

From a microscopic to a macroscopic model for  
Alzheimer disease: Two-scale homogenization of the  
Smoluchowski equation in perforated domains.

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**Abstract**

In this paper, we study the homogenization of a set of Smoluchowski's discrete diffusion-coagulation equations modeling the aggregation and diffusion of  $\beta$ -amyloid peptide ( $A\beta$ ), a process associated with the development of Alzheimer's disease. In particular, we define a periodically perforated domain  $\Omega_\epsilon$ , obtained by removing from the fixed domain  $\Omega$  (the cerebral tissue) infinitely many small holes of size  $\epsilon$  (the neurons), which support a non-homogeneous Neumann boundary condition describing the production of  $A\beta$  by the neuron membranes. Then, we prove that, when  $\epsilon \rightarrow 0$ , the solution of this micro-model two-scale converges to the solution of a macro-model asymptotically consistent with the original one. Indeed, the information given on the microscale by the non-homogeneous Neumann boundary condition is transferred into a source term appearing in the limiting (homogenized) equations. Furthermore, on the macroscale, the geometric structure of the perforated domain induces a correction in that the scalar diffusion coefficients defined at the microscale are replaced by tensorial quantities.

# 1 Introduction

The Smoluchowski equation [47] is a system of partial differential equations which describes the evolving densities of diffusing particles that are prone to coagulate in pairs [6], [7], [8], [10], [22], [23], [25], [26], [34], [36], [49], [50], [51]. In spite of the large literature concerning the use of the Smoluchowski equation in many branches of science (e.g. in aerosol science, polymer science, astrophysics, chemistry), this equation does not seem to have been considered extensively in the field of biomedical research. Applications of Smoluchowski equation to the description of the agglomeration of  $\beta$ -amyloid peptide ( $A\beta$ ), a process associated with the development of Alzheimer's disease (AD), seem to appear for the first time in Murphy and Pallitto [37].

Nowadays, Alzheimer's disease is the most common form of senile dementia with enormous socio-economic implications. In recent years, besides *in vivo* and *in vitro* experimental models, there has been an increasing interest in mathematical modeling and computer simulations (the so-called *in silico* approach) [1], [9], [20], [24], [28], [45], in order to better understand the mechanisms for the onset and the evolution of AD. It is largely accepted that  $A\beta$  peptide (especially in soluble form) has a substantial role in the process of synaptic degeneration leading to neuronal death and eventually to dementia (the so-called *amyloid cascade hypothesis* [32]).  $A\beta$ , in monomeric form, is a normal product of cleavage of the amyloid precursor protein (APP), an integral membrane protein involved in signal transduction pathways. By unknown reasons (partially genetic), some neurons start to present an imbalance between production and clearance of  $A\beta$  amyloid during aging. Soluble  $A\beta$  (in the form of monomers) diffuses freely through neuronal tissue. At elevated levels, it produces pathological aggregates (that cannot be readily cleared): long insoluble amyloid fibrils, which accumulate in spherical deposits known as senile plaques. In addition, it has been recognised that  $A\beta$  is able to initiate an inflammatory response, which implicates the activation of microglia (the resident immune cells in the central nervous system) and therefore the release of neurotoxic products that are involved in neuronal and synaptic damage.

In [37], the authors compare experimental data with numerical simulations based

on the Smoluchowski equation without diffusion, in order to clarify the kinetics of conversion of monomeric  $\beta$ -amyloid peptide into macroscopic fibril aggregates. Very recently, the important role of Smoluchowski equation in modeling the evolution of AD at different scales has been investigated in [1], [27], [9]. In [1], the authors present a mathematical model for the aggregation and diffusion of  $\beta$ -amyloid in the brain affected by AD at a microscopic scale (the size of a single neuron) and at the early stage of the disease when small amyloid fibrils are free to move and to coalesce. In the model proposed in [1], a very small portion of the cerebral tissue is described by a bounded smooth region  $\Omega \subset \mathbb{R}^3$ , whereas the neurons are represented by a family of regular disjoint regions  $\Omega_j$  (for  $1 \leq j \leq \overline{M}$ ). Moreover, the production of  $A\beta$  in monomeric form at the level of neuron membranes is modeled by a non-homogeneous Neumann condition on the boundary of  $\Omega_j$ , for  $j = 1, \dots, \overline{M}$ . On the other hand, in [9] the authors present a model for the evolution of AD at a macroscopic scale and over the entire lifetime of the patient. In this case, the whole brain is represented by a region of the three-dimensional space, and the process of diffusion and aggregation of  $A\beta$  is modeled by a Smoluchowski system with a source term, coupled with a kinetic-type transport equation that keeps into account the spreading of the disease. Clearly, at this scale, neurons are no more visible so that they can be described mathematically as points.

Passing from a microscopic model to a macroscopic one has always been a common issue in mathematical modeling. As a matter of fact, while being closer to the actual physical nature, a mathematical model for a physical system that resolves smaller scales is usually more complicated and sometimes even virtually impossible to solve. Moreover, experimental data are often available for macroscale quantities only, but not for the microscale. Therefore, for quite a long time, the key issue has been how to formulate laws on a scale that is larger than the microscale and to justify these laws on the basis of a microscopic approach. In practice, one wants to start from differential equations that are assumed to hold on the micro-scale and to transform them into equations on the macro-scale, by performing a sort of 'averaging process'. To do that, in the seventies, mathematicians have developed a new method called homogenization [16], [17], [21]. This method allows to perform certain limits

of the solutions of partial differential equations describing media with microstructures and to determine equations which the limits are solution of. Roughly speaking, what one does is to consider media with microstructures, to average out the physical and chemical processes arising at the microscale and to calculate effective properties of the media on the macroscale.

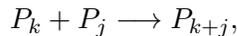
This is precisely what has been done in the present work, where the homogenization method has been applied to the model presented in [1], in order to describe the effects of the production of  $A\beta$  by the neuron membranes at the macroscopic level and to derive rigorously the equations in [9]. In particular, a periodically perforated domain  $\Omega_\epsilon$ , obtained by removing from the fixed domain  $\Omega$  (the cerebral tissue) infinitely many small holes of size  $\epsilon$  (the neurons), which support a non-homogeneous Neumann boundary condition, has been defined. Then, the limiting behavior as  $\epsilon \rightarrow 0$  of the Smoluchowski-type equations in  $\Omega_\epsilon$  has been studied in the framework of two-scale convergence [3], [4], [5], [11], [18], [19], [29], [30], [31], [38], [40]. The peculiarity of the two-scale convergence method, introduced by Gabriel Nguetseng and Gregoire Allaire, is that, in a single process one can find the homogenized equations and prove the convergence of a sequence of solutions to the problem at hand. Moreover, while previous approaches were originally defined only for certain problem classes, two-scale convergence allows to pass to the limit in all sorts of problems featuring periodic microstructures.

The paper is organized as follows. Section 2 summarizes the main features of the discrete diffusive Smoluchowski equation, while in Section 3, a mathematical model describing the self-association and diffusion of  $\beta$ -amyloid peptide (which is the main trigger of Alzheimer's disease) is presented. Then, in Section 4 we define the perforated geometry and prove all the a priori estimates needed for two-scale homogenization. Finally, Section 5 is devoted to derive our main results on the homogenization of the Smoluchowski equation in perforated domains.

