
(A_{\text{eff}}w_0,[\psi])_{L^2(\Omega)}:=\frac{1}{c_m}\int_\Omega a_i^{\text{eff}}\partial_{x_1}\widetilde{z}_0^i\,\partial_{x_1}\psi^i dx+\frac{1}{c_m}\int_\Omega a_e^{\text{eff}}\nabla\widetilde{z}_0^e\cdot\nabla\psi^e\,dx,
$$

and $(\widetilde{z}_0^i,\widetilde{z}_0^e)$ solve (34). In operator form one writes

$$
\begin{aligned}
&\partial_t W_0+\mathbb{A}_0(t,W_0)=F_0(t),\quad (t,x)\in(0,T)\times\Omega,\\
&W_0(0,x)=W_0^0(x),\quad x\in\Omega.
\end{aligned}
\tag{35}
$$

Therein, we have the following operators

$$
\mathbb{A}_0(t,W_0):=B_0^{(1)}(t,W_0)+B_0^{(2)}(t,W_0),
$$

$$B_0^{(1)}(t,W_0) := \begin{pmatrix} \frac{1}{c_m}A_{\text{eff}}w_0 + (\lambda - \frac{1}{c_m})w_0 - \frac{1}{c_m}h_0 \\ (b+\lambda)h_0 - \theta w_0 \end{pmatrix},$$

$$B_0^{(2)}(t,W_0) := \begin{pmatrix} \frac{e^{2\lambda t}}{3c_m}w_0^3 \\ 0 \end{pmatrix},$$

$$F_0(t) := e^{-\lambda t}\begin{pmatrix} a_i^{\text{eff}}\partial^2_{x_1x_1}q_0 \\ a \end{pmatrix}.$$

Introducing the spaces

$$\begin{aligned} &H_0 = L^2(\Omega) \times L^2(\Omega), \\ &V_1 = X_0 \times L^2(\Omega), \quad V_1' = X_0' \times L^2(\Omega), \\ &V_2 = L^4(\Omega) \times L^2(\Omega), \quad V_2' = L^{4/3}(\Omega) \times L^2(\Omega), \end{aligned}$$

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 (35). It follows, as in Section 2.3, from Theorem 1.4 in [27] and Remark 1.8 in Chapter 2.

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Appendix A. 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 $A_\varepsilon v_\varepsilon = \varepsilon f$ for some smooth function $f = f(x)$. Specifically, we write

$$\begin{aligned} &-\text{div}\,(a_\varepsilon \nabla u_\varepsilon) = 0, && x \in \Omega_\varepsilon^i \cup \Omega_\varepsilon^e, \\ &a_e \nabla u_\varepsilon^e \cdot \nu = a_i \nabla u_\varepsilon^i \cdot \nu = \varepsilon f(x), && x \in \Gamma_\varepsilon, \\ &u_\varepsilon^i - u_\varepsilon^e = v_\varepsilon, && x \in \Gamma_\varepsilon, \\ &a_e \nabla u_\varepsilon \cdot \nu = 0, && x \in \Gamma_\varepsilon^m \cup \Sigma, \\ &u_\varepsilon = 0, && x \in (S_0 \cup S_L). \end{aligned} \tag{A.1}$$

Take

$$u_\varepsilon^l(x) \sim u_0^l(x,y) + \varepsilon u_1^l(x,y) + \varepsilon^2 u_2^l(x,y) + \cdots, \quad y = \frac{x}{\varepsilon},$$

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

$$\begin{aligned} \text{div}(a_l \nabla u_\varepsilon^l) \sim\ & \frac{1}{\varepsilon^2}\text{div}_y(a_l \nabla_y u_0^l) \\ &+ \frac{1}{\varepsilon}\left(\text{div}_y(a_l \nabla_x u_0^l) + \text{div}_y(a_l \nabla_y u_1^l) + \text{div}_x(a_l \nabla_y u_0^l)\right) \\ &+ \text{div}_x(a_l \nabla_x u_0^l) + \text{div}_x(a_l \nabla_y u_1^l) + \text{div}_y(a_l \nabla_x u_1^l) + \text{div}_y(a_l \nabla_y u_2^l) \end{aligned}$$

$$\begin{aligned}&+ \varepsilon \left(\mathrm{div}_x(a_l \nabla_x u_1^l) + \mathrm{div}_x(a_l \nabla_y u_2^l) + \mathrm{div}_y(a_l \nabla_x u_2^l)\right)\\ &+ \varepsilon^2 \mathrm{div}_x(a_l \nabla_x u_2^l).\end{aligned}$$

