

Homogenization of a nonlinear multiscale model of calcium dynamics in biological cells

Isabell Graf^a, Malte A. Peter^{a,b}, James Sneyd^c

^a*Institute of Mathematics, University of Augsburg, Augsburg, Germany*

^b*Augsburg Centre for Innovative Technologies, Augsburg, Germany*

^c*Department of Mathematics, University of Auckland, Auckland, New Zealand*

Abstract

Calcium is one of the most important intracellular messengers, which occurs in the cytosol and the endoplasmic reticulum of animal cells. While most calcium dynamics models either do not account properly for the fact that the endoplasmic reticulum constitutes a microstructure of the cell or are infeasible by resolving the fine structure very explicitly, Goel et al. [1] derived an effective macroscopic model by formal homogenization. In this paper, this approach is made rigorous using periodic homogenization techniques to upscale the nonlinear coupled system of reaction–diffusion equations and, moreover, the appropriate scaling of the interfacial exchange term is taken into consideration.

Keywords: Calcium bidomain equations, periodic homogenization, reaction–diffusion, interfacial exchange, nonlinear

2010 MSC: 35B27, 35K51, 35K58, 92B05, 92C40

1. Introduction

The calcium bidomain equations are a widely used model for the dynamics of calcium ions, which act as intracellular messengers between the extracellular space, the cytosol and the endoplasmic reticulum inside animal cells. The calcium bidomain equations consist of one reaction–diffusion equation for the concentration of calcium ions in the cytosol and one for the concentration of calcium ions in the endoplasmic reticulum, which are coupled through a nonlinear (volume) reaction term. Of course, the model is based on an averaging idea as the endoplasmic reticulum is a finely structured domain extending throughout the cell and surrounded by cytosol. Thereby, it constitutes a microstructure of the cell and the exchange of calcium between the cytosol and the endoplasmic reticulum in fact occurs at their common interface, i.e. the immersed surface of the endoplasmic reticulum. We refer to [2] for the general physiological background.

Email address: peter@math.uni-augsburg.de (Malte A. Peter)

A first approach to derive the calcium bidomain equations from a homogenization approach explicitly taking into account the multiscale nature of the problem was undertaken by [1] and we also refer the reader to this article for a much more detailed introduction into the modelling aspects of the calcium dynamics problem under consideration here. The homogenization approach there was only formal, however, and no rigorous proofs were provided. In this paper, the approach is made rigorous based on periodic homogenization.

Periodic homogenization is a method for upscaling rigorously mathematical models of multiscale processes. In many cases, the multiscale nature of the problem stems from a microstructure of the material under consideration. While it is infeasible to resolve the microstructure in detail in numerical simulations (and often unnecessary), upscaled models describing the processes on an observation scale much larger than the characteristic size of the microstructure are required. In periodic homogenization, such upscaled models are obtained by assuming the microstructure of the material to be periodic with respect to a reference cell and considering the limit as the periodicity length approaches zero. Monographs on the subject include [3, 4, 5, 6, 7, 8].

There are two main difficulties in upscaling the calcium dynamics problem by periodic homogenization. On the one hand, it is important to choose the correct scaling of the material parameters with the homogenization parameter as it is well known that this has a large influence on the limit problems. In particular, different scalings may lead to different types of limit problems, cf. e.g. [9, 10, 11]. On the other hand, the notions of convergence in periodic homogenization are of weak type, which implies that they are not compatible with nonlinear terms a priori. Thus, additional problem-specific considerations are required in order to characterise the limit problems. We refer the reader to e.g. [12, 13, 14, 15] for this aspect. It is worth pointing out that the homogenization of a linear version of the problem considered here follows as a special case of the general considerations in [10].

Bidomain models based on averaging ideas arise in other contexts in mathematical biology as well. For example, the cardiac bidomain equations model electrical conduction in a biological tissue, i.e. formations of many cells, where the microstructure is due to the single cells [16, 17]. Similar to the problem under consideration here, a key interest is in the effective condition describing the exchange at the boundary between the two (microscopically) spatially separate domains. Rigorous homogenization results for such related models can be found in [18, 19].

The paper is organized as follows. In §2 the microscale problem is introduced and the mathematical assumptions on the setup are stated. The resulting homogenized limit problem is given in §3. The remaining sections contain the details of the rigorous homogenization procedure: well-posedness and a-priori estimates of the microproblem (§4), convergence (§5) and the identification of the limit problems (§6). Finally, uniqueness of the homogenized limit problems is proven in §7.

2. Problem setting

We consider an open bounded material body $\Omega \subset \mathbb{R}^d$ with Lipschitz boundary, which is a mixture of two different phases. The geometry under consideration is basically the same as in [10]. We repeat the relevant facts for the reader's convenience in the context and the notation required here. The part of Ω made up of the first material is denoted by Ω^1 while the other part is labelled with Ω^2 . We assume Ω to be periodic with respect to a scaled representative cell $Y = (0, 1)^d$, which contains a volume of cytosol, Z^1 , and a piece of endoplasmic reticulum, Z^2 (each being an open bounded domain with Lipschitz boundary), i.e. Ω is the union of translated versions of εY . Then, $\Omega_\varepsilon^\alpha$ is defined as $\bigcup_{k \in \mathcal{I}} \varepsilon \overline{Z_k^\alpha}$, $\alpha \in \{1, 2\}$, which is assumed connected, for some bounded index set $\mathcal{I} \subset \mathbb{Z}^d$. Here, the subscript k indicates translation of the set by $k \in \mathbb{Z}^d$ and ε denotes the ε -periodicity of the domain. The characteristic function of Z^α is given by $\chi^\alpha : Y \rightarrow \{0, 1\}$, $\alpha \in \{1, 2\}$, and we write $\chi_\varepsilon^\alpha(x) = \chi^\alpha(\frac{x}{\varepsilon})$, where χ^α has been extended periodically. The common interface of Ω_ε^1 and Ω_ε^2 (internal to Ω) is labelled with Γ_ε . We set $\Gamma = \text{int}(\partial Z^1 \cap \partial Z^2)$ and the time interval under consideration is denoted by $S = (0, T)$.

The idea of periodic homogenization (e.g. cf. [20, 21]) is then to examine the limit as ε approaches zero in order to obtain averaged problems defined in all of Ω , which are easier to treat numerically and give useful information about macroscopically observable processes.

We consider the dynamics of the concentration of calcium ions in a biological cell, represented by u_ε in the cytosol Ω_ε^1 and by v_ε in the endoplasmic reticulum Ω_ε^2 . Cf. [1], the ε -periodic problem is given by

$$\partial_t u_\varepsilon(x, t) - \nabla \cdot (D_\varepsilon \nabla u_\varepsilon) = f(u_\varepsilon) \quad \text{in } \Omega_\varepsilon^1, \quad (1a)$$

$$\partial_t v_\varepsilon(x, t) - \nabla \cdot (E_\varepsilon \nabla v_\varepsilon) = g(v_\varepsilon) \quad \text{in } \Omega_\varepsilon^2, \quad (1b)$$

$$E_\varepsilon \nabla v_\varepsilon \cdot n_\varepsilon^2 = -D_\varepsilon \nabla u_\varepsilon \cdot n_\varepsilon^1 = \varepsilon^m h(u_\varepsilon, v_\varepsilon) \quad \text{on } \Gamma_\varepsilon, \quad (1c)$$

where n^j are the outward normal vectors on $\overline{Z^j} \cap \Gamma$. For technical simplicity, we assume no-flux conditions for both concentrations at the outer cell membrane. The non-negative initial conditions are denoted by $u_\varepsilon(x, 0) = u_0(x)$, $v_\varepsilon(x, 0) = v_0(x)$. The scaling exponent $m \geq 0$ is a real number. The value of the scaling number m is related to the speed of the interfacial exchange, cf. [10, 11] for details.

Let $\mathcal{V}(\Omega) = L^2(0, T; W^{1,2}(\Omega))$, $\mathcal{W}(\Omega) = \{u \in \mathcal{V}(\Omega) \mid \partial_t u \in L^2(\Omega \times (0, T))\}$, $(u(t) \mid v(t))_\Omega = \int_\Omega u(x, t)v(x, t) dx$, $(u \mid v)_{\Omega, t} = \int_0^t (u(t) \mid v(t))_\Omega dt$, $\|u(t)\|_\Omega^2 = (u(t) \mid u(t))_\Omega$ and $\|u\|_{\Omega, t}^2 = (u \mid u)_{\Omega, t}$. Then, the (standard) weak form of problem (1) reads: Find $(u_\varepsilon, v_\varepsilon) \in \mathcal{W}(\Omega_\varepsilon^1) \times \mathcal{W}(\Omega_\varepsilon^2)$ such that $(u_\varepsilon(0), v_\varepsilon(0)) = (u_0, v_0) \in [L^2(\Omega)]^2$ and

$$(\partial_t u_\varepsilon(t) \mid \varphi(t))_{\Omega_\varepsilon^1} + (D_\varepsilon(t) \nabla u_\varepsilon(t) \mid \nabla \varphi(t))_{\Omega_\varepsilon^1} = (f(u_\varepsilon(t)) \mid \varphi(t))_{\Omega_\varepsilon^1} - \varepsilon^m (h(u_\varepsilon(t), v_\varepsilon(t)) \mid \varphi(t))_{\Gamma_\varepsilon}, \quad (2a)$$

$$(\partial_t v_\varepsilon(t) \mid \psi(t))_{\Omega_\varepsilon^2} + (E_\varepsilon(t) \nabla v_\varepsilon(t) \mid \nabla \psi(t))_{\Omega_\varepsilon^2} = (g(v_\varepsilon(t)) \mid \psi(t))_{\Omega_\varepsilon^2} + \varepsilon^m (h(u_\varepsilon(t), v_\varepsilon(t)) \mid \psi(t))_{\Gamma_\varepsilon} \quad (2b)$$

for all $(\varphi, \psi) \in \mathcal{V}(\Omega_\varepsilon^1) \times \mathcal{V}(\Omega_\varepsilon^2)$ and a.e. $t \in S$.

For the coefficient functions, we assume that their spatial dependence can each be split into a macroscopic and a microscopic component: It is assumed that there exist bounded matrix-valued functions $D = D(x, y, t)$, $x \in \Omega_\varepsilon^1$, $y \in Z^1$, $t \in S$ and $E = E(x, y, t)$, $x \in \Omega_\varepsilon^2$, $y \in Z^2$, $t \in S$, uniformly elliptic and extended periodically in the y -variable, such that $D_\varepsilon = D(x, \frac{x}{\varepsilon}, t)$, $E_\varepsilon = E(x, \frac{x}{\varepsilon}, t)$ are uniformly elliptic and $\partial_t D_\varepsilon, \partial_t E_\varepsilon \in [L^\infty(\Omega_\varepsilon \times S)]^{d \times d}$. Moreover, for the matrix elements, we require

$$\lim_{\varepsilon \rightarrow 0} \|D_{\varepsilon, ij}(t)\|_{\Omega_\varepsilon^1}^2 = \|D_{ij}(t)\|_{\Omega \times Y}^2, \quad \lim_{\varepsilon \rightarrow 0} \|E_{\varepsilon, ij}(t)\|_{\Omega_\varepsilon^2}^2 = \|E_{ij}(t)\|_{\Omega \times Y}^2. \quad (3)$$

We assume f, g, h to be Lipschitz-continuous with constants L_f, L_g, L_{h_u} and L_{h_v} and $f(0) = g(0) = 0$. For simplicity and since this is the relevant case in applications, we assume $h(r, s)$ to be of the form $h(r, s) = \bar{h}(r, s)(r - s)$ with $0 < h_{\min} \leq \bar{h}(r, s) \leq h_{\max} < \infty$. This condition can be somewhat relaxed, however, as will be discussed below.