## 2 The Smoluchowski equation

The Smoluchowski coagulation equation models various kind of phenomena as for example: the evolution of a system of solid or liquid particles suspended in a gas (in

aerosol science), polymerisation (in chemistry), aggregation of colloidal particles (in physics), formation of stars and planets (in astrophysics), red blood cell aggregation (in hematology), behaviour of fuel mixtures in engines (in engineering), etc. The original model proposed by Smoluchowski [47] was introduced to describe the binary coagulation of colloidal particles moving according to Brownian motions and several additional physical processes have been subsequently incorporated into the model (fragmentation, condensation, influence of external fields, see, e.g. [22], [34], [49], [50], [51]). In view of our subsequent applications, we present the appearance of the Smoluchowski equation in polymerisation [22], [34], [50]. For  $k \in \mathbb{N}$ , let  $P_k$  denote a polymer of size  $k$ , that is a set of  $k$  identical particles (monomers). As time advances, the polymers evolve and, if they approach each other sufficiently close, there is some chance that they merge into a single polymer whose size equals the sum of the sizes of the two polymers which take part in this reaction. By convention, we admit only binary reactions. This phenomenon is called coalescence and we write formally



for the coalescence of a polymer of size  $k$  with a polymer of size  $j$ .

In the model studied further on, we restrict ourselves to the following physical situation: the approach of two clusters leading to aggregation is assumed to result only from Brownian movement or diffusion (thermal coagulation). Other effects such as multiple coagulation or condensation, together with the influence of other external force fields are neglected. Under these assumptions, the discrete diffusive coagulation equations read [34], [50]

$$\frac{\partial u_i}{\partial t}(t, x) - d_i \Delta_x u_i(t, x) = Q_i(u) \quad \text{in } [0, T] \times \Omega, \quad (1)$$

with appropriate initial and boundary conditions.

The variable  $u_i(t, x) \geq 0$  (for  $i \geq 1$ ) represents the concentration of  $i$ -clusters, that is, clusters consisting of  $i$  identical elementary particles, and

$$Q_i(u) = Q_{g,i}(u) - Q_{l,i}(u) \quad i \geq 1 \quad (2)$$

with the gain ( $Q_{g,i}$ ) and loss ( $Q_{l,i}$ ) terms given by

$$Q_{g,i} = \frac{1}{2} \sum_{j=1}^{i-1} a_{i-j,j} u_{i-j} u_j \quad (3)$$

$$Q_{l,i} = u_i \sum_{j=1}^{\infty} a_{i,j} u_j. \quad (4)$$

where  $u = (u_i)_{i \geq 1}$ . The coagulation rates  $a_{i,j}$  are non negative constants such that  $a_{i,j} = a_{j,i}$  and  $d_i$  denotes the diffusion coefficient of an  $i$ -cluster,  $d_i > 0 \quad \forall i \geq 1$ . The kinetic coefficient  $a_{i,j}$  represents reaction in which an  $(i+j)$ -cluster is formed from an  $i$ -cluster and a  $j$ -cluster. Possible breakup of clusters is not taken into account. The term  $Q_{g,i}$ , given by (3), describes the creation of polymers of size  $i$  by coagulation of polymers of size  $j$  and  $i-j$ . The term  $Q_{l,i}$ , given by (4), corresponds to the depletion of polymers of size  $i$  after coalescence with other polymers. Since the size of clusters is not limited a priori, Eq. (1) describes a non-linear evolution equation of infinite dimension, for which even the existence of a local solution is not guaranteed by the general theory of reaction-diffusion equations. According to the form of the coalescence kernel  $a_{i,j}$  we obtain or not solutions for the system of equations (1). In general, the coagulation rates are determined by the statistical probabilities of bond formation and depend upon the details of the physical process being considered. If there are no sources nor sinks of clusters in the reactions described by the initial-boundary value problem (1), the total mass of clusters is expected to be constant throughout the time evolution of the system, provided it is initially finite. It turns out however that this property may fail to be true in general for some physically relevant kinetic coefficients. The break-down of the mass conservation is then related to the so-called gelation phenomenon which corresponds to the appearance of an infinite cluster called gel, caused by the cascading growth of larger and larger clusters. We will however not consider this issue in the following.

### 3 A mathematical model for the aggregation and diffusion of $\beta$ -amyloid peptide

In the present paper, we consider a mathematical model based on the discrete Smoluchowski equation in order to describe the aggregation and diffusion of  $\beta$ -

amyloid peptide ( $A\beta$ ) in the brain affected by Alzheimer's disease (AD) [1].  $A\beta$  is naturally present in the brain and cerebrospinal fluid of humans throughout life, even if its role is currently unknown. By now, it is recognized that the mere presence of  $A\beta$  in the brain is not sufficient to support the diagnosis of AD. Neuronal injury is rather the result of ordered  $A\beta$  self-association [13], [24], [35], [39], [43], [52]. The amyloid plaques, which serve as a hallmark for AD, have been found to contain large amounts of  $A\beta$  organized into amyloid fibrils. There is no clear correlation, however, between the presence of the  $A\beta$  containing plaques in the brain and the severity of AD neurodegeneration. Therefore, in recent years, the research in this area has shifted its focus from senile plaques toward oligomeric conformations of  $A\beta$ . This oligomeric form of  $A\beta$  is highly toxic to the brain and is the trigger for loss of synapses and neuronal damage. However, the transient nature of small oligomeric aggregates makes it difficult to shed light on their formation process or structure. Most proposed pathways for the initial stages of  $A\beta$  amyloid fibril formation amount to a sequence of events that can be summarized as follows: unordered monomeric  $A\beta$  in solution converts into an 'activated' monomer that then recruits other  $A\beta$  molecules to form oligomers. The length-wise association of individual protofibrils produces the mature amyloid fibrils, whose structure has been studied in most detail due to their high stability under a wide range of physicochemical conditions. The mature fibrillar form and monomeric  $A\beta$  have both been confirmed on many occasions as the only non-toxic species.

In the present work, we are interested in considering the early stage of Alzheimer's disease (AD) when small amyloid fibrils are free to move and to coalesce in the brain. In addition, we discard fibril fragmentation, which can be considered as a secondary process in the mechanism of amyloid self-assembly, especially when oligomers of small size are involved (for a model with fragmentation, we refer to [27]). Since the fibrils at this stage are relatively small, diffusion plays a key role in the description of the behavior of oligomeric  $\beta$ -amyloid peptide ( $A\beta$ ). In the mathematical model proposed in [1] and reported below, the authors consider a portion of the hippocampus or of the cerebral cortex (the regions of the brain mainly affected by AD) whose size is comparable to a multiple of the size of a neuron, thus avoiding the description of

intracellular phenomena. With this choice of scale, it is coherent to consider that the diffusion is uniform. Moreover, it is assumed that 'large' assemblies do not aggregate with each other. This assumption prevents blow-up phenomena for solutions at a finite time, but it is also consistent with experimental data [24], [37]. The portion of cerebral tissue considered in the following is represented by a bounded smooth region  $\Omega_0 \subset \mathbb{R}^3$ , whereas the neurons are represented by a family of regular regions  $\Omega_j$  such that

- (i)  $\overline{\Omega}_j \subset \Omega_0$  if  $j = 1, 2, \dots, \overline{M}$ ;
- (ii)  $\overline{\Omega}_i \cap \overline{\Omega}_j = \emptyset$  if  $i \neq j$ .