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

$$\begin{aligned}&-\mathrm{div}_y(a_l \nabla_y u_0^l) = 0, && y \in Y_l,\\ &a_l \nabla_y u_0^l \cdot \nu = 0 && y \in \Gamma \cup \Gamma^m,\\ &u_0^i \text{ is 1-periodic in } y_1,\\ &\text{and } u_0^e \text{ is } Y\text{-periodic.}\end{aligned}$$

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

$$u_0^l(x,y) = u_0^l(x), \quad l = i, e. \tag{A.2}$$

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

$$\begin{aligned}&-\mathrm{div}_y(a_l \nabla_y u_1^l) = 0, && y \in Y_l,\\ &a_l \nabla_y u_1^l \cdot \nu = -a_l \nabla_x u_0^l \cdot \nu, && y \in \Gamma \cup \Gamma_m,\\ &u_1^i \text{ is 1-periodic in } y_1\\ &\text{and } u_1^e \text{ is } Y\text{-periodic.}\end{aligned} \tag{A.3}$$

The solvability condition reads $-\int_\Gamma a_l \nabla_x u_0^l \cdot \nu = 0$, which is fulfilled thanks to (A.2). By seeking a solution of (A.3) in the form $u_1^l(x,y) = \mathbf{N}^l(y) \cdot \nabla_x u_0^l(x)$, we obtain

$$a^l \nabla_y u_1^l(x,y) \cdot \nu = a^l \partial_{y_j} N_i^l(y) \nu_j \partial_{x_i} u_0^l(x),$$

where we assume summation over the repeated indexes. The boundary condition in (A.3) yields a boundary condition for N_i on $\Gamma \cup \Gamma_m$:

$$\left(\partial_{y_j} N_i^l(y) + \delta_{i,j}\right) \nu_j = 0.$$

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

$$\begin{aligned}&-\Delta N_k^e = 0, && y \in Y_e,\\ &\nabla N_k^e \cdot \nu = -\nu_k, && y \in \Gamma \cup \Gamma_m,\\ &y \mapsto N_k^e(y) \ \text{ is } \ Y-\text{periodic;}\end{aligned} \tag{A.4}$$

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 $\partial_{l \neq k} N_k^i = 0$. The first component N_1^i solves the problem

$$\begin{aligned}&-\Delta N_1^i = 0, && y \in Y_i,\\ &\nabla N_1^i \cdot \nu = -\nu_1, && y \in \Gamma \cup \Gamma_m,\\ &y \mapsto N_1^i(y) \ \text{ is } \ 1-\text{periodic;}\end{aligned} \tag{A.5}$$

Finally, taking the terms of order 1 in the volume and the ones of order ϵ^1 on the boundary, we obtain the following problem for u_2^l:

$$\begin{aligned}&-\mathrm{div}_y(a^l \nabla_y u_2^l) = \mathrm{div}_x(a^l \nabla_x u_0^l) + \mathrm{div}_x(a^l \nabla_y u_1^l) + \mathrm{div}_y(a^l \nabla_x u_1^l), && y \in Y_l,\\ &a^l \nabla_y u_2^l \cdot \nu^l = -a^l \nabla_x u_1^l \cdot \nu^l + f(x), && y \in \Gamma,\end{aligned}$$

$$a^l \nabla_y u_2^l \cdot \nu = 0, \qquad y \in \Gamma_m,$$
u_2^i is 1-periodic in y_1
and u_2^e is Y-periodic.