3. Macroscopic limit problems – summary of results

The macroscopic limit problems of problem (2) are now stated. We denote the limit functions of u_ε and v_ε as $\varepsilon \rightarrow 0$ by u and v , respectively. Obviously, different choices of the scaling exponents m need to be distinguished.

It is useful to distinguish the cases $m < 1$ and $m \geq 1$ as they correspond to particularly different limit behaviours. It turns out that independently of the choice of m , the concentrations u and v are independent of y . Moreover, the homogeneous Neumann boundary conditions on the external boundary of Ω are recovered.

For the statement of the limit problems, we require a couple of cell problems, which are discussed first.

3.1. Cell problems

The solutions of two cell problems are required. Let μ_j, ν_j , $j = 1, \dots, d$, be the Y -periodic solution of the cell problems

$$\begin{aligned} -\nabla_y \cdot (D(x, y, t)(\nabla_y \mu_j(y, t) + e_j)) &= 0, & y \in Z^1, x \in \Omega, t \in S, \\ -D(x, y, t)(\nabla_y \mu_j(y, t) + e_j) \cdot n^1 &= 0, & y \in \Gamma, x \in \Omega, t \in S, \\ -\nabla_y \cdot (E(x, y, t)(\nabla_y \nu_j(y, t) + e_j)) &= 0, & y \in Z^2, x \in \Omega, t \in S, \\ -E(x, y, t)(\nabla_y \nu_j(y, t) + e_j) \cdot n^2 &= 0, & y \in \Gamma, x \in \Omega, t \in S, \end{aligned} \quad (4)$$

the weak forms of which are given by

$$\begin{aligned} (D(x, \cdot, t)(\nabla_y \mu_j(x, \cdot, t) + e_j) | \nabla_y \varphi)_{Z^1} &= 0, \\ (E(x, \cdot, t)(\nabla_y \nu_j(x, \cdot, t) + e_j) | \nabla_y \varphi)_{Z^2} &= 0 \end{aligned} \quad (5)$$

for all Y -periodic test functions φ . The vector e_j is the j th unit vector in d -dimensional Euclidean space. It is well-known that the solution of each of these cell problems exists and is unique up to addition of a constant [7, 22].

The solutions of the cell problems allow the definition of the tensors $P^u = [P_{ij}^u]_{ij=1\dots n}$, $P^v = [P_{ij}^v]_{ij=1\dots n}$ via

$$\begin{aligned} P_{ij}^u(x, t) &= \int_{Z^1} D(x, y, t)(e_i + \nabla_y \mu_i(y, t))(e_j + \nabla_y \mu_j(y, t)) dy, \\ P_{ij}^v(x, t) &= \int_{Z^2} E(x, y, t)(e_i + \nabla_y \nu_i(y, t))(e_j + \nabla_y \nu_j(y, t)) dy, \end{aligned} \quad (6)$$

which turn out to be the macroscopic diffusion tensors in the limit problems. The tensors are uniquely defined, symmetric and positive definite.

3.2. The case $m < 1$

For $m < 1$, it turns out that the limit functions satisfy $u(x, t) = v(x, t)$ for a.e. $x \in \Omega$, $y \in Y$, $t \in S$. Therefore, it make sense to replace v by u and to look for the one equation satisfied by u . For ease of notation, we also define

$$F(u(x, t)) = \int_Y (\chi^1(y)f(u(x, t)) + \chi^2(y)g(u(x, t))) dy = |Z^1|f(u(x, t)) + |Z^2|g(u(x, t)) \quad (7)$$

If $m < 1$ the macroscopic limit problem of problem (2) reads as follows: find $u \in \mathcal{W}(\Omega)$ such that $u(0) = |Z^1|u_0 + |Z^2|v_0$ and

$$((|Z^1| + |Z^2|)\partial_t u(t) | \varphi(t))_\Omega + ((P^u(t) + P^v(t))\nabla u(t) | \nabla \varphi(t))_\Omega = (F(u(t)) | \varphi(t))_\Omega \quad (8)$$

for all $\varphi \in \mathcal{V}(\Omega)$ and a.e. $t \in S$.

Obviously, this is not the bidomain equation(s) but it is an appropriate model when the interfacial exchange of calcium between the cytosol and the endoplasmic reticulum is very fast.

3.3. The case $m \geq 1$

If $m \geq 1$, the limit functions u and v need to be considered separately. In order to be able to write the macroscopic limit equations in a simple way, the limit of the interfacial-exchange term is written as

$$h^{\text{ex}}(u, v) = |\Gamma|h(u, v) \quad \text{for } m = 1, \quad h^{\text{ex}}(u, v) = 0 \quad \text{for } m > 1. \quad (9)$$

The macroscopic limit problem is given by: find $u, v \in \mathcal{W}(\Omega)$ such that $u(0) = |Z^1|u_0$, $v(0) = |Z^2|v_0$ and

$$|Z^1|(\partial_t u(t) | \varphi(t))_\Omega + (P^u(t)\nabla u(t) | \nabla \varphi(t))_\Omega = \left(\int_{Z^1} f(\cdot, y, t) dy | \varphi(t) \right)_\Omega - (h^{\text{ex}}(u(t), v(t)) | \varphi(t))_\Omega, \quad (10a)$$

$$|Z^2|(\partial_t v(t) | \varphi(t))_\Omega + (P^v(t)\nabla v(t) | \nabla \varphi(t))_\Omega = \left(\int_{Z^2} g(\cdot, y, t) dy | \varphi(t) \right)_\Omega + (h^{\text{ex}}(u(t), v(t)) | \varphi(t))_\Omega. \quad (10b)$$

for all $\varphi \in \mathcal{V}(\Omega)$ and a.e. $t \in S$.

These equations are of the form of the calcium bidomain equations, where all effective parameters and sink and source terms are given explicitly in dependence on the microscopic representation.

4. Well-posedness and a-priori estimates

In this section, the well-posedness of the microscopic problem (2) as well as a-priori estimates required for the limit passage as ε tends to zero are proven.

Lemma 4.1

The functions u_ε and v_ε are non-negative almost everywhere.

PROOF We define

$$u_{\varepsilon-} := \begin{cases} -u_\varepsilon(x, t), & \text{if } u_\varepsilon(x, t) \leq 0, \\ 0, & \text{else,} \end{cases} \quad v_{\varepsilon-} := \begin{cases} -v_\varepsilon(x, t), & \text{if } v_\varepsilon(x, t) \leq 0, \\ 0, & \text{else.} \end{cases}$$

Testing the weak formulation (2) with $-u_{\varepsilon-}$, $-v_{\varepsilon-}$, respectively, and adding gives

$$\begin{aligned} & (\partial_t u_{\varepsilon-}(t) | u_{\varepsilon-}(t))_{\Omega_\varepsilon^1} + (\partial_t v_{\varepsilon-}(t) | v_{\varepsilon-}(t))_{\Omega_\varepsilon^2} + (D_\varepsilon(t) \nabla u_{\varepsilon-}(t) | \nabla u_{\varepsilon-}(t))_{\Omega_\varepsilon^1} + (E_\varepsilon(t) \nabla v_{\varepsilon-}(t) | \nabla v_{\varepsilon-}(t))_{\Omega_\varepsilon^2} \\ & = -(f(u_\varepsilon) | u_{\varepsilon-}(t))_{\Omega_\varepsilon^1} - (g(v_\varepsilon) | v_{\varepsilon-}(t))_{\Omega_\varepsilon^2} + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_{\varepsilon-} - v_{\varepsilon-})(t))_{\Gamma_\varepsilon}. \end{aligned}$$

Noting that the initial values are non-negative, integration with respect to time gives

$$\begin{aligned} & \frac{1}{2} \|u_{\varepsilon-}(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_{\varepsilon-}(t)\|_{\Omega_\varepsilon^2}^2 + (D_\varepsilon \nabla u_{\varepsilon-} | \nabla u_{\varepsilon-})_{\Omega_\varepsilon^1, t} + (E_\varepsilon \nabla v_{\varepsilon-} | \nabla v_{\varepsilon-})_{\Omega_\varepsilon^2, t} \\ & = -(f(u_\varepsilon) | u_{\varepsilon-})_{\Omega_\varepsilon^1, t} - (g(v_\varepsilon) | v_{\varepsilon-})_{\Omega_\varepsilon^2, t} + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_{\varepsilon-} - v_{\varepsilon-}))_{\Gamma_\varepsilon, t}. \end{aligned}$$

Making use of the ellipticity of D_ε and E_ε and the Lipschitz-continuity of f and g , we can estimate,

$$\frac{1}{2} \|u_{\varepsilon-}(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_{\varepsilon-}(t)\|_{\Omega_\varepsilon^2}^2 \leq L_f \|u_{\varepsilon-}\|_{\Omega_\varepsilon^1, t}^2 + L_g \|v_{\varepsilon-}\|_{\Omega_\varepsilon^2, t}^2 + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_{\varepsilon-} - v_{\varepsilon-}))_{\Gamma_\varepsilon, t}.$$

Using Gronwall's lemma, it easily follows that $u_{\varepsilon-} = v_{\varepsilon-} = 0$ a.e. if h is such that $(h(u_\varepsilon, v_\varepsilon) | (u_{\varepsilon-} - v_{\varepsilon-}))_{\Gamma_\varepsilon, T} \leq 0$ for all possible $u_\varepsilon, v_\varepsilon$. This is satisfied since $h(u_\varepsilon, v_\varepsilon) = \bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)$ with \bar{h} non-negative. \blacktriangleleft

Lemma 4.2

The functions u_ε and v_ε are bounded almost everywhere.