Let us set

$$\Omega := \Omega_0 \setminus \bigcup_{j=1}^{\overline{M}} \overline{\Omega}_j$$

and consider a vector-valued function  $u = (u_1, \dots, u_M)$ , where  $M \in \mathbb{N}$  and  $u_j = u_j(t, x)$ ,  $t \in \mathbb{R}$ ,  $t \geq 0$  (the time), and  $x \in \Omega$ . If  $1 \leq j < M - 1$ , then  $u_j(t, x)$  is the (molar) concentration at the point  $x$  and at the time  $t$  of an  $A\beta$  assembly of  $j$  monomers, while  $u_M$  takes into account aggregations of more than  $M - 1$  monomers. The production of  $A\beta$  in the monomeric form at the level of neuron membranes is modeled by a non-homogeneous Neumann condition on  $\partial\Omega_j$ , the boundary of  $\Omega_j$ , for  $j = 1, \dots, \overline{M}$ . Finally, an homogeneous Neumann condition on  $\partial\Omega_0$  is meant to artificially isolate the portion of tissue considered from its environment. Thus, the following Cauchy-Neumann problem can be defined [1]:

$$\left\{ \begin{array}{ll} \frac{\partial u_1}{\partial t}(t, x) - d_1 \Delta_x u_1(t, x) + u_1(t, x) - \sum_{j=1}^M a_{1,j} u_j(t, x) = 0 & \\ \frac{\partial u_1}{\partial \nu} \equiv \nabla_x u_1 \cdot n = 0 & \text{on } \partial\Omega_0 \\ \frac{\partial u_1}{\partial \nu} \equiv \nabla_x u_1 \cdot n = \psi_j & \text{on } \partial\Omega_j, \quad j = 1, \dots, \overline{M} \\ u_1(0, x) = U_1 \geq 0 & \end{array} \right. \quad (5)$$



Let us remark that the meaning of  $u_M$  differs from that of  $u_m$ ,  $m < M$ , since it describes the sum of the densities of all the 'large' assemblies. It is assumed that large assemblies exhibit all the same coagulation properties and do not coagulate with each other. Indeed, the present model only takes into account the evolution of the  $A\beta$  and ignores the role played by the microglia and astrocytes in neuronal death and in the formation of senile plaques.

## 4 Setting of the problem and preliminary results

Let  $\Omega$  be a bounded open set in  $\mathbb{R}^3$  with a smooth boundary  $\partial\Omega$ . Let  $Y$  be the unit periodicity cell  $[0, 1]^3$  having the paving property. We perforate  $\Omega$  by removing from it a set  $T_\epsilon$  of periodically distributed holes defined as follows. Let us denote by  $T$  an open subset of  $Y$  with a smooth boundary  $\Gamma$ , such that  $\bar{T} \subset \text{Int } Y$ . Set  $Y^* = Y \setminus T$  which is called in the literature the solid or material part. According to the model presented in Section 3, the set  $T$  represents a generic neuron, and  $Y^*$  the supporting cerebral tissue. We define  $\tau(\epsilon\bar{T})$  to be the set of all translated images of  $\epsilon\bar{T}$  of the form  $\epsilon(k + \bar{T})$ ,  $k \in \mathbb{Z}^3$ . Then,

$$T_\epsilon := \Omega \cap \tau(\epsilon\bar{T}).$$

Introduce now the periodically perforated domain  $\Omega_\epsilon$  defined by

$$\Omega_\epsilon = \Omega \setminus \bar{T}_\epsilon.$$

For the sake of simplicity, we make the following standard assumption on the holes [17], [21]:

there exists a 'security' zone around  $\partial\Omega$  without holes, i.e.

$$\exists \delta > 0 \text{ such that } \text{dist}(\partial\Omega, T_\epsilon) \geq \delta. \quad (8)$$

Therefore,  $\Omega_\epsilon$  is a connected set ([17]). The boundary  $\partial\Omega_\epsilon$  of  $\Omega_\epsilon$  is then composed of two parts. The first one is the union of the boundaries of the holes strictly contained in  $\Omega$ . It is denoted by  $\Gamma_\epsilon$  and is defined by

$$\Gamma_\epsilon := \cup \left\{ \partial(\epsilon(k + \bar{T})) \mid \epsilon(k + \bar{T}) \subset \Omega \right\}.$$

The second part of  $\partial\Omega_\epsilon$  is its fixed exterior boundary denoted by  $\partial\Omega$ . It is easily seen that (see [4], Eq. (3))

$$\lim_{\epsilon \rightarrow 0} \epsilon |\Gamma_\epsilon|_{N-1} = |\Gamma|_{N-1} \frac{|\Omega|_N}{|Y|_N} \quad (9)$$

where  $|\cdot|_N$  is the  $N$ -dimensional Hausdorff measure.

Throughout this paper,  $\epsilon$  will denote the general term of a sequence of positive reals which converges to zero.

Let us rewrite the model problem presented in Section 3 as a family of equations in  $\Omega_\epsilon$ :

$$\left\{ \begin{array}{ll} \frac{\partial u_1^\epsilon}{\partial t} - \operatorname{div}(d_1 \nabla_x u_1^\epsilon) + u_1^\epsilon \sum_{j=1}^M a_{1,j} u_j^\epsilon = 0 & \text{in } [0, T] \times \Omega_\epsilon \\ \frac{\partial u_1^\epsilon}{\partial \nu} \equiv \nabla_x u_1^\epsilon \cdot n = 0 & \text{on } [0, T] \times \partial\Omega \\ \frac{\partial u_1^\epsilon}{\partial \nu} \equiv \nabla_x u_1^\epsilon \cdot n = \epsilon \psi(t, x, \frac{x}{\epsilon}) & \text{on } [0, T] \times \Gamma_\epsilon \\ u_1^\epsilon(0, x) = U_1 & \text{in } \Omega_\epsilon \end{array} \right. \quad (10)$$

where  $\psi$  is a given bounded function satisfying the following conditions:

(i)  $\psi(t, x, \frac{x}{\epsilon}) \in C^1(0, T; B)$  with  $B = C^1[\bar{\Omega}; C^1_{\#}(Y)]$ , where  $C^1_{\#}(Y)$  is the subset of  $C^1(\mathbb{R}^N)$  of  $Y$ -periodic functions;

(ii)  $\psi(t = 0, x, \frac{x}{\epsilon}) = 0$

and  $U_1$  is a positive constant such that

$$U_1 \leq \|\psi\|_{L^\infty(0, T; B)}. \quad (11)$$

Typically,  $\psi$  has the form  $\psi(t, x, \frac{x}{\epsilon}) = \psi_0(\frac{x}{\epsilon})\psi_1(t - g(x))$ , where the function  $\psi_1(s) \equiv 0$  for  $s$  near 0 and  $\psi_1(s) \equiv 1$  for large  $s > 0$ . The function  $g$  takes into account that different cerebral regions are affected at different times. However, we stress that this system corresponds to an evolution model based only on genetic causes, since it ignores any spreading (like, e.g., a possible prion-type diffusion ([28]).