Here ν^l is the exterior unit normal, and $\nu^e = -\nu^i$ on Γ. The solvability condition reads

$$\int_{Y_l} \left(\mathrm{div}_x(a^l \nabla_x u_0^l) + \mathrm{div}_x(a^l \nabla_y u_1^l) + \mathrm{div}_y(a^l \nabla_x u_1^l)\right) dY - \int_{\Gamma} a^l \nabla_x u_2^l \cdot \nu^l d\sigma = 0.$$

Integrating by parts in the third term of the volume integral, substituting the expression $u_1^l(x,y) = N_i^l(y)\partial_{x_i} u_0^l(x)$, and taking into account that $N_k^i(y) = -y_k$ and $\int_{Y_i} \partial_{l\neq 1} N_1^i dy = 0$, we obtain

$$\begin{aligned} &- \partial_{kj} u_0^e(x) \int_{Y_e} a^e \left(\partial_j N_k^e(y) + \delta_{kj}\right) dy = |\Gamma| f(x), \\ &|Y_i| a_i \partial_{11} u_0^i(x) = |\Gamma| f(x). \end{aligned}$$

Introducing the effective coefficient

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

and adding the boundary conditions on $S_0 \cup S_L$ and Σ, we arrive at

$$\begin{aligned} &\frac{|Y_i|}{|\Gamma|} a_i \partial_{11} u_0^i = -a_e^{\mathrm{eff}} \Delta u_0^e = f(x), && x \in \Omega, \\ &u_0^{i,e} = 0, && x \in S_0 \cup S_L, \\ &a_e^{\mathrm{eff}} \nabla u^e \cdot \nu = 0, && x \in \Sigma. \end{aligned}$$

Appendix B. Monotonicity method

The passage to the limit in the microscopic problem requires us to adapt the method of monotone operators due to G. Minty [30]. The application of the method to problem (1) is given in Section 3.2. 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 ε. In [31], 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

$$\begin{aligned} &\partial_t u_\varepsilon + A(u_\varepsilon) = f_\varepsilon, \\ &u_\varepsilon\big|_{t=0} = V_\varepsilon^0. \end{aligned} \tag{B.1}$$

Assume that we know that u_ε 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 (B.1), we get

$$
\begin{aligned}
0 &\le \int_0^t (A(u_\varepsilon) - A(u_0+\delta\varphi), u_\varepsilon - (u_0+\delta\varphi))d\tau. \\
&= \int_0^t (f_\varepsilon, u_\varepsilon - (u_0+\delta\varphi))d\tau - \int_0^t (\partial_\tau u_\varepsilon, u_\varepsilon)d\tau + \int_0^t (\partial_\tau u_\varepsilon, (u_0+\delta\varphi))d\tau. \\
&- \int_0^t (A(u_0+\delta\varphi), u_\varepsilon - (u_0+\delta\varphi))d\tau.
\end{aligned} \tag{B.2}
$$

Integrating by parts, we get

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

Then inequality (B.2) transforms into

$$
\begin{aligned}
&\frac{1}{2}\|u_\varepsilon(t,\cdot)\|_H^2 - \frac{1}{2}\|u_0(t,\cdot)\|_H^2 - \frac{1}{2}\|V_\varepsilon^0\|_H^2 + \frac{1}{2}\|V^0\|_H^2 \\
&\le \int_0^t (f_\varepsilon, u_\varepsilon - (u_0+\delta\varphi))d\tau - \int_0^t (\partial_\tau u_0, u_0)d\tau \\
&+ \int_0^t (\partial_\tau u_\varepsilon, (u_0+\delta\varphi))d\tau - \int_0^t (A(u_0+\delta\varphi), u_\varepsilon - (u_0+\delta\varphi))d\tau.
\end{aligned} \tag{B.3}
$$

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

$$
\begin{aligned}
0 &\le \frac{1}{2}\limsup_{\varepsilon\to 0}\left(\|u_\varepsilon(t,\cdot)\|_H^2 - \|u_0(t,\cdot)\|_H^2\right) \\
&\le \delta\int_0^t (-f + \partial_\tau u_0 + A(u_0+\delta\varphi), \varphi)d\tau.
\end{aligned}
$$

Since the left-hand side is positive and δ is arbitrary, that delivers the strong convergence of u_ε

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

Furthermore,

$$
\int_0^t (\partial_\tau u_0 + A(u_0+\delta\varphi) - f, \delta\varphi)d\tau \ge 0. \tag{B.4}
$$

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

$$
\int_0^t (\partial_\tau u_0 + A(u_0) - f, \varphi)d\tau \ge 0.
$$

Then, dividing (B.4) by $\delta < 0$ and passing to the limit, as $\delta \to 0$, we have the opposite inequality

$$
\int_0^t (\partial_\tau u_0 + A(u_0) - f, \varphi)d\tau \le 0.
$$

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 $\partial_t u_0 + A(u_0) = f$.

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

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