PROOF Let $M(t) = \max\{\|u_0\|_\infty, \|v_0\|_\infty\} e^{kt}$ with a $k \in \mathbb{R}$ to be specified later. We define

$$(u_\varepsilon - M)_+(x, t) := \begin{cases} u_\varepsilon(x, t) - M(t), & \text{if } u_\varepsilon(x, t) - M(t) \geq 0, \\ 0, & \text{else.} \end{cases}$$

Testing the weak formulation (2) with $(u_\varepsilon - M)_+$, $(v_\varepsilon - M)_+$, respectively, and adding gives

$$\begin{aligned} & (\partial_t u_\varepsilon(t) | (u_\varepsilon - M)_+(t))_{\Omega_\varepsilon^1} + (\partial_t v_\varepsilon(t) | (v_\varepsilon - M)_+(t))_{\Omega_\varepsilon^2} \\ & + (D_\varepsilon(t) \nabla u_\varepsilon(t) | \nabla (u_\varepsilon - M)_+(t))_{\Omega_\varepsilon^1} + (E_\varepsilon(t) \nabla v_\varepsilon(t) | \nabla (v_\varepsilon - M)_+(t))_{\Omega_\varepsilon^2} \\ & = (f(u_\varepsilon(t)) | (u_\varepsilon - M)_+(t))_{\Omega_\varepsilon^1} + (g(v_\varepsilon(t)) | (v_\varepsilon - M)_+(t))_{\Omega_\varepsilon^2} - \varepsilon^m (h(u_\varepsilon(t), v_\varepsilon(t)) | (u_\varepsilon - M)_+(t) - (v_\varepsilon - M)_+(t))_{\Gamma_\varepsilon}. \end{aligned}$$

This implies, after integration with respect to time,

$$\begin{aligned} & \frac{1}{2} \|(u_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|(v_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^2}^2 + \|\sqrt{D_\varepsilon} \nabla (u_\varepsilon - M)_+\|_{\Omega_\varepsilon^1, t}^2 + \|\sqrt{E_\varepsilon} \nabla (v_\varepsilon - M)_+\|_{\Omega_\varepsilon^2, t}^2 \\ &= (f(u_\varepsilon) | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t} + (g(v_\varepsilon) | (v_\varepsilon - M)_+)_{\Omega_\varepsilon^2, t} - \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_\varepsilon - M)_+ - (v_\varepsilon - M)_+)_{\Gamma_\varepsilon, t} \\ & \quad - (kM | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t} - (kM | (v_\varepsilon - M)_+)_{\Omega_\varepsilon^2, t}. \end{aligned}$$

Let us look at the reaction terms on the second line. If both reaction terms are negative we can choose $k = 0$ and obtain the estimate

$$\frac{1}{2} \|(u_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|(v_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^2}^2 \leq -\varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_\varepsilon - M)_+ - (v_\varepsilon - M)_+)_{\Gamma_\varepsilon, t}.$$

If one of the reaction terms is non-negative, we choose k to be the Lipschitz constant associated with this reaction function. If both reaction terms are non-negative, we choose $k = \max\{L_f, L_g\}$, where L_f and L_g are the Lipschitz constants associated with f and g , respectively. Then, we can estimate

$$(f(u_\varepsilon) - kM | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t} \leq (L_f u_\varepsilon - kM | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t} \leq k(u_\varepsilon - M | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t}$$

and, analogously, for the reaction term in Ω_ε^2 . Moreover, since we have $h(u_\varepsilon, v_\varepsilon) = \bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)$, it follows that $-\varepsilon^m (h(u_\varepsilon, v_\varepsilon) | (u_\varepsilon - M)_+ - (v_\varepsilon - M)_+)_{\Gamma_\varepsilon, t} \leq 0$ and, altogether, we obtain

$$\begin{aligned} & \frac{1}{2} \|(u_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|(v_\varepsilon - M)_+(t)\|_{\Omega_\varepsilon^2}^2 \\ & \leq k((u_\varepsilon - M)_+ | (u_\varepsilon - M)_+)_{\Omega_\varepsilon^1, t} + k((v_\varepsilon - M)_+ | (v_\varepsilon - M)_+)_{\Omega_\varepsilon^2, t} \end{aligned}$$

with k equal to 0, L_f , L_g or $\max\{L_f, L_g\}$ depending on the reaction terms. From this, the assertion follows using Gronwall's inequality. \blacktriangleleft

Lemma 4.3

For the functions u_ε and v_ε there exists a constant $C \geq 0$, independent of ε , such that

$$\|u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \|v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 + \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 + \|\nabla v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | u_\varepsilon - v_\varepsilon)_{\Gamma_\varepsilon, t} \leq C \quad (11)$$

for a.e. $t \in S$.

PROOF Testing the weak formulation (2) with $(u_\varepsilon, v_\varepsilon)$, adding and integrating with respect to time gives

$$\begin{aligned} & \frac{1}{2} \|u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 + \|\sqrt{D_\varepsilon} \nabla u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 + \|\sqrt{E_\varepsilon} \nabla v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | u_\varepsilon - v_\varepsilon)_{\Gamma_\varepsilon, t} \\ &= (f(u_\varepsilon) | u_\varepsilon)_{\Omega_\varepsilon^1, t} + (g(v_\varepsilon) | v_\varepsilon)_{\Omega_\varepsilon^2, t} + \frac{1}{2} \|u_0\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_0\|_{\Omega_\varepsilon^2}^2. \end{aligned}$$

Since u_ε and v_ε are bounded and non-negative, we obtain the estimate

$$\begin{aligned} & \frac{1}{2} \|u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 + \|\sqrt{D_\varepsilon} \nabla u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 + \|\sqrt{E_\varepsilon} \nabla v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | u_\varepsilon - v_\varepsilon)_{\Gamma_\varepsilon, t} \\ & \leq L_f \|u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 + L_g \|v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 + \frac{1}{2} \|u_0\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|v_0\|_{\Omega_\varepsilon^2}^2. \end{aligned}$$

Then, we obtain using Gronwall's inequality

$$\frac{1}{2}\|u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2}\|v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 + \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 + \|\nabla v_\varepsilon\|_{\Omega_\varepsilon^2,t}^2 + \varepsilon^m(h(u_\varepsilon, v_\varepsilon) | u_\varepsilon - v_\varepsilon)_{\Gamma_\varepsilon,t} \leq C. \quad \blacktriangleleft$$

We state the following trace lemma without proof (e.g. see [7]).

Lemma 4.4

There exists a positive constant c_0 , independent of ε , such that $\|u\|_{\Gamma_\varepsilon}^2 \leq c_0 \left(\frac{1}{\varepsilon} \|u\|_{\Omega_\varepsilon}^2 + \varepsilon \|\nabla u\|_{\Omega_\varepsilon}^2 \right)$ for any $u \in \mathcal{V}(\Omega_\varepsilon)$.

We need the trace lemma above to prove the next result.

Lemma 4.5

Let $m \geq 1$. There exists a positive constant C , independent of ε , such that

$$\|\partial_t u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \|\partial_t v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 \leq C. \quad (12)$$

PROOF Taking the time derivative of the strong formulation and testing with $\partial_t u_\varepsilon$ (this can be made rigorous by considering difference quotients and passing to the limit, cf. e.g. [23]) gives

$$\begin{aligned} & (\partial_{tt} u_\varepsilon(t) | \partial_t u_\varepsilon(t))_{\Omega_\varepsilon^1} + (\partial_t D_\varepsilon \nabla u_\varepsilon(t) | \nabla \partial_t u_\varepsilon(t))_{\Omega_\varepsilon^1} + (D_\varepsilon \nabla \partial_t u_\varepsilon(t) | \nabla \partial_t u_\varepsilon(t))_{\Omega_\varepsilon^1} \\ & + \varepsilon^m (\partial_t h(u_\varepsilon(t), v_\varepsilon(t)) | \partial_t u_\varepsilon(t))_{\Gamma_\varepsilon} = (f'(u_\varepsilon(t)) \partial_t u_\varepsilon(t) | \partial_t u_\varepsilon(t))_{\Omega_\varepsilon^1}. \end{aligned}$$

Integration with respect to time and standard estimation gives

$$\begin{aligned} & \frac{1}{2} \|\partial_t u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \|\sqrt{D_\varepsilon} \nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \\ & = -(\partial_t D_\varepsilon \nabla u_\varepsilon, \nabla \partial_t u_\varepsilon)_{\Omega_\varepsilon^1,t} - \varepsilon^m (\partial_u h \partial_t u_\varepsilon + \partial_v h \partial_t v_\varepsilon | \partial_t u_\varepsilon)_{\Gamma_\varepsilon,t} + (f'(u_\varepsilon) \partial_t u_\varepsilon | \partial_t u_\varepsilon)_{\Omega_\varepsilon^1,t} + \frac{1}{2} \|\partial_t u_\varepsilon(0)\|_{\Omega_\varepsilon^1}^2 \\ & \leq C_0 \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1,t} \|\nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t} + \varepsilon^m \|\partial_u h\|_\infty \|\partial_t u_\varepsilon\|_{\Gamma_\varepsilon,t}^2 + \varepsilon^m \|\partial_v h\|_\infty \|\partial_t u_\varepsilon\|_{\Gamma_\varepsilon,t} \|\partial_t v_\varepsilon\|_{\Gamma_\varepsilon,t} + \|f'\|_\infty \|\partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 + c \end{aligned}$$

for constants $c, C_0 > 0$. Using the trace inequality, we arrive at

$$\begin{aligned} & \frac{1}{2} \|\partial_t u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \|\sqrt{D_\varepsilon} \nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \\ & \leq \|\partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \left(L_{h_u} c_0 \varepsilon^{m-1} + L_{h_v} \frac{c_0 \delta_2}{2} \varepsilon^{m-1} + L_f \right) \\ & + \|\nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \left(\frac{1}{2\delta_1} C_0 + L_{h_u} c_0 \varepsilon^{m+1} + L_{h_v} \frac{c_0 \delta_2}{2} \varepsilon^{m+1} \right) + \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \left(C_0 \frac{\delta_1}{2} \right) \\ & + \|\partial_t v_\varepsilon\|_{\Omega_\varepsilon^2,t}^2 L_{h_v} \frac{c_0}{2\delta_2} \varepsilon^{m-1} + \|\nabla \partial_t v_\varepsilon\|_{\Omega_\varepsilon^2,t}^2 L_{h_v} \frac{c_0}{2\delta_2} \varepsilon^{m+1} + c. \end{aligned}$$

for arbitrary $\delta_1, \delta_2 > 0$. Since D_ε and E_ε are elliptic, there are $\alpha, \beta > 0$ such that

$$\|\sqrt{D_\varepsilon} \nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2 \geq \alpha \|\nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1,t}^2, \quad \|\sqrt{E_\varepsilon} \nabla \partial_t v_\varepsilon\|_{\Omega_\varepsilon^2,t}^2 \geq \beta \|\nabla \partial_t v_\varepsilon\|_{\Omega_\varepsilon^2,t}^2.$$

We use this estimate to continue with

$$\begin{aligned} & \frac{1}{2} \|\partial_t u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \|\nabla \partial_t u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 \left(\alpha - \frac{1}{2\delta_1} C_0 - L_{h_u} c_0 \varepsilon^{m+1} - L_{h_v} \frac{c_0 \delta_2}{2} \varepsilon^{m+1} \right) \\ & \leq \|\partial_t u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 \left(L_{h_u} c_0 \varepsilon^{m-1} + L_f + L_{h_v} \frac{c_0 \delta_2}{2} \varepsilon^{m-1} \right) + \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 \left(C_0 \frac{\delta_1}{2} \right) \\ & \quad + \|\partial_t v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 \left(L_{h_v} \frac{c_0}{2\delta_2} \varepsilon^{m-1} \right) + \|\nabla \partial_t v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 \left(L_{h_v} \frac{c_0}{2\delta_2} \varepsilon^{m+1} \right) + c. \end{aligned}$$