In addition, if  $1 < m < M$ ,

$$\left\{ \begin{array}{l} \frac{\partial u_m^\epsilon}{\partial t} - \operatorname{div}(d_m \nabla_x u_m^\epsilon) + u_m^\epsilon \sum_{j=1}^M a_{m,j} u_j^\epsilon = f^\epsilon \quad \text{in } [0, T] \times \Omega_\epsilon \\ \frac{\partial u_m^\epsilon}{\partial \nu} \equiv \nabla_x u_m^\epsilon \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \\ \frac{\partial u_m^\epsilon}{\partial \nu} \equiv \nabla_x u_m^\epsilon \cdot n = 0 \quad \text{on } [0, T] \times \Gamma_\epsilon \\ u_m^\epsilon(0, x) = 0 \quad \text{in } \Omega_\epsilon \end{array} \right. \quad (12)$$

and

$$\left\{ \begin{array}{l} \frac{\partial u_M^\epsilon}{\partial t} - \operatorname{div}(d_M \nabla_x u_M^\epsilon) = g^\epsilon \quad \text{in } [0, T] \times \Omega_\epsilon \\ \frac{\partial u_M^\epsilon}{\partial \nu} \equiv \nabla_x u_M^\epsilon \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \\ \frac{\partial u_M^\epsilon}{\partial \nu} \equiv \nabla_x u_M^\epsilon \cdot n = 0 \quad \text{on } [0, T] \times \Gamma_\epsilon \\ u_M^\epsilon(0, x) = 0 \quad \text{in } \Omega_\epsilon \end{array} \right. \quad (13)$$

where the gain terms  $f^\epsilon$  and  $g^\epsilon$  in (12) and (13) are given by

$$f^\epsilon = \frac{1}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon \quad (14)$$

$$g^\epsilon = \frac{1}{2} \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} u_j^\epsilon u_k^\epsilon. \quad (15)$$

**Theorem 4.1.** *If  $\epsilon > 0$  the system (10) - (13) has a unique solution*

$$(u_1^\epsilon, \dots, u_M^\epsilon) \in C^{1+\alpha/2, 2+\alpha}([0, T] \times \Omega_\epsilon) \quad (\alpha \in (0, 1))$$

such that

$$u_j^\epsilon(t, x) > 0 \quad \text{for } (t, x) \in (0, T) \times \Omega_\epsilon, \quad j = 1, \dots, M.$$

*Proof.* The proof can be carried out as in [1], using Theorem 1, p.111 of [46] for the function  $(u_1^\epsilon - g^\epsilon, \dots, u_M^\epsilon)$ , where  $g^\epsilon \in C^{1+\alpha/2, 2+\alpha}([0, T] \times \Omega_\epsilon)$  solves the Cauchy-Neumann problem:

$$\left\{ \begin{array}{ll} \frac{\partial g^\epsilon}{\partial t} - \operatorname{div}(d_1 \nabla_x g^\epsilon) = 0 & \text{in } [0, T] \times \Omega_\epsilon \\ \frac{\partial g^\epsilon}{\partial \nu} \equiv \nabla_x g^\epsilon \cdot n = 0 & \text{on } [0, T] \times \partial\Omega \\ \frac{\partial g^\epsilon}{\partial \nu} \equiv \nabla_x g^\epsilon \cdot n = \epsilon \psi(t, x, \frac{x}{\epsilon}) & \text{on } [0, T] \times \Gamma_\epsilon \\ g^\epsilon(0, x) = 0 & \text{in } \Omega_\epsilon. \end{array} \right.$$

Notice that the function  $g^\epsilon$  is bounded in  $[0, T] \times \Omega_\epsilon$ , uniformly with respect to  $\epsilon > 0$ . This can be proven, for instance, following the arguments used in the proof of Lemmas 4.1 and 4.2 below. □

Our aim is to study the homogenization of the set of equations (10)-(13) as  $\epsilon \rightarrow 0$ , i.e., to study the behaviour of  $u_j^\epsilon (1 \leq j \leq M)$  as  $\epsilon \rightarrow 0$  and obtain the equations satisfied by the limit. There is no clear notion of convergence for the sequence  $u_j^\epsilon (1 \leq j \leq M)$  which is defined on a varying set  $\Omega_\epsilon$ . This difficulty is specific to the case of perforated domains. A natural way to get rid of this difficulty is given by Nguetseng-Allaire two-scale convergence [3], [40].

We first obtain the a priori estimates for the sequences  $u_j^\epsilon, \nabla u_j^\epsilon, \partial_t u_j^\epsilon$  in  $[0, T] \times \Omega_\epsilon$ , that are independent of  $\epsilon$ .

Since

$$\operatorname{div}(d_1 \nabla_x u_1^\epsilon) - \frac{\partial u_1^\epsilon}{\partial t} \geq 0,$$

by the classical maximum principle [44] the following estimate holds.

**Lemma 4.1.** *Let  $T > 0$  be arbitrary and  $u_1^\epsilon$  be a classical solution of (10). Then,*

$$\|u_1^\epsilon\|_{L^\infty(0, T; L^\infty(\Omega_\epsilon))} \leq |U_1| + \|u_1^\epsilon\|_{L^\infty(0, T; L^\infty(\Gamma_\epsilon))}. \quad (16)$$

Thus, the boundedness of  $u_1^\epsilon(t, x)$  in  $L^\infty([0, T] \times \Gamma_\epsilon)$ , uniformly in  $\epsilon$ , can be immediately deduced from Lemma 4.2 below.

**Lemma 4.2.** *Let  $T > 0$  be arbitrary and  $u_1^\epsilon$  be a classical solution of (10). Then,*

$$\|u_1^\epsilon\|_{L^\infty(0, T; L^\infty(\Gamma_\epsilon))} \leq c \|\psi\|_{L^\infty(0, T; B)} \quad (17)$$

where  $c$  is independent of  $\epsilon$ .

In order to establish Lemma 4.2, we will first need the following preliminary results [33], [41].

**Lemma 4.3** ([33], Lemma 5.6). *Let  $(\tilde{z}_n)_{n \in \mathbb{N}_0}$  be a sequence of non-negative real numbers such that*

$$\tilde{z}_{n+1} \leq c b^n \tilde{z}_n^{r/2} \quad (18)$$

for all  $n \in \mathbb{N}_0$ , with fixed positive constants  $c, b, r$ , where  $b > 1$  and

$$r = \frac{2(N+1)}{N} > 2.$$

If

$$\tilde{z}_0 \leq \theta := c^{-N} b^{-N^2} \quad (19)$$

then,

$$\tilde{z}_n \leq \theta b^{-nN} \quad (20)$$

for all  $n \in \mathbb{N}_0$ .

**Theorem 4.2.** *Assume that there exist positive constants  $T, \hat{k} = \|\psi\|_{L^\infty(0, T; B)}, \gamma$ , such that for all  $k \geq \hat{k}$  we have*

$$\|u_\epsilon^{(k)}\|_{Q_\epsilon(T)}^2 := \sup_{0 \leq t \leq T} \int_{\Omega_\epsilon} |u_\epsilon^{(k)}|^2 dx + \int_0^T dt \int_{\Omega_\epsilon} |\nabla u_\epsilon^{(k)}|^2 dx \leq \epsilon \gamma k^2 \int_0^T dt |B_k^\epsilon(t)| \quad (21)$$

where  $u_\epsilon^{(k)}(t) := (u_1^\epsilon(t) - k)_+$  and  $B_k^\epsilon(t)$  is the set of points on  $\Gamma_\epsilon$  at which  $u_1^\epsilon(t, x) > k$ .

Then

$$\text{ess sup}_{(t,x) \in [0,T] \times \Gamma_\epsilon} u_1^\epsilon(t,x) \leq 2m\hat{k} \quad (22)$$

where the positive constant  $m$  is independent of  $\epsilon$ .