We perform analogous estimations for v_ε and add the result to the inequality above. After carefully choosing the δ_i , it follows for ε sufficiently small

$$\frac{1}{2} \|\partial_t u_\varepsilon(t)\|_{\Omega_\varepsilon^1}^2 + \frac{1}{2} \|\partial_t v_\varepsilon(t)\|_{\Omega_\varepsilon^2}^2 \leq \|\partial_t u_\varepsilon\|_{\Omega_\varepsilon^1, t}^2 C_1 + \|\partial_t v_\varepsilon\|_{\Omega_\varepsilon^2, t}^2 C_2 + C_3.$$

Using Gronwall's lemma, we obtain the desired result. \blacktriangleleft

If $m < 1$, we still get the following result:

Lemma 4.6

Let $m \geq 0$. There exists a positive constant C , independent of ε , such that

$$\|\partial_t u_\varepsilon\|_{L^2(S, H^{-1}(\Omega_\varepsilon^1))} + \|\partial_t v_\varepsilon\|_{L^2(S, H^{-1}(\Omega_\varepsilon^2))} \leq C. \quad (13)$$

PROOF Using the definition of the H^{-1} -norm and noting that the boundary terms vanish, we can estimate

$$\begin{aligned} & \|\partial_t u_\varepsilon\|_{H^{-1}(\Omega_\varepsilon^1)} + \|\partial_t v_\varepsilon\|_{H^{-1}(\Omega_\varepsilon^2)} \\ & = \sup_{\varphi \in H_0^1(\Omega_\varepsilon^1)} (\partial_t u_\varepsilon | \varphi)_{(H^{-1}(\Omega_\varepsilon^1) | H_0^1(\Omega_\varepsilon^1))} / \|\varphi\|_{H_0^1(\Omega_\varepsilon^1)} + \sup_{\psi \in H_0^1(\Omega_\varepsilon^2)} (\partial_t v_\varepsilon | \psi)_{(H^{-1}(\Omega_\varepsilon^2) | H_0^1(\Omega_\varepsilon^2))} / \|\psi\|_{H_0^1(\Omega_\varepsilon^2)} \\ & = \sup_{\varphi \in H_0^1(\Omega_\varepsilon^1)} \left((-D_\varepsilon \nabla u_\varepsilon | \nabla \varphi)_{(L^2(\Omega_\varepsilon^1) | L^2(\Omega_\varepsilon^1))} + (f(u_\varepsilon) | \varphi)_{(H^{-1}(\Omega_\varepsilon^1) | H_0^1(\Omega_\varepsilon^1))} \right) / \|\varphi\|_{H_0^1(\Omega_\varepsilon^1)} \\ & \quad + \sup_{\psi \in H_0^1(\Omega_\varepsilon^2)} \left((-E_\varepsilon \nabla v_\varepsilon | \nabla \psi)_{(L^2(\Omega_\varepsilon^2) | L^2(\Omega_\varepsilon^2))} + (g(v_\varepsilon) | \psi)_{(H^{-1}(\Omega_\varepsilon^2) | H_0^1(\Omega_\varepsilon^2))} \right) / \|\psi\|_{H_0^1(\Omega_\varepsilon^2)} \\ & \leq \sup_{\varphi \in H_0^1(\Omega_\varepsilon^1)} (C_1 \|\nabla u_\varepsilon\|_{\Omega_\varepsilon^1} \|\nabla \varphi\|_{\Omega_\varepsilon^1} + \|f\|_{H^{-1}(\Omega_\varepsilon^1)} \|\varphi\|_{H_0^1(\Omega_\varepsilon^1)}) / \|\varphi\|_{H_0^1(\Omega_\varepsilon^1)} \\ & \quad + \sup_{\psi \in H_0^1(\Omega_\varepsilon^2)} (C_2 \|\nabla v_\varepsilon\|_{\Omega_\varepsilon^2} \|\nabla \psi\|_{\Omega_\varepsilon^2} + \|g\|_{H^{-1}(\Omega_\varepsilon^2)} \|\psi\|_{H_0^1(\Omega_\varepsilon^2)}) / \|\psi\|_{H_0^1(\Omega_\varepsilon^2)} \end{aligned}$$

Integration with respect to time and use of lemma 4.3 gives the result. \blacktriangleleft

Proposition 4.7 (Existence)

There exists at least one solution $(u_\varepsilon, v_\varepsilon)$ of problem (2).

PROOF We begin with showing existence of solutions for a (possibly short) time interval $(0, \tau)$. For convenience, the spaces \mathcal{V} and \mathcal{W} refer to this time interval in this proof.

Fix δ with $0 < \delta < \frac{1}{2}$ and let $\hat{u}_\varepsilon \in V = L^2(0, \tau; H^{1-\delta}(\Omega_\varepsilon^1))$ and $\hat{v}_\varepsilon \in W = L^2(0, \tau; H^{1-\delta}(\Omega_\varepsilon^2))$ be given functions. Since the Nemytskii operators associated with f , g and h , F , G and H say, are bounded and continuous as mappings $V \rightarrow L^2(0, \tau, L^2(\Omega_\varepsilon^1))$, $W \rightarrow L^2(0, \tau, L^2(\Omega_\varepsilon^2))$ and $[L^2(0, \tau; L^2(\Gamma_\varepsilon))]^2 \rightarrow L^2(0, \tau; H^{-1/2}(\Gamma_\varepsilon))$, problem (2), in which the concentration-dependent reaction terms and interfacial-exchange terms have been replaced by the given functions $f(\hat{u}_\varepsilon)$, $g(\hat{v}_\varepsilon)$ and $h(\hat{u}_\varepsilon, \hat{v}_\varepsilon)$, has a unique solution in the space $\mathcal{W}(\Omega_\varepsilon^1) \times \mathcal{W}(\Omega_\varepsilon^2)$ and the associated solution operator is continuous in this setting. Since the embeddings $\mathcal{W}(\Omega_\varepsilon^1) \hookrightarrow V$ and $\mathcal{W}(\Omega_\varepsilon^2) \hookrightarrow W$ are compact, the solution mapping is continuous and compact as a mapping into $V \times W$. Hence, the fixed-point operator mapping $(\hat{u}_\varepsilon, \hat{v}_\varepsilon) \in V \times W$ to a new solution $(u_\varepsilon, v_\varepsilon) \in V \times W$ is compact and continuous.

It remains to show that $\|u_\varepsilon\|_V, \|v_\varepsilon\|_W \leq R$, if $\|\hat{u}_\varepsilon\|_V, \|\hat{v}_\varepsilon\|_W \leq R$ for some $R > 0$. Then, by Schauder's fixed-point theorem, there exists at least one fixed point.

This can be shown easily making use of an interpolation inequality,

$$\|u_\varepsilon\|_{L^2((0, \tau), H^{1-\delta}(\Omega_\varepsilon^1))} \leq C \|u_\varepsilon\|_{L^2((0, \tau) \times \Omega_\varepsilon^1)}^\delta \|u_\varepsilon\|_{L^2((0, \tau), H^1(\Omega_\varepsilon^1))}^{1-\delta},$$

[24, p. 135], and the already obtained a-priori estimate (11) from Lemma 4.3 (noting that the estimate for $\|u_\varepsilon(t)\|_{\Omega_\varepsilon^1}$ is uniform in time), where R has been chosen large enough such that the initial conditions are within the ball of radius R , $\|u_0\|_{\Omega_\varepsilon^1} < R$ and $\|v_0\|_{\Omega_\varepsilon^2} < R$. This yields

$$\|u_\varepsilon\|_V \leq C \|u_\varepsilon\|_{L^2((0, \tau) \times \Omega_\varepsilon^1)}^\delta \|u_\varepsilon\|_{V(\Omega_\varepsilon^1)}^{1-\delta} \leq C(C_1 R \tau)^\delta (C_2 R)^{1-\delta} = C_3 R \tau^\delta.$$

This can be made smaller than R for τ small enough. The same argument can be used for $\|v_\varepsilon\|_W$.

Noting that the argument above is independent of the initial time, the argument can be repeated so that, after a finite number of times, the solution has been extended to the whole time interval $(0, T)$. \blacktriangleleft

5. Convergence

In this section, we want to investigate the convergence of the sequences of solutions as $\varepsilon \rightarrow 0$. We use the notion of two-scale convergence.

5.1. Two-scale convergence

Details of classical results on two-scale convergence can be found in [25, 26, 27, 28, 29, 30] and, in the context of reaction–diffusion systems, in [10] in particular. For the sake of convenience, we discuss two-scale convergence for sequences independent of time. Note that this is no restriction since time is only a parameter with respect to the convergence with respect to the spatial variables, cf. e.g. [31].

Definition 5.1 (Two-scale convergence)

A sequence of functions v_ε in $L^2(\Omega)$ is said to two-scale converge to a limit function $v_0(x, y) \in L^2(\Omega \times Y)$ iff

$$\lim_{\varepsilon \rightarrow 0} \int_{\Omega} v_\varepsilon(x) \varphi(x, x/\varepsilon) dx = \int_{\Omega} \int_Y v_0(x, y) \varphi(x, y) dy dx \quad (14)$$

for all $\varphi \in C_0^\infty(\Omega; C_\#^\infty(Y))$ where the subscript $\#$ denotes periodicity. A sequence of functions v_ε in $L^2(\Gamma_\varepsilon)$ is said to two-scale converge to a limit function $v_0(x, y) \in L^2(\Omega \times \Gamma)$ iff

$$\lim_{\varepsilon \rightarrow 0} \varepsilon \int_{\Gamma_\varepsilon} v_\varepsilon(x) \varphi(x, x/\varepsilon) d\sigma_x = \int_{\Omega} \int_{\Gamma} v_0(x, y) \varphi(x, y) d\sigma_y dx \quad (15)$$

for all $\varphi \in C_0^\infty(\Omega; C_\#^\infty(Y))$.

The following theorem is fundamental to the notion of two-scale convergence (cf. theorem 1 in [25] or theorem 1.2 in [26]).

Theorem 5.2

Let u_ε be a bounded sequence in $L^2(\Omega)$. Then, there exists a subsequence such that u_ε two-scale converges to a limit function $u_0 \in L^2(\Omega \times Y)$.

For the formulation of the next theorem, the proof of which is found in [10], the following notation is introduced: For a function $v^\alpha \in L^2(\Omega_\varepsilon^\alpha)$, its zero extension to Ω is denoted by \tilde{v}^α . Clearly this yields $\tilde{v}^\alpha \in L^2(\Omega)$, $\alpha = 1, 2$.

Theorem 5.3

Let $j = 1$ or $j = 2$ and let u_ε be a bounded sequence in $W^{1,2}(\Omega_\varepsilon^j)$. Then, there exist limit functions $u \in W^{1,2}(\Omega^j)$ as well as $u_1 \in L^2(\Omega^j; W_\#^{1,2}(Y)/\mathbb{R})$ such that for a subsequence the following convergence results hold in two-scale sense: $\tilde{u}_\varepsilon \rightarrow \chi^j u$ and $\widetilde{\nabla_x u_\varepsilon} \rightarrow \chi^j (\nabla_x u + \nabla_y u_1)$. Moreover, the trace of u_ε on Γ_ε two-scale converges to the trace of the limit function on Γ in the sense of (15).

We also cite a result stating when the product of two two-scale convergent sequences converges to the product of their limits (cf. theorem 1.8 of [26]):

Theorem 5.4

Assume that u_ε and v_ε are two bounded sequences of functions in $L^2(\Omega)$ which two-scale converge to limits u_0 and v_0 in $L^2(\Omega \times Y)$, respectively. Assume further that

$$\lim_{\varepsilon \rightarrow 0} \|u_\varepsilon\|_{\Omega} = \|u_0\|_{\Omega \times Y}. \quad (16)$$

Then, we have

$$u_\varepsilon v_\varepsilon \rightarrow \int_Y u_0(x, y) v_0(x, y) dy \quad (17)$$

weakly in $C_0^\infty(\Omega)'$.

A sufficient condition for (16) to hold, is that u_ε is a sum of functions belonging to the following classes,

- functions being continuous with respect to one space variable,
- products of functions which only depend on one space variable and time.

An analogous result holds for sequences given on Γ_ε , cf. [27], where condition (16) needs to be replaced by

$$\lim_{\varepsilon \rightarrow 0} \varepsilon \|u_\varepsilon\|_{\Gamma_\varepsilon}^2 = \|u_0\|_{\Omega \times \Gamma}^2. \quad (18)$$

The a-priori estimate (11) ensures that these standard two-scale convergence results apply to the sequences u_ε and v_ε , whose limits we denote by u and v , respectively.

5.2. Nonlinearities

As a notion of convergence of weak type, two-scale convergence is well suited for linear terms. In order to handle the nonlinearities, the following additional considerations are required.

In order to be able to talk about sequences defined on the entire domain Ω , we first extend each solution $(u_\varepsilon, v_\varepsilon)$ to the entire domain. This can be achieved by the following result from [32]:

Theorem 5.5

Let $j = 1$ or $j = 2$. A function $u_\varepsilon \in W^{1,2}(\Omega_\varepsilon^j)$ can be extended to a function \tilde{u}_ε defined on all of Ω such that

$$\|\tilde{u}_\varepsilon\|_{W^{1,2}(\Omega)}^2 \leq C \|u_\varepsilon\|_{W^{1,2}(\Omega_\varepsilon^j)}^2. \quad (19)$$

For $u_\varepsilon \in L^2(\Omega_\varepsilon^j)$, the extension satisfies

$$\|\tilde{u}_\varepsilon\|_{\Omega}^2 \leq C \|u_\varepsilon\|_{\Omega_\varepsilon^j}^2. \quad (20)$$

Note that such an extension does not hold if the domain is disconnected [33]. Furthermore, for the extensions from theorem 5.5, analogous estimates to (19) hold for the L^∞ -norm, if the L^∞ -norms of the original functions are bounded.

If the function to be extended depends on additional variables, the time-dependence in $u_\varepsilon \in \mathcal{V}(\Omega_\varepsilon^1)$ for example, it also makes sense to consider its extension in the sense of theorem 5.5 since the extension operator is linear and $u_\varepsilon(\cdot, t) \in W^{1,2}(\Omega_\varepsilon^1)$ for a.e. $t \in S$. Thus, a linear and continuous extension operator $E: \mathcal{V}(\Omega_\varepsilon^1) \rightarrow \mathcal{V}(\Omega)$ exists whose norm is independent of ε .

If the sequence of solutions u_ε is bounded in $L^2(0, T; W^{1,2}(\Omega)) \cap W^{1,2}(0, T; H_0^1(\Omega)') \cap L^\infty(\Omega \times S)$, it is actually strongly convergent in any L^p with $p < \infty$ to some u (see the next lemma). Then, if the Nemytskii operator associated with the nonlinear function f is continuous, $f(u_\varepsilon)$ converges to $f(u)$.

Lemma 5.6

Let u_ε be a bounded sequence in $L^2(0, T; W^{1,2}(\Omega)) \cap W^{1,2}(0, T; H_0^1(\Omega)') \cap L^\infty(\Omega \times S)$ and let u be the corresponding two-scale limit. Then, at least a subsequence of u_ε strongly converges to u in $L^p(\Omega \times S)$ with $1 \leq p < \infty$.

PROOF Let u_ε be a subsequence which converges to u in $\mathcal{W}(\Omega)$ weakly as well as in two-scale sense.

Since the embedding $L^2(\Omega) \hookrightarrow H_0^1(\Omega)'$ is continuous and the embedding $W^{1,2}(\Omega) \hookrightarrow L^2(\Omega)$ is compact, the same applies to the embedding $\mathcal{W}(\Omega) \hookrightarrow L^2(0, T; L^2(\Omega))$ (by the lemma of Lions–Aubin, cf. [34], p. 106) and at least a subsequence of u_ε (denoted by the same symbol) converges strongly to u in $L^2(\Omega \times S)$. Therefore, u_ε strongly converges to u in $L^p(\Omega \times S)$ with $1 \leq p \leq 2$ as well.

It remains to be shown that convergence also holds in $L^p(\Omega \times S)$ with $2 \leq p < \infty$. Since u_ε converges to u strongly in $L^2(\Omega \times S)$, a subsequence of u_ε exists (denoted by the same symbol) which converges to u pointwise almost everywhere in $\Omega \times S$. Since u_ε belongs to the space $L^\infty(\Omega \times S)$ and since

$$\|u(x, t)\| = \lim_{\varepsilon \rightarrow 0} \|u_\varepsilon(x, t)\| \leq C \quad \text{a.e. in } \Omega \times S,$$

u belongs to this space as well. Using an interpolation inequality [24, p. 27],

$$\|u\|_{L^p} \leq \|u\|_{L^{p_1}}^{1-\theta} \|u\|_{L^{p_2}}^\theta \quad \text{for } 1 \leq p_1, p_2 \leq \infty, 0 \leq \theta \leq 1 \text{ and } \frac{1}{p} = \frac{1-\theta}{p_1} + \frac{\theta}{p_2}$$

with $p_1 = \infty$ and $p_2 = 2$ gives

$$\|u_\varepsilon - u\|_{L^{\frac{2}{\theta}}(\Omega \times S)} \leq \|u_\varepsilon - u\|_{L^\infty(\Omega \times S)}^{1-\theta} \|u_\varepsilon - u\|_{L^2(\Omega \times S)}^\theta$$

for fixed $0 \leq \theta \leq 1$. Therefore, u_ε converges to u in $L^p(\Omega \times S)$ with $2 \leq p < \infty$ strongly. \blacktriangleleft

5.3. Interfacial exchange term

From (11), we immediately obtain the estimate

$$\varepsilon^m \|\sqrt{\bar{h}(u_\varepsilon, v_\varepsilon)}(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 \leq C \tag{21}$$

Using that $0 < h_{\min} \leq \bar{h}(u_\varepsilon, v_\varepsilon) \leq h_{\max} < \infty$, this also implies

$$\varepsilon^m \|\bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 \leq C \quad \text{and} \quad \varepsilon^m \|u_\varepsilon - v_\varepsilon\|_{\Gamma_\varepsilon}^2 \leq C. \tag{22}$$

If we have $m < 1$, we further find that

$$\varepsilon \|\bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 \leq \varepsilon^{1-m} C \leq C \quad \text{and} \quad \varepsilon \|u_\varepsilon - v_\varepsilon\|_{\Gamma_\varepsilon}^2 \leq \varepsilon^{1-m} C \leq C. \tag{23}$$

Thus, $\bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)$ two-scale converges in trace sense to some function $\xi \in L^2(\Omega \times \Gamma)$ and we have that

$$\|\xi\|_{\Omega \times \Gamma}^2 \leq \lim_{\varepsilon \rightarrow 0} \varepsilon \|\bar{h}(u_\varepsilon, v_\varepsilon)(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 \leq \lim_{\varepsilon \rightarrow 0} \varepsilon^{1-m} C = 0. \tag{24}$$

Thus, $\xi = 0$ almost everywhere. Using the same argument, we find that $u_\varepsilon - v_\varepsilon$ two-scale converges to 0 in trace sense. On the other hand, since u_ε and v_ε two-scale converge in $H^1(\Omega_\varepsilon^1)$ and $H^1(\Omega_\varepsilon^2)$ respectively, we also know that their traces converge to the traces of the (domain) limits. Thus, we find that $u = v$ a.e. on $\Omega \times \Gamma$.

If we have $m > 1$, we find that

$$\varepsilon^m \|\sqrt{\bar{h}(u_\varepsilon, v_\varepsilon)}(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 = \varepsilon^{m-1} \varepsilon \|\sqrt{\bar{h}(u_\varepsilon, v_\varepsilon)}(u_\varepsilon - v_\varepsilon)\|_{\Gamma_\varepsilon}^2 \xrightarrow{\varepsilon \rightarrow 0} 0, \quad (25)$$

since the second term is bounded, cf. estimate (11). Thus, the interfacial exchange term disappears in the limit equation, $h^{\text{ex}} = 0$.

In the case $m = 1$, the limit needs to be characterised further. For this purpose, we proof the following lemma, which is an adaptation of a lemma of Conca et al. [12].

Lemma 5.7

For $m = 1$, we have

$$\lim_{\varepsilon \rightarrow 0} \varepsilon (h(u_\varepsilon, v_\varepsilon) \mid \varphi)_{L^2(\Gamma^\varepsilon), t} = (|\Gamma| h(u_0, v_0) \mid \varphi)_{\Omega, t} \quad (26)$$

for any $\varphi \in C_0^\infty(\Omega)$.

PROOF We prove the assertion in two steps. In the first step, we show that the linear form μ_λ^ε defined in (**) below strongly converges in $(W^{1,p}(\Omega))'$ for $1 \leq p < \infty$. Therefore, we mainly adopt and rearrange section 3 ‘‘Lemmes de base’’ from [35]. In the second step, we use the form μ_λ^ε to complete the proof.

1. Let $\lambda \in L^{p'}(\Gamma)$ be a Y -periodic function and $1 < p' \leq \infty$. We define

$$C_\lambda = \frac{1}{|Z^1|} \int_\Gamma \lambda(y) d\sigma_y.$$

Let Ψ_λ be the solution of the problem

$$\begin{cases} -\Delta \Psi_\lambda = -C_\lambda & \text{in } Z^1, \\ \nabla \Psi_\lambda \cdot n = \lambda & \text{on } \Gamma, \\ \Psi_\lambda & Y\text{-periodic.} \end{cases}$$

The solution Ψ_λ exists, since $-\int_{Z^1} C_\lambda dy = \int_\Gamma \lambda d\sigma_y$. Furthermore, we define the function $\Psi_\lambda^\varepsilon(x) = \Psi_\lambda(\frac{x}{\varepsilon})$ satisfying

$$\begin{cases} -\Delta \Psi_\lambda^\varepsilon = -\frac{1}{\varepsilon^2} C_\lambda & \text{in } \Omega_\varepsilon^1, \\ \nabla \Psi_\lambda^\varepsilon \cdot n = \frac{1}{\varepsilon} \lambda(\frac{x}{\varepsilon}) & \text{on } \Gamma_\varepsilon. \end{cases}$$

Testing this problem with $v \in W^{1,p}(\Omega_\varepsilon^1)$ ($\frac{1}{p} + \frac{1}{p'} = 1$) and integrating by parts leads to

$$\varepsilon \int_{\Gamma_\varepsilon} \lambda(\frac{x}{\varepsilon}) v(x) d\sigma_x = \varepsilon \int_{\Omega_\varepsilon} \nabla_y \Psi_\lambda(\frac{x}{\varepsilon}) \nabla v(x) dx + \int_{\Omega_\varepsilon} C_\lambda v(x) dx. \quad (*)$$

Here we used that $\varepsilon \nabla_x \Psi_\lambda^\varepsilon(x) = \nabla_y \Psi_\lambda(\frac{x}{\varepsilon})$.