*Proof.* Let us choose

$$r = \frac{2(N+1)}{N} > 2$$

Then, it holds

$$\frac{1}{r} + \frac{(N-1)}{2r} = \frac{N}{4} \quad (23)$$

Let  $\mathcal{M} \geq \hat{k}$  be arbitrary and define

$$k_n := (2 - 2^{-n}) \mathcal{M} \geq \hat{k},$$

$$z_n := \epsilon^{2/r} \left[ \int_0^T dt |B_{k_n}^\epsilon(t)| \right]^{2/r} \quad (24)$$

for all  $n \in \mathbb{N}_0$ . We prove that the sequence  $(z_n)$  satisfies the assumptions of Lemma 4.3. To this end, let  $n \in \mathbb{N}_0$  be fixed. From the trivial estimate

$$|u_\epsilon^{(k_n)}(t)|^2 \geq (k_{n+1} - k_n)^2 \mathbb{1}_{B_{k_{n+1}}^\epsilon(t)} \quad (25)$$

we get

$$\begin{aligned} z_{n+1} &\leq \epsilon^{2/r} \left[ \int_0^T dt (k_{n+1} - k_n)^{-r} \int_{\Gamma_\epsilon} |u_\epsilon^{(k_n)}(t)|^r d\sigma_\epsilon(x) \right]^{2/r} \\ &= (k_{n+1} - k_n)^{-2} \epsilon^{2/r} \left[ \int_0^T dt \int_{\Gamma_\epsilon} |u_\epsilon^{(k_n)}(t)|^r d\sigma_\epsilon(x) \right]^{2/r} \end{aligned} \quad (26)$$

Hence, since the condition (23) holds, by using (146) we obtain

$$\begin{aligned} 2^{-2(n+1)} \mathcal{M}^2 z_{n+1} &= (k_{n+1} - k_n)^2 z_{n+1} \\ &\leq c \epsilon^{2/r} \epsilon^{-N - [\frac{2(1-N)}{r}]} \|u_\epsilon^{(k_n)}\|_{Q_\epsilon(T)}^2 \end{aligned} \quad (27)$$

where  $c$  is a positive constant independent of  $\epsilon$ . Therefore,

$$2^{-2(n+1)} \mathcal{M}^2 z_{n+1} \leq c \epsilon^{-\frac{N}{(1+N)}} \|u_\epsilon^{(k_n)}\|_{Q_\epsilon(T)}^2 \quad (28)$$

Moreover, from (21) and (24) we get

$$\begin{aligned} \|u_\epsilon^{(k_n)}\|_{Q_\epsilon(T)}^2 &\leq \gamma k_n^2 z_n^{r/2} \leq \gamma (2 - 2^{-n})^2 \mathcal{M}^2 z_n^{r/2} \\ &\leq 4\gamma \mathcal{M}^2 z_n^{r/2} \end{aligned} \quad (29)$$

Combining (28) and (29), we obtain

$$z_{n+1} \leq c_0 \epsilon^{-\frac{N}{(1+N)}} 2^{2n} z_n^{r/2} \quad (30)$$

where  $c_0$  is a positive constant independent of  $\epsilon$ .

Let us define

$$d := \frac{(r-2)}{r}$$

$$\lambda := (c_0)^{-\frac{r}{(r-2)}} 2^{-\frac{4}{(r-2)d}}$$

and choose

$$\mathcal{M} := \hat{k} + \lambda^{-1/r} \sqrt{c'} \hat{k} \equiv m \hat{k} \quad (31)$$

where  $c'$  is defined in (32) and  $m > 1$ . Now we want to estimate  $z_0$  for the fixed value of  $\mathcal{M}$  given by (31). From the definition (24) and (9), by following the same strategy which leads to (28) and (29), where we substitute  $\hat{k}$  for  $k_n$  and  $\mathcal{M}$  for  $k_{n+1}$ , we have

$$\begin{aligned} (\mathcal{M} - \hat{k})^2 z_0 &\leq c \epsilon^{-\frac{N}{(1+N)}} \|u_\epsilon^{(\hat{k})}\|_{Q_\epsilon(T)}^2 \leq c \epsilon^{-\frac{N}{(1+N)}} \left[ \gamma \hat{k}^2 T \frac{|\Gamma|_{N-1} |\Omega|_N}{|Y|_N} \right] \\ &:= c' \epsilon^{-\frac{N}{(1+N)}} \hat{k}^2 \end{aligned} \quad (32)$$

so that

$$z_0 \leq \frac{c' \epsilon^{-\frac{N}{(1+N)}} \hat{k}^2}{(\mathcal{M} - \hat{k})^2} \quad (33)$$

for all  $\mathcal{M} \geq \hat{k}$ . Therefore, from (33) and (31) we obtain that

$$z_0 \leq \epsilon^{-\frac{N}{(1+N)}} \lambda^{2/r}. \quad (34)$$

For a fixed  $\epsilon$ , we set

$$\tilde{z}_n = \epsilon^{\frac{N}{(1+N)}} z_n \quad (35)$$

for all  $n \in \mathbb{N}_0$ . Then, the recursion inequality (30) and the estimate (34) can be rewritten as follows:

$$\begin{cases} \tilde{z}_{n+1} \leq c_0 2^{2n} \epsilon^{-1} \tilde{z}_n^{r/2} \\ \tilde{z}_0 \leq \lambda^{2/r} = (c_0)^{-N} 2^{-2N^2} \end{cases} \quad (36)$$

Keeping in mind (36), it is easy to see that the sequence  $(\tilde{z}_n)$  satisfies the assumptions of Lemma 4.3 with

$$c := \max \left\{ c_0, \frac{c_0}{\epsilon} \right\} \text{ and } b := 4.$$

Therefore, in view of Lemma 4.3, one can conclude that  $z_n \rightarrow 0$  as  $n \rightarrow \infty$ , which implies

$$u_1^\epsilon \leq \lim_{n \rightarrow \infty} k_n = 2\mathcal{M}$$

almost everywhere on  $\Gamma_\epsilon$  for almost every  $t \in [0, T]$  if we define  $\mathcal{M}$  as in (31). This gives (22).

□

*Proof of Lemma 4.2.* Let  $T > 0$  and  $k \geq 0$  be fixed. Define:  $u_\epsilon^{(k)}(t) := (u_1^\epsilon(t) - k)_+$  for  $t \geq 0$ , with derivatives:

$$\frac{\partial u_\epsilon^{(k)}}{\partial t} = \frac{\partial u_1^\epsilon}{\partial t} \mathbb{1}_{\{u_1^\epsilon > k\}} \quad (37)$$

$$\nabla_x u_\epsilon^{(k)} = \nabla_x u_1^\epsilon \mathbb{1}_{\{u_1^\epsilon > k\}}. \quad (38)$$

Moreover,

$$u_\epsilon^{(k)}|_{\partial\Omega} = (u_1^\epsilon|_{\partial\Omega} - k)_+ \quad (39)$$

$$u_\epsilon^{(k)}|_{\Gamma_\epsilon} = (u_1^\epsilon|_{\Gamma_\epsilon} - k)_+ \quad (40)$$

Let us assume  $k \geq \hat{k}$ , where  $\hat{k} := \|\psi\|_{L^\infty(0,T;B)}$ . Then, by (11),

$$u_1^\epsilon(0, x) = U_1 \leq \hat{k} \leq k. \quad (41)$$

For  $t \in [0, T_1]$  with  $T_1 \leq T$ , we get

$$\begin{aligned} \frac{1}{2} \int_{\Omega_\epsilon} |u_\epsilon^{(k)}(t)|^2 dx &= \int_0^t \frac{d}{ds} \left[ \frac{1}{2} \int_{\Omega_\epsilon} |u_\epsilon^{(k)}(s)|^2 dx \right] ds \\ &= \int_0^t ds \int_{\Omega_\epsilon} \frac{\partial u_\epsilon^{(k)}(s)}{\partial s} u_\epsilon^{(k)}(s) dx. \end{aligned} \quad (42)$$