We define the linear form on $W^{1,p}(\Omega)$ by

$$\langle \mu_\lambda^\varepsilon | \varphi \rangle = \varepsilon \int_{\Gamma_\varepsilon} \lambda(\frac{x}{\varepsilon}) \varphi(x) d\sigma_x \quad \forall \varphi \in W^{1,p}(\Omega) \quad (**)$$

with $\frac{1}{p} + \frac{1}{p'} = 1$. With equation (*) we estimate

$$\varepsilon \int_{\Gamma_\varepsilon} \lambda(\frac{x}{\varepsilon}) v(x) d\sigma_x \leq \varepsilon C \|\nabla_y \Psi_\lambda\|_{[L^{p'}(Z^1)]^n} \|\nabla v\|_{[L^p(\Omega_\varepsilon)]^n} + C' C_\lambda \|v\|_{L^p(\Omega_\varepsilon)}.$$

In this setup, the following convergence holds

$$\mu_\lambda^\varepsilon \rightarrow \mu_\lambda \quad \text{strongly in } (W^{1,p}(\Omega))'$$

with

$$\langle \mu_\lambda, \varphi \rangle = \underbrace{\frac{1}{|Y|} \int_\Gamma \lambda(y) d\sigma_y}_{=\mu_\lambda} \int_\Omega \varphi dx.$$

To prove this statement, we define the following using equation (*)

$$\mu_\lambda^\varepsilon = \tilde{\mu}_\lambda^\varepsilon + C_\lambda \chi_{\Omega_\varepsilon}$$

with

$$\langle \tilde{\mu}_\lambda^\varepsilon | \varphi \rangle = \varepsilon \int_{\Omega_\varepsilon} \nabla_y \Psi_\lambda(\frac{x}{\varepsilon}) \nabla v(x) dx.$$

It holds that

$$|\langle \tilde{\mu}_\lambda^\varepsilon | \varphi \rangle| \leq \varepsilon C \|\nabla_y \Psi_\lambda\|_{[L^{p'}(Z^1)]^n} \|\nabla \varphi\|_{[L^p(\Omega_\varepsilon)]^n},$$

where the first norm on the right-hand side is bounded since $\Psi_\lambda \in W^{1,p'}(Z^1)$ and the second norm is bounded since $\varphi \in W^{1,p}(\Omega)$. Hence, $\tilde{\mu}_\lambda^\varepsilon \xrightarrow{\varepsilon \rightarrow 0} 0$ strongly in $(W^{1,p}(\Omega))'$.

Furthermore, we have

$$C_\lambda \chi_{\Omega_\varepsilon} \rightarrow C_\lambda \frac{|Z^1|}{|Y|} = \mu_\lambda \quad \text{weak* in } L^\infty(\Omega).$$

Since $L^\infty(\Omega)$ is compactly embedded in $W^{-1,\infty}(\Omega)$, it follows that

$$C_\lambda \chi_{\Omega_\varepsilon} \rightarrow C_\lambda \frac{|Z^1|}{|Y|} = \mu_\lambda \quad \text{strongly in } W^{-1,\infty}(\Omega)$$

and hence, also strongly in $(W^{1,p}(\Omega))'$.

- Now we are going to use part 1 of the proof, where we take $\lambda = 1$ and $p' = p = 2$. Notice that in this case $\mu_\lambda = \mu_1 = |\Gamma|$.

If a sequence of functions $z^\varepsilon \in H^1(\Omega)$ is such that $z^\varepsilon \rightharpoonup z$ weakly in $H^1(\Omega)$, then

$$\langle \mu_\lambda^\varepsilon | z^\varepsilon \rangle \rightarrow \mu_\lambda \int_\Omega z dx. \quad (+)$$

With $u_\varepsilon \rightarrow u_0$ and $v_\varepsilon \rightarrow v_0$ strongly in $L^2(S \times \Omega)$ and continuity of H , which is the Nemytskii operator associated with h , we obtain

$$H(u_\varepsilon, v_\varepsilon) \rightarrow H(u_0, v_0) \quad \text{strongly in } L^2(\Omega \times S).$$

Moreover, $\|\nabla h(u_\varepsilon, v_\varepsilon)\|_{L^2(\Omega \times S)} = \|\partial_u h(u_\varepsilon, v_\varepsilon) \nabla u_\varepsilon + \partial_v h(u_\varepsilon, v_\varepsilon) \nabla v_\varepsilon\|_{L^2(\Omega \times S)}$ is bounded, since h is Lipschitz-continuous in both arguments and $\|u_\varepsilon\|_{L^2(S; W^{1,2}(\Omega))}$ and $\|v_\varepsilon\|_{L^2(S; W^{1,2}(\Omega))}$ are bounded. Hence, we deduce a weakly converging subsequence $h(u_\varepsilon, v_\varepsilon)$ in $L^2(S; H^1(\Omega))$ and for any $\varphi \in C^\infty(\Omega)$ it holds that

$$\varphi h(u_\varepsilon, v_\varepsilon) \xrightarrow{\varepsilon \rightarrow 0} \varphi h(u_0, v_0) \quad \text{weakly in } L^2(S; H^1(\Omega)).$$

Combining this with (+) yields for $z^\varepsilon = \varphi h(u_\varepsilon(t), v_\varepsilon(t))$

$$\langle \mu_1^\varepsilon \mid \varphi h(u_\varepsilon(t), v_\varepsilon(t)) \rangle \xrightarrow{\varepsilon \rightarrow 0} |\Gamma| \int_\Omega \varphi h(u_0(t), v_0(t)) dx$$

for almost every $t \in S$. Finally, we are in the position to use Lebesgue's convergence theorem and get

$$\lim_{\varepsilon \rightarrow 0} \varepsilon (h(u_\varepsilon, v_\varepsilon) \mid \varphi)_{\Gamma_\varepsilon, t} = (|\Gamma| h(u_0, v_0) \mid \varphi)_{\Omega, t}, \quad \blacktriangleleft$$

which concludes the proof.

6. Identification of the limit problems

Proposition 6.1

If $m \geq 1$ the limit functions u and v associated with the sequence of solutions u_ε and v_ε satisfy the weak macroproblem (10).

PROOF Owing to the convergence results for the nonlinear terms of the previous section, the proof is similar to that of proposition 4.3 in [10] (which deals with the identification of the homogenization limit of a related linear problem), which is why we only give it in short form.

We integrate the weak micromodel (2) with respect to time and choose the test functions to be of the form

$$\varphi(x, t) = \varphi_0(x, t) + \varepsilon \varphi_1(x, x/\varepsilon, t),$$

$$\psi(x, t) = \psi_0(x, t) + \varepsilon \psi_1(x, x/\varepsilon, t),$$

where $(\varphi_0, \varphi_1), (\psi_0, \psi_1) \in C_0^\infty(S; C^\infty(\Omega)) \times C_0^\infty(S; C^\infty(\Omega; C_\#^\infty(Y)))$. Since the determination of the limit problems for u and v is completely analogous except for a sign difference, we only show it for u .

With the choice of test functions above, equation (2a) reads

$$\begin{aligned}
0 &= \int_{S \times \Omega} \partial_t u_\varepsilon(x, t) \chi^1\left(\frac{x}{\varepsilon}\right) [\varphi_0(x, t) + \varepsilon \varphi_1\left(x, \frac{x}{\varepsilon}, t\right)] dx dt \\
&\quad + \int_{S \times \Omega} D_\varepsilon\left(x, \frac{x}{\varepsilon}, t\right) \nabla_x u_\varepsilon(x, t) \chi^1\left(\frac{x}{\varepsilon}\right) \\
&\quad \quad \quad \times \left[\nabla_x \varphi_0(x, t) + \varepsilon \nabla_x \varphi_1\left(x, \frac{x}{\varepsilon}, t\right) + \nabla_y \varphi_1\left(x, \frac{x}{\varepsilon}, t\right) \right] dx dt \quad (\dagger) \\
&\quad - \int_{S \times \Omega} f(u_\varepsilon(x, t)) \chi^1\left(\frac{x}{\varepsilon}\right) [\varphi_0(x, t) + \varepsilon \varphi_1\left(x, \frac{x}{\varepsilon}, t\right)] dx dt \\
&\quad + \int_{S \times \Gamma_\varepsilon} \varepsilon^m h(u_\varepsilon(x, t), v_\varepsilon(x, t)) [\varphi_0(x, t) + \varepsilon \varphi_1\left(x, \frac{x}{\varepsilon}, t\right)] d\sigma_x dt.
\end{aligned}$$

Now, we pass to the limit as $\varepsilon \rightarrow 0$. In this context, u and u_1 are understood as the limit functions from theorem 5.3.

The limits of the four terms in (\dagger) can each be determined separately. Lemma 4.5 together with theorem 5.2 applies to the first term. For the limit passage in the second term, we use theorem 5.4 with (3) and theorem 5.3. For the third term, the assumption on f and lemma 5.6 is used. The limit of the fourth term is found using the results from lemma 5.7. Altogether, we find

$$\begin{aligned}
0 &= |Z^1| \int_{S \times \Omega} \partial_t u(x, t) \varphi_0(x, t) dx dt \\
&\quad + \int_{S \times \Omega} \int_{Z^1} D(x, y, t) (\nabla_x u(x, t) + \nabla_y u_1(x, y, t)) [\nabla_x \varphi_0(x, t) + \nabla_y \varphi_1(x, y, t)] dy dx dt \\
&\quad - \int_{S \times \Omega} \int_{Z^1} f(u(x, t)) dy \varphi_0(x, t) dx dt \\
&\quad + \int_{S \times \Omega} h^{\text{ex}}(u(t), v(t)) \varphi_0(x, t) dx dt
\end{aligned}$$

for all (φ_0, φ_1) . Choosing $\varphi_0 \equiv 0$ yields the cell problem and $u_1 = \sum_{j=1}^d \partial_{x_j} u(x, t) \mu_j(y, t)$ by standard arguments (also see the proof of proposition 6.2).