Taking into account (37), (10) and Lemma A.1, we obtain that for all  $s \in [0, T_1]$

$$\begin{aligned} \int_{\Omega_\epsilon} \frac{\partial u_\epsilon^{(k)}(s)}{\partial s} u_\epsilon^{(k)}(s) dx &= \int_{\Omega_\epsilon} \frac{\partial u_1^\epsilon(s)}{\partial s} u_\epsilon^{(k)}(s) dx \\ &= \int_{\Omega_\epsilon} \left[ d_1 \Delta_x u_1^\epsilon - u_1^\epsilon \sum_{j=1}^M a_{1,j} u_j^\epsilon \right] u_\epsilon^{(k)}(s) dx \\ &= - \int_{\Omega_\epsilon} u_1^\epsilon(s) \sum_{j=1}^M a_{1,j} u_j^\epsilon(s) u_\epsilon^{(k)}(s) dx + \epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( s, x, \frac{x}{\epsilon} \right) u_\epsilon^{(k)}(s) d\sigma_\epsilon(x) \\ &\quad - d_1 \int_{\Omega_\epsilon} \nabla_x u_1^\epsilon(s) \cdot \nabla_x u_\epsilon^{(k)}(s) dx \\ &\leq \epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( s, x, \frac{x}{\epsilon} \right) u_\epsilon^{(k)}(s) d\sigma_\epsilon(x) - d_1 \int_{\Omega_\epsilon} \nabla_x u_1^\epsilon(s) \cdot \nabla_x u_\epsilon^{(k)}(s) dx \\ &\leq \frac{\epsilon d_1}{2} \int_{B_k^\epsilon(s)} \left| \psi \left( s, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) + \frac{\epsilon d_1}{2} \int_{\Gamma_\epsilon} |u_\epsilon^{(k)}(s)|^2 d\sigma_\epsilon(x) \\ &\quad - d_1 \int_{\Omega_\epsilon} \nabla_x u_1^\epsilon(s) \cdot \nabla_x u_\epsilon^{(k)}(s) dx \\ &\leq \frac{\epsilon d_1}{2} \int_{B_k^\epsilon(s)} \left| \psi \left( s, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) + \frac{C_1 d_1}{2} \int_{A_k^\epsilon(s)} |u_\epsilon^{(k)}(s)|^2 dx \\ &\quad - d_1 \left( 1 - \frac{C_1 \epsilon^2}{2} \right) \int_{\Omega_\epsilon} |\nabla_x u_\epsilon^{(k)}(s)|^2 dx \end{aligned} \quad (43)$$

where we denote by  $A_k^\epsilon(t)$  and  $B_k^\epsilon(t)$  the set of points in  $\Omega_\epsilon$  and on  $\Gamma_\epsilon$ , respectively, at which  $u_1^\epsilon(t, x) > k$ . It holds:

$$|A_k^\epsilon(t)| \leq |\Omega_\epsilon|$$

$$|B_k^\epsilon(t)| \leq |\Gamma_\epsilon|$$

with  $|\cdot|$  being the Hausdorff measure.

Plugging (43) into (42) and varying over  $t$ , we arrive at the estimate:

$$\begin{aligned} & \sup_{0 \leq t \leq T_1} \left[ \frac{1}{2} \int_{\Omega_\epsilon} |u_\epsilon^{(k)}(t)|^2 dx \right] + d_1 \left( 1 - \frac{C_1 \epsilon^2}{2} \right) \int_0^{T_1} dt \int_{\Omega_\epsilon} |\nabla u_\epsilon^{(k)}(t)|^2 dx \\ & \leq \frac{C_1 d_1}{2} \int_0^{T_1} dt \int_{A_k^\epsilon(t)} |u_\epsilon^{(k)}(t)|^2 dx + \frac{\epsilon d_1}{2} \int_0^{T_1} dt \int_{B_k^\epsilon(t)} \left| \psi \left( t, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) \end{aligned} \quad (44)$$

Introducing the following norm

$$\|u\|_{Q_\epsilon(T)}^2 := \sup_{0 \leq t \leq T} \int_{\Omega_\epsilon} |u(t)|^2 dx + \int_0^T dt \int_{\Omega_\epsilon} |\nabla u(t)|^2 dx \quad (45)$$

the inequality (44) can be rewritten as follows

$$\begin{aligned} \min \left\{ \frac{1}{2}, d_1 \left( 1 - \frac{C_1 \epsilon^2}{2} \right) \right\} \|u_\epsilon^{(k)}\|_{Q_\epsilon(T_1)}^2 & \leq \frac{C_1 d_1}{2} \int_0^{T_1} dt \int_{A_k^\epsilon(t)} |u_\epsilon^{(k)}(t)|^2 dx \\ & + \frac{\epsilon d_1}{2} \int_0^{T_1} dt \int_{B_k^\epsilon(t)} \left| \psi \left( t, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) \end{aligned} \quad (46)$$

We estimate the right-hand side of (46). From Hölder's inequality we obtain

$$\int_0^{T_1} dt \int_{A_k^\epsilon(t)} |u_\epsilon^{(k)}(t)|^2 dx \leq \|u_\epsilon^{(k)}\|_{L^{\bar{r}_1}(0, T_1; L^{\bar{q}_1}(\Omega_\epsilon))}^2 \|\mathbb{1}_{A_k^\epsilon}\|_{L^{r'_1}(0, T_1; L^{q'_1}(\Omega_\epsilon))} \quad (47)$$

with  $r'_1 = \frac{r_1}{r_1 - 1}$ ,  $q'_1 = \frac{q_1}{q_1 - 1}$ ,  $\bar{r}_1 = 2r_1$ ,  $\bar{q}_1 = 2q_1$ , where, for  $N > 2$ ,  $\bar{r}_1 \in (2, \infty)$  and  $\bar{q}_1 \in (2, \frac{2N}{N-2})$  have been chosen such that

$$\frac{1}{\bar{r}_1} + \frac{N}{2\bar{q}_1} = \frac{N}{4}$$

In particular,  $r'_1, q'_1 < \infty$ , so that (47) yields

$$\int_0^{T_1} dt \int_{A_k^\epsilon(t)} |u_\epsilon^{(k)}(t)|^2 dx \leq \|u_\epsilon^{(k)}\|_{L^{\bar{r}_1}(0, T_1; L^{\bar{q}_1}(\Omega_\epsilon))}^2 |\Omega|^{1/q'_1} T_1^{1/r'_1}. \quad (48)$$

If we choose

$$T_1^{1/r'_1} < \frac{\min\{1, d_1\}}{2C_1 d_1} |\Omega|^{-1/q'_1} \leq \frac{\min\left\{ \frac{1}{2}, d_1 \left( 1 - \frac{C_1 \epsilon^2}{2} \right) \right\}}{C_1 d_1} |\Omega|^{-1/q'_1},$$

then from (48) it follows that

$$\frac{C_1 d_1}{2} \int_0^{T_1} dt \int_{A_k^\epsilon(t)} |u_\epsilon^{(k)}(t)|^2 dx \leq \frac{1}{2} \min \left\{ \frac{1}{2}, d_1 \left( 1 - \frac{C_1 \epsilon^2}{2} \right) \right\} \|u_\epsilon^{(k)}\|_{Q_\epsilon(T_1)}^2. \quad (49)$$

Analogously, from Hölder's inequality we have, for  $k \geq \hat{k}$

$$\begin{aligned} \frac{\epsilon d_1}{2} \int_0^{T_1} dt \int_{B_k^\epsilon(t)} \left| \psi \left( t, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) &\leq \frac{\epsilon d_1 k^2}{2} \left( \frac{\hat{k}^2}{k^2} \right) \|\mathbb{1}_{B_k^\epsilon}\|_{L^1(0, T_1; L^1(\Gamma_\epsilon))} \\ &\leq \frac{\epsilon d_1 k^2}{2} \int_0^{T_1} dt |B_k^\epsilon(t)|. \end{aligned} \quad (50)$$

Thus (46) yields

$$\|u_\epsilon^{(k)}\|_{Q_\epsilon(T_1)}^2 \leq \epsilon \gamma k^2 \int_0^{T_1} dt |B_k^\epsilon(t)|. \quad (51)$$

Hence, by Theorem 4.2 we obtain

$$\|u_1^\epsilon\|_{L^\infty(0, T_1; L^\infty(\Gamma_\epsilon))} \leq 2m\hat{k}$$

where the positive constant  $m$  is independent of  $\epsilon$ . Analogous arguments are valid for the cylinder  $[T_s, T_{s+1}] \times \Omega_\epsilon$ ,  $s = 1, 2, \dots, p-1$  with

$$\left[ T_{s+1} - T_s \right]^{1/r_1'} < \frac{\min\{1, d_1\}}{2C_1 d_1} |\Omega|^{-1/q_1'}$$

and  $T_p \equiv T$ . Thus, after a finite number of steps, we obtain the estimate (17).  $\square$

**Lemma 4.4.** *The sequence  $\nabla_x u_1^\epsilon$  is bounded in  $L^2([0, T] \times \Omega_\epsilon)$ , uniformly in  $\epsilon$ .*

*Proof.* Let us multiply the first equation in (10) by the function  $u_1^\epsilon(t, x)$ . Integrating, the divergence theorem yields

$$\begin{aligned} \frac{1}{2} \int_{\Omega_\epsilon} \frac{\partial}{\partial t} |u_1^\epsilon|^2 dx + d_1 \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx + \int_{\Omega_\epsilon} |u_1^\epsilon|^2 \sum_{j=1}^M a_{1,j} u_j^\epsilon dx \\ = \epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) u_1^\epsilon(t, x) d\sigma_\epsilon(x) \end{aligned} \quad (52)$$

By Hölder's and Young's inequalities, the right-hand side of Eq. (52) can be rewritten as

$$\int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) u_1^\epsilon(t, x) d\sigma_\epsilon(x) \leq \frac{1}{2} \|\psi(t, \cdot, \frac{\cdot}{\epsilon})\|_{L^2(\Gamma_\epsilon)}^2 + \frac{1}{2} \|u_1^\epsilon(t, \cdot)\|_{L^2(\Gamma_\epsilon)}^2 \quad (53)$$

The following estimate holds [see Lemma 5.1]

$$\epsilon \int_{\Gamma_\epsilon} |\psi(t, x, \frac{x}{\epsilon})|^2 d\sigma_\epsilon(x) \leq C_2 \|\psi(t)\|_B^2 \quad (54)$$

where  $C_2$  is a positive constant independent of  $\epsilon$  and  $B = C^1[\bar{\Omega}; C^1_{\#}(Y)]$ . Therefore, by combining Eqs. (52)-(54) and by using Lemma A.1, we deduce

$$\begin{aligned} & \int_{\Omega_\epsilon} \frac{\partial}{\partial t} |u_1^\epsilon|^2 dx + d_1 (2 - \epsilon^2 C_1) \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx \\ & \leq d_1 C_2 \|\psi(t)\|_B^2 + d_1 C_1 \int_{\Omega_\epsilon} |u_1^\epsilon|^2 dx \end{aligned} \quad (55)$$

since the third term on the left-hand side of (52) is non-negative. Integrating over  $[0, t]$  with  $t \in [0, T]$ , we get

$$\|u_1^\epsilon(t)\|_{L^2(\Omega_\epsilon)}^2 + d_1 (2 - \epsilon^2 C_1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx \leq C_3 + d_1 C_1 \|u_1^\epsilon\|_{L^2(0,T;L^2(\Omega_\epsilon))}^2 \quad (56)$$

where  $C_1$  and  $C_3$  are positive constants independent of  $\epsilon$  since, by (11),

$$u_1^\epsilon(0, x) = U_1 \leq \|\psi\|_{L^\infty(0,T;B)}.$$

Taking into account that the first term on the left-hand side of (56) is non-negative and the sequence  $u_1^\epsilon$  is bounded in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ , one has

$$d_1 (2 - \epsilon^2 C_1) \|\nabla_x u_1^\epsilon\|_{L^2(0,T;L^2(\Omega_\epsilon))}^2 \leq C_4 \quad (57)$$

Thus the boundedness of  $\nabla_x u_1^\epsilon(t, x)$  follows, provided that  $\epsilon$  is close to zero.

□

**Lemma 4.5.** *Let  $u_m^\epsilon(t, x)$  ( $1 < m < M$ ) be a classical solution of (12). Then*

$$\|u_m^\epsilon\|_{L^\infty(0,T;L^\infty(\Omega_\epsilon))} \leq K_m \quad (58)$$

*uniformly with respect to  $\epsilon$ , where*

$$K_m = 1 + \frac{\left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right]}{a_{m,m}} \quad (59)$$

*Proof.* We prove the Lemma directly by induction. By using Lemmas 4.1 and 4.2, it can be deduced that

$$\|u_1^\epsilon\|_{L^\infty(0,T;L^\infty(\Omega_\epsilon))} \leq K_1$$

where  $K_1$  is a positive constant independent of  $\epsilon$ . Let us suppose that

$$\|u_j^\epsilon\|_{L^\infty(0,T;L^\infty(\Omega_\epsilon))} \leq K_j$$

for  $1 \leq j \leq m-1$ . We shall show that

$$\|u_m^\epsilon\|_{L^\infty(0,T;L^\infty(\Omega_\epsilon))} \leq K_m \quad (60)$$

where  $K_m$  is given by (59). To this end, let us test the  $m$ th equation of (12) with the function

$$\phi_m \equiv p(u_m^\epsilon)^{(p-1)} \quad p \geq 2.$$

We stress that the functions  $\phi_m$  are strictly positive and continuously differentiable in  $[0, t] \times \overline{\Omega}$ , for all  $t > 0$ . Integrating, the divergence theorem yields

$$\begin{aligned} \int_0^t ds \int_{\Omega_\epsilon} \frac{\partial}{\partial s} (u_m^\epsilon)^p(s) dx &= -d_m p \int_0^t ds \int_{\Omega_\epsilon} \nabla_x u_m^\epsilon \cdot \nabla \left[ (u_m^\epsilon)^{(p-1)} \right] dx \\ &\quad - p \int_0^t ds \int_{\Omega_\epsilon} u_m^\epsilon \sum_{j=1}^M a_{m,j} u_j^\epsilon (u_m^\epsilon)^{(p-1)} dx \\ &\quad + \frac{p}{2} \int_0^t ds \int_{\Omega_\epsilon} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon (u_m^\epsilon)^{(p-1)} dx \end{aligned} \quad (61)$$

Hence

$$\begin{aligned} \|u_m^\epsilon\|_{L^p(\Omega_\epsilon)}^p + d_m p(p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla u_m^\epsilon|^2 (u_m^\epsilon)^{(p-2)} dx \\ = -p \int_0^t ds \int_{\Omega_\epsilon} u_m^\epsilon \sum_{j=1}^M a_{m,j} u_j^\epsilon (u_m^\epsilon)^{(p-1)} dx \\ + \frac{p}{2} \int_0^t ds \int_{\Omega_\epsilon} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon (u_m^\epsilon)^{(p-1)} dx \end{aligned} \quad (62)$$