Choosing $\varphi_1 \equiv 0$ gives

$$\begin{aligned}
0 &= |Z^1| \int_{S \times \Omega} \partial_t u(x, t) \varphi_0(x, t) dx dt \\
&\quad + \int_{S \times \Omega} \int_{Z^1} D(x, y, t) (\nabla_x u(x, t) + \nabla_y u_1(x, y, t)) \nabla_x \varphi_0(x, t) dy dx dt \\
&\quad - \int_{S \times \Omega} \int_{Z^1} f(u(x, t)) dy \varphi_0(x, t) dx dt \\
&\quad + \int_{S \times \Omega} h^{\text{ex}}(u(t), v(t)) \varphi_0(x, t) dx dt
\end{aligned}$$

for all $\varphi_0 \in C_0^\infty(S; C^\infty(\Omega))$. Using $u_1 = \sum_{j=1}^d \partial_{x_j} u(x, t) \mu_j(y, t)$, the second term can be simplified to

$$\int_{S \times \Omega} P^u(x, t) \nabla_x u(x, t) \nabla_x \varphi_0(x, t) dx dt,$$

where P^u is defined in (6). Thus,

$$\begin{aligned} |Z^1| \int_{S \times \Omega} \partial_t u(x, t) \varphi_0(x, t) \, dx \, dt + \int_{S \times \Omega} P^u(x, t) \nabla_x u(x, t) \nabla_x \varphi_0(x, t) \, dx \, dt \\ = \int_{S \times \Omega} \int_{Z^1} f(u(x, t)) \, dy \, \varphi_0(x, t) \, dx \, dt - \int_{S \times \Omega} h^{\text{ex}}(u(t), v(t)) \varphi_0(x, t) \, dx \, dt \end{aligned}$$

for all $\varphi_0 \in C_0^\infty(S; C^\infty(\Omega))$.

Taking the analogous steps for the function v_ε we get

$$\begin{aligned} |Z^2| \int_{S \times \Omega} \partial_t v(x, t) \varphi_0(x, t) \, dx \, dt + \int_{S \times \Omega} P^v(x, t) \nabla_x v(x, t) \nabla_x \varphi_0(x, t) \, dx \, dt \\ = \int_{S \times \Omega} \int_{Z^2} g(v(x, t)) \, dy \, \varphi_0(x, t) \, dx \, dt + \int_{S \times \Omega} h^{\text{ex}}(u(t), v(t)) \varphi_0(x, t) \, dx \, dt \end{aligned}$$

for all $\varphi_0 \in C_0^\infty(S; C^\infty(\Omega))$, where the tensor P^v is defined in (6). \blacktriangleleft

Proposition 6.2

If $m < 1$ the limit functions u and v associated with the sequences of solutions u_ε and v_ε , respectively, satisfy the weak macromodel equation (8).

PROOF From (24) we know that $u = v$ on $\Omega \times \Gamma$ in the limit. Addition of the equations (2a) and (2b) gives

$$\begin{aligned} (\partial_t u_\varepsilon | \varphi)_{\Omega_\varepsilon^1} + (D_\varepsilon \nabla u_\varepsilon | \nabla \varphi)_{\Omega_\varepsilon^1} + (\partial_t v_\varepsilon | \varphi)_{\Omega_\varepsilon^2} + (E_\varepsilon \nabla v_\varepsilon | \nabla \varphi)_{\Omega_\varepsilon^2} \\ + \varepsilon^m (h(u_\varepsilon, v_\varepsilon) | \varphi|_{\Omega_\varepsilon^1} - \varphi|_{\Omega_\varepsilon^2})_{\Gamma_\varepsilon} = (f(u_\varepsilon) | \varphi)_{\Omega_\varepsilon^1} + (g(v_\varepsilon) | \varphi)_{\Omega_\varepsilon^2}. \end{aligned}$$

Choosing the test function as

$$\varphi(x, t) = \begin{cases} \varphi_0(x, t) + \varepsilon \varphi^1(x, \frac{x}{\varepsilon}, t), & x \in \Omega_\varepsilon^1 \\ \varphi_0(x, t) + \varepsilon \varphi^2(x, \frac{x}{\varepsilon}, t), & x \in \Omega_\varepsilon^2 \end{cases}$$

with (φ_0, φ^1) and $(\varphi_0, \varphi^2) \in C_0^\infty(S; C^\infty(\Omega)) \times C_0^\infty(S; C^\infty(\Omega; C_\#^\infty(Y)))$ gives

$$\begin{aligned} \int_{S \times \Omega} \chi_1\left(\frac{x}{\varepsilon}\right) \partial_t u_\varepsilon(x, t) \left[\varphi_0(x, t) + \varepsilon \varphi^1\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt \\ + \int_{S \times \Omega} \chi_2\left(\frac{x}{\varepsilon}\right) \partial_t v_\varepsilon(x, t) \left[\varphi_0(x, t) + \varepsilon \varphi^2\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt \\ + \int_{S \times \Omega} \chi_1\left(\frac{x}{\varepsilon}\right) D\left(x, \frac{x}{\varepsilon}, t\right) \nabla u_\varepsilon(x, t) \left[\nabla_x \varphi_0(x, t) + \varepsilon \nabla_x \varphi^1\left(x, \frac{x}{\varepsilon}, t\right) + \nabla_y \varphi^1\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt \\ + \int_{S \times \Omega} \chi_2\left(\frac{x}{\varepsilon}\right) E\left(x, \frac{x}{\varepsilon}, t\right) \nabla v_\varepsilon(x, t) \left[\nabla_x \varphi_0(x, t) + \varepsilon \nabla_x \varphi^2\left(x, \frac{x}{\varepsilon}, t\right) + \nabla_y \varphi^2\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt \\ + \int_{S \times \Gamma_\varepsilon} \varepsilon^m h(u_\varepsilon, v_\varepsilon) \left[\varphi_0(x, t) + \varepsilon \varphi^1\left(x, \frac{x}{\varepsilon}, t\right) - \varphi_0(x, t) - \varepsilon \varphi^2\left(x, \frac{x}{\varepsilon}, t\right) \right] \, d\sigma \, dt \\ = \int_{S \times \Omega} \chi_1\left(\frac{x}{\varepsilon}\right) f(u_\varepsilon(x, t)) \left[\varphi_0(x, t) + \varepsilon \varphi^1\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt \\ + \int_{S \times \Omega} \chi_2\left(\frac{x}{\varepsilon}\right) g(v_\varepsilon(x, t)) \left[\varphi_0(x, t) + \varepsilon \varphi^2\left(x, \frac{x}{\varepsilon}, t\right) \right] \, dx \, dt. \end{aligned}$$

Using (24) we receive for $\varepsilon \rightarrow 0$

$$\begin{aligned}
& \int_{S \times \Omega} \left(\int_{Z^1} \partial_t u(x, t) \, dy + \int_{Z^2} \partial_t v(x, t) \, dy \right) \varphi_0(x, t) \, dx \, dt \\
& + \int_{S \times \Omega} \int_{Z^1} D(x, y, t) [\nabla_x u(x, t) + \nabla_y u_1(x, y, t)] [\nabla_x \varphi_0(x, t) + \nabla_y \varphi^1(x, y, t)] \, dy \, dx \, dt \\
& + \int_{S \times \Omega} \int_{Z^2} E(x, y, t) [\nabla_x v(x, t) + \nabla_y v_1(x, y, t)] [\nabla_x \varphi_0(x, t) + \nabla_y \varphi^2(x, y, t)] \, dy \, dx \, dt \\
& = \int_{S \times \Omega} \left(\int_{Z^1} f(u(x, t)) \, dy + \int_{Z^2} g(v(x, t)) \, dy \right) \varphi_0(x, t) \, dx \, dt
\end{aligned}$$

and we deduce that $u = v$ on $\Omega \times \Gamma$. Because u and v is independent of y we immediately have $u = v$ on the whole domain $\Omega \times Y$. Hence, we replace v by u and define the right-hand side $F(u(x, t)) = \int_{Z^1} f(u(x, t)) \, dy + \int_{Z^2} g(u(x, t)) \, dy$ so that

$$\begin{aligned}
& \int_{S \times \Omega} [|Z^1| |\partial_t u(x, t)| + |Z^2| |\partial_t u(x, t)|] \varphi_0(x, t) \, dx \, dt \\
& + \int_{S \times \Omega} \int_{Z^1} D(x, y, t) [\nabla_x u(x, t) + \nabla_y u_1(x, y, t)] [\nabla_x \varphi_0(x, t) + \nabla_y \varphi^1(x, y, t)] \, dy \, dx \, dt \\
& + \int_{S \times \Omega} \int_{Z^2} E(x, y, t) [\nabla_x u(x, t) + \nabla_y v_1(x, y, t)] [\nabla_x \varphi_0(x, t) + \nabla_y \varphi^2(x, y, t)] \, dy \, dx \, dt \\
& = \int_{S \times \Omega} F(u(x, t)) \varphi_0(x, t) \, dx \, dt.
\end{aligned}$$

We assume $\varphi_0 = 0$ and it follows that for all $\varphi^1, \varphi^2 \in C_0^\infty(S; C^\infty(\Omega; C_\#^\infty(Y)))$

$$\int_{Z^1} D(x, y, t) (\nabla_x u(x, t) + \nabla_y u_1(x, y, t)) \nabla_y \varphi^1 \, dy + \int_{Z^2} E(x, y, t) (\nabla_x u(x, t) + \nabla_y v_1(x, y, t)) \nabla_y \varphi^2 \, dy = 0.$$

Assuming $u_1 = \sum_{j=1}^d \partial_{x_j} u(x, t) \mu_j(y, t)$ and $v_1 = \sum_{j=1}^d \partial_{x_j} u(x, t) \nu_j(y, t)$ we get

$$\begin{aligned}
0 = & \int_{Z^1} D(x, y, t) \left(\nabla_x u(x, t) + \sum_{j=1}^d \partial_{x_j} u(x, t) \nabla_y \mu_j(y, t) \right) \nabla_y \varphi^1 \, dy \\
& + \int_{Z^2} E(x, y, t) \left(\nabla_x u(x, t) + \sum_{j=1}^d \partial_{x_j} u(x, t) \nabla_y \nu_j(y, t) \right) \nabla_y \varphi^2 \, dy,
\end{aligned}$$

which is satisfied by virtue of the cell problem (5).

Now we assume $\varphi^1 = \varphi^2 = 0$ and it follows that for all φ_0

$$\begin{aligned}
& \int_{S \times \Omega} (|Z^1| + |Z^2|) \partial_t u(x, t) \varphi_0(x, t) \, dx \, dt + \int_{S \times \Omega} \sum_{ijk} \partial_{x_k} u \left(\int_{Z^1} D_{ij}(x, y, t) (\delta_{jk} + \nabla_{y_j} \mu_k(y, t)) \, dy \right. \\
& \quad \left. + \int_{Z^2} E_{ij}(x, y, t) (\delta_{jk} + \nabla_{y_j} \nu_k(y, t)) \, dy \right) \partial_{x_i} \varphi_0 \, dx \, dt = \int_{S \times \Omega} F(u(x, t)) \varphi_0 \, dx \, dt.
\end{aligned}$$

With $P_{ij}^u(x, t) = \int_{Z^1} D(x, y, t) (e_i + \nabla_y \mu_i(y, t)) (e_j + \nabla_y \mu_j(y, t)) \, dy$ and $P_{ij}^v(x, t) = \int_{Z^2} E(x, y, t) (e_i + \nabla_y \nu_i(y, t)) (e_j + \nabla_y \nu_j(y, t)) \, dy$ we abbreviate this equation to (8). \blacktriangleleft

7. Uniqueness of the limit problems

Finally, we show uniqueness of the macroscopic limit problems of §3.

Proposition 7.1 (Uniqueness)

There is at most one solution of the weak problem (8).

PROOF Let us suppose that there exist two solutions U_1 and $U_2 \in \mathcal{W}(\Omega)$ of the weak problem (8) with $U_1(0) = U_2(0)$. It holds that

$$(\partial_t(U_1 - U_2) | \varphi)_\Omega + ((P^u + P^v)\nabla(U_1 - U_2) | \varphi)_\Omega = (F(U_1) - F(U_2) | \varphi)_\Omega.$$

Testing with $\varphi = U_1 - U_2$ and integrating from 0 to t gives us

$$\frac{1}{2}\|U_1 - U_2\|_\Omega^2 + \|\sqrt{P^u + P^v}\nabla(U_1 - U_2)\|_{\Omega,t}^2 = (F(U_1) - F(U_2) | U_1 - U_2)_{\Omega,t} + \frac{1}{2}\|U_1(0) - U_2(0)\|_\Omega^2.$$

The function F is Lipschitz continuous, because f and g are Lipschitz continuous. So we conclude

$$\frac{1}{2}\|U_1 - U_2\|_\Omega^2 \leq L_F\|U_1 - U_2\|_{\Omega,t}^2$$

With Gronwall's Lemma we deduce that $\|U_1 - U_2\|_\Omega^2 \leq 0$, so $U_1 = U_2$ almost everywhere. \blacktriangleleft

Proposition 7.2 (Uniqueness)

There is at most one solution of the weak problem (10).

PROOF Let us suppose that there exist two solutions (u_1, v_1) and $(u_2, v_2) \in \mathcal{W}(\Omega)^2$ of the weak problem (10) with $u_1(0) = u_2(0)$ and $v_1(0) = v_2(0)$. It holds that

$$\begin{aligned} |Z^1|(\partial_t u_1 - \partial_t u_2 | \nabla \varphi)_\Omega + (P^u \nabla(u_1 - u_2) | \nabla \varphi)_\Omega \\ = \left(\int_{Z^1} (f(u_1) - f(u_2)) \, dy | \varphi \right)_\Omega - (h^{\text{ex}}(u_1, v_1) - h^{\text{ex}}(u_2, v_2) | \varphi)_\Omega. \end{aligned}$$

for all test functions φ . We take $\varphi = u_1 - u_2$ and integrate from 0 to t noting that $u_1(0) = u_2(0)$ to obtain

$$\begin{aligned} |Z^1| \frac{1}{2} \|u_1 - u_2\|_\Omega^2 + \|\sqrt{P^u} \nabla_y(u_1 - u_2)\|_{\Omega,t}^2 \\ = \left(\int_{Z^1} (f(u_1) - f(u_2)) \, dy | u_1 - u_2 \right)_{\Omega,t} - (h^{\text{ex}}(u_1, v_1) - h^{\text{ex}}(u_2, v_2) | u_1 - u_2)_{\Omega,t} \\ \leq \left(\int_{Z^1} L_f |u_1 - u_2| \, dy | |u_1 - u_2| \right)_{\Omega,t} + (|h^{\text{ex}}(u_1, v_1) - h^{\text{ex}}(u_2, v_1)| | |u_1 - u_2|)_{\Omega,t} \\ \quad + (|h^{\text{ex}}(u_2, v_1) - h^{\text{ex}}(u_2, v_2)| | |u_1 - u_2|)_{\Omega,t} \\ \leq |Z^1| L_f \|u_1 - u_2\|_{\Omega,t}^2 + |\Gamma| L_{h_u} \|u_1 - u_2\|_{\Omega,t}^2 + |\Gamma| L_{h_v} (\|v_1 - v_2\|_{\Omega,t}^2 + \|u_1 - u_2\|_{\Omega,t}^2). \end{aligned}$$

where we have used that f is Lipschitz with constant L_f , the functions u_1 and u_2 are independent of y and h is Lipschitz with constants L_{h_u} and L_{h_v} .

We perform the analogous estimations starting from the equation for v and get

$$\begin{aligned} |Z^2| \frac{1}{2} \|v_1 - v_2\|_{\Omega}^2 + \|\sqrt{P^v} \nabla(v_1 - v_2)\|_{\Omega, t}^2 \\ \leq |Z^2| L_g \|v_1 - v_2\|_{\Omega, t}^2 + |\Gamma| L_{h_v} \|v_1 - v_2\|_{\Omega, t}^2 + |\Gamma| L_{h_u} (\|u_1 - u_2\|_{\Omega, t}^2 + \|v_1 - v_2\|_{\Omega, t}^2). \end{aligned}$$

Adding the equations we get

$$\|u_1 - u_2\|_{\Omega}^2 + \|v_1 - v_2\|_{\Omega}^2 \leq C (\|u_1 - u_2\|_{\Omega, t}^2 + \|v_1 - v_2\|_{\Omega, t}^2)$$

for a $C > 0$. With Gronwall's Lemma we conclude that $\|u_1 - u_2\|_{\Omega}^2 + \|v_1 - v_2\|_{\Omega}^2 = 0$ so that $u_1 = u_2$ and $v_1 = v_2$. ◀

References

- [1] P. Goel, J. Sneyd, A. Friedman, Homogenization of the cell cytoplasm: The calcium bidomain equations, *Multiscale Model. Simul.* 5 (4) (2006) 1045–1062.
- [2] J. Keener, J. Sneyd, *Mathematical Physiology*, Springer, 2008.
- [3] A. Bensoussan, J.-L. Lions, G. Papanicolaou, *Asymptotic analysis for periodic structures*, North-Holland, 1978.
- [4] E. Sanchez-Palencia, *Non-homogeneous media and vibration theory*, Springer, 1980.
- [5] N. Panasenko, N. S. Bakhvalov, *Homogenization: Averaging Processes in Periodic Media: Mathematical Problems in the Mechanics of Composite Materials*, Kluwer Academic, 1989.
- [6] V. V. Jikov, S. M. Kozlov, O. A. Oleinik, *Homogenization of differential operators and integral functionals*, Springer, 1994.
- [7] D. Cioranescu, P. Donato, *An introduction to homogenization*, Oxford University Press, 1999.
- [8] V. A. Marchenko, E. Y. Khruslov, *Homogenization of partial differential equations*, Birkhäuser, 2006.
- [9] É. Canon, J.-N. PERNIN, Homogenization of diffusion in composite media with interfacial barrier, *Rev. Roumaine Math. Pures Appl.* 44 (1) (1999) 23–36.
- [10] M. A. Peter, M. Böhm, Different choices of scaling in homogenization of diffusion and interfacial exchange in a porous medium, *Math. Meth. Appl. Sci.* 31 (2008) 1257–1282.
- [11] M. A. Peter, M. Böhm, Multi-scale modelling of chemical degradation mechanisms in porous media with evolving microstructure, *SIAM Multiscale Mod. Sim.* 7 (2009) 1643–1668.
- [12] C. Conca, J. I. Díaz, C. Timofte, Effective chemical processes in porous media, *Math. Mod. Meth. Appl. Sci.* 13 (10) (2003) 1437–1462.
- [13] C. Conca, J. I. Diaz, C. Timofte, On the homogenization of a transmission problem arising in chemistry, *Rom. Rep. Phys.* 56 (4) (2004) 613–622.
- [14] P. Donato, A. Nabil, Homogenization of semilinear parabolic equations in perforated domains, *Chin. Ann. Math.* 25B (2) (2004) 143–156.
- [15] M. A. Peter, Coupled reaction–diffusion processes inducing an evolution of the microstructure: analysis and homogenization, *Nonlin. Anal* 70 (2) (2009) 806–821.
- [16] C. Neu, W. Krassowska, Homogenization of syncytial tissues, *Crit. Rev. Biomedical Eng.* 21 (2) (1993) 137–199.
- [17] W. Krassowska, C. Neu, Effective boundary conditions for syncytial tissue, *IEEE Trans. Biomedical Eng.* 41 (2) (1994) 143–150.

- [18] M. Amar, D. Andreucci, R. Gianni, Evolution and memory effects in the homogenization limit for electrical conduction in biological tissues, *Math. Mod. Meth. Appl. Sci.* 14 (9) (2004) 1261–1295.
- [19] M. Amar, D. Andreucci, P. Bisegna, R. Gianni, On a hierarchy of models for electrical conduction in biological tissues, *Math. Meth. Appl. Sci.* 29 (2006) 767–787.
- [20] A. Bensoussan, J.-L. Lions, G. Papanicolaou, *Asymptotic analysis for periodic structures*, North-Holland, 1978.
- [21] E. Sanchez-Palencia, *Non-homogeneous media and vibration theory*, Springer, 1980.
- [22] U. Hornung (Ed.), *Homogenization and porous media*, Springer, 1997.
- [23] D. Gilbarg, N. S. Trudinger, *Elliptic partial differential equations of second order*, 3rd Edition, Springer, 1998.
- [24] R. A. Adams, J. J. F. Fournier, *Sobolev Spaces*, 2nd Edition, Academic Press, 2003.
- [25] G. Nguetseng, A general convergence result for a functional related to the theory of homogenization, *SIAM J. Math. Anal.* 20 (3) (1989) 608–629.
- [26] G. Allaire, Homogenization and two-scale convergence, *SIAM J. Math. Anal.* 23 (6) (1992) 1482–1518.
- [27] G. Allaire, A. Damlamian, U. Hornung, Two-scale convergence on periodic surfaces and applications, in: A. P. Bourgeat, C. Carasso, S. Luckhaus, A. Mikelić (Eds.), *Proceedings of the international conference on mathematical modelling of flow through porous media*, World Scientific, 1995, pp. 15–25.
- [28] M. Neuss-Radu, Some extensions of two-scale convergence, *C. R. Acad. Sci. Paris, Ser. I* 322 (1996) 899–904.
- [29] G. Allaire, M. Briane, Multiscale convergence and reiterated homogenisation, *Proc. Roy. Soc. Edinb.* 126A (1996) 297–342.
- [30] D. Lukkassen, G. Nguetseng, P. Wall, Two-scale convergence, *Int. J. Pure Appl. Math.* 2 (1) (2002) 35–86.
- [31] A. Holmbom, Homogenization of parabolic equations an alternative approach and some corrector-type results, *Appl. Math.* 42 (5) (1997) 321–343.
- [32] M. Höpker, M. Böhm, A note on the existence of extension operators for Sobolev spaces on periodic domains, preprint, submitted for publication (2013).
- [33] S. Monsurrò, Homogenization of a two-component composite with interfacial thermal barrier, *Adv. Math. Sci. Appl.* 13 (1) (2003) 44–63.
- [34] R. E. Showalter, *Monotone operators in Banach space and nonlinear partial differential equations*, American Mathematical Society, 1997.
- [35] D. Cioranescu, P. Donato, Homogenisation du probleme de Neumann non homogene dans des ouverts perfores, *Asympt. Anal.* 1 (1988) 115–138.