Rearranging the terms of the summations, we obtain

$$\begin{aligned}
& \|u_m^\epsilon\|_{L^p(\Omega_\epsilon)}^p + d_m p(p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla u_m^\epsilon|^2 (u_m^\epsilon)^{(p-2)} dx \\
&= \int_0^t ds \int_{\Omega_\epsilon} \left[ \frac{1}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon - a_{m,m} |u_m^\epsilon|^2 \right] p (u_m^\epsilon)^{(p-1)} dx \\
&- \int_0^t ds \int_{\Omega_\epsilon} \left[ \sum_{j=1}^{m-1} a_{m,j} u_m^\epsilon u_j^\epsilon + \sum_{j=m+1}^M a_{m,j} u_m^\epsilon u_j^\epsilon \right] p (u_m^\epsilon)^{(p-1)} dx
\end{aligned} \tag{63}$$

By using the induction hypothesis, Eq. (63) becomes

$$\begin{aligned}
& \|u_m^\epsilon\|_{L^p(\Omega_\epsilon)}^p + d_m p(p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla u_m^\epsilon|^2 (u_m^\epsilon)^{(p-2)} dx \\
&\leq \int_0^t ds \int_{\Omega_\epsilon} \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} - a_{m,m} (u_m^\epsilon)^2 \right] p (u_m^\epsilon)^{(p-1)} dx \\
&- \int_0^t ds \int_{\Omega_\epsilon} \left[ \sum_{j=1}^{m-1} a_{m,j} u_m^\epsilon u_j^\epsilon + \sum_{j=m+1}^M a_{m,j} u_m^\epsilon u_j^\epsilon \right] p (u_m^\epsilon)^{(p-1)} dx =: I_1 - I_2
\end{aligned} \tag{64}$$

From the nonnegativity of solutions,  $I_2 \geq 0$ . In order to estimate  $I_1$ , it is now convenient to use Young's inequality in the following form [12]:

$$ab \leq \eta a^{p'} + \eta^{1-p} b^p \quad \forall a \geq 0, b \geq 0 \tag{65}$$

with  $p' = \frac{p}{p-1}$ . We find

$$\begin{aligned}
I &=: \int_0^t ds \int_{\Omega_\epsilon} \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right] p (u_m^\epsilon)^{(p-1)} dx \\
&\leq \int_0^t ds \int_{\Omega_\epsilon} p^p \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right]^p \eta^{1-p} dx + \int_0^t ds \int_{\Omega_\epsilon} \eta \left[ (u_m^\epsilon)^{(p-1)} \right]^{\frac{p}{p-1}} dx \\
&\leq p^{p-1} \left( \frac{p}{p-1} \right)^{1-p} \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right]^p \eta^{1-p} |\Omega_\epsilon| t \\
&+ \eta \int_0^t ds \int_{\Omega_\epsilon} (u_m^\epsilon)^p dx
\end{aligned} \tag{66}$$

By using the estimate (66),  $I_1$  reads:

$$\begin{aligned}
I_1 &\leq p^{p-1} \left( \frac{p}{p-1} \right)^{1-p} \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right]^p \eta^{1-p} |\Omega_\epsilon| t \\
&\quad + \eta \int_0^t ds \int_{\Omega_\epsilon} (u_m^\epsilon)^p dx - p a_{m,m} \int_0^t ds \int_{\Omega_\epsilon} (u_m^\epsilon)^{(p+1)} dx \\
&\leq p^{p-1} \left( \frac{p}{p-1} \right)^{1-p} \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right]^p \eta^{1-p} |\Omega_\epsilon| t \\
&\quad + \eta \int_0^t ds \int_{\Omega_\epsilon} (u_m^\epsilon)^p dx + p a_{m,m} \int_0^t ds \int_{\Omega_\epsilon} \left[ 1 - (u_m^\epsilon)^p \right] dx
\end{aligned} \tag{67}$$

Taking  $\eta = p a_{m,m}$  yields

$$I_1 \leq \left[ \left( \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right)^p a_{m,m}^{1-p} \right] |\Omega_\epsilon| T + p a_{m,m} |\Omega_\epsilon| T \tag{68}$$

Finally from (64) and (68) it follows that

$$\begin{aligned}
&\|u_m^\epsilon\|_{L^p(\Omega_\epsilon)}^p + d_m p (p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla u_m^\epsilon|^2 (u_m^\epsilon)^{(p-2)} dx \\
&\leq \left[ \left( \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right)^p a_{m,m}^{1-p} + p a_{m,m} \right] |\Omega_\epsilon| T
\end{aligned} \tag{69}$$

Since the second term on the left-hand side of (69) is non-negative, we conclude that

$$\begin{aligned}
&\sup_{t \in [0, T]} \lim_{p \rightarrow \infty} \left[ \int_{\Omega_\epsilon} (u_m^\epsilon(t, x))^p dx \right]^{1/p} \\
&\leq \left[ \sum_{j=1}^{m-1} a_{j,m-j} K_j K_{m-j} \right] a_{m,m}^{-1} + 1
\end{aligned} \tag{70}$$

which yields (60). □

**Lemma 4.6.** *The sequence  $\nabla_x u_m^\epsilon$  ( $1 < m < M$ ) is bounded in  $L^2([0, T] \times \Omega_\epsilon)$ , uniformly in  $\epsilon$ .*

*Proof.* Let us multiply the first equation in (12) by the function  $u_m^\epsilon(t, x)$ . Integrating, the divergence theorem yields

$$\begin{aligned}
\frac{1}{2} \int_{\Omega_\epsilon} \frac{\partial}{\partial t} |u_m^\epsilon|^2 dx + d_m \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon|^2 dx + \int_{\Omega_\epsilon} |u_m^\epsilon|^2 \sum_{j=1}^M a_{m,j} u_j^\epsilon dx \\
= \int_{\Omega_\epsilon} f^\epsilon u_m^\epsilon dx
\end{aligned} \tag{71}$$

By Hölder's inequality, the right-hand side of Eq. (71) can be rewritten as follows

$$\int_{\Omega_\epsilon} f^\epsilon(t, x) u_m^\epsilon(t, x) dx \leq \|f^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)} \cdot \|u_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)} \quad (72)$$

Thus

$$\begin{aligned} \|f^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)} &=: \left[ \int_{\Omega_\epsilon} \left| \frac{1}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon \right|^2 dx \right]^{1/2} \\ &\leq \frac{1}{2} \sum_{j=1}^{m-1} \left[ \int_{\Omega_\epsilon} a_{j,m-j}^2 |u_j^\epsilon|^2 |u_{m-j}^\epsilon|^2 dx \right]^{1/2} \\ &\leq \frac{1}{2} \sum_{j=1}^{m-1} a_{j,m-j} \int_{\Omega_\epsilon} K_j^2 K_{m-j}^2 dx \leq C_3 \end{aligned} \quad (73)$$

due to the boundedness of  $u_j^\epsilon(t, x)$  ( $1 \leq j \leq m-1$ ) in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ , where  $C_3$  is a constant which does not depend on  $\epsilon$ . Therefore, by combining (72) and (73), Eq. (71) reads

$$\frac{1}{2} \int_{\Omega_\epsilon} \frac{\partial}{\partial t} |u_m^\epsilon|^2 dx + d_m \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon|^2 dx \leq C_3 \|u_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)} \quad (74)$$

since the third term on the left-hand side of (71) is non-negative. Dividing by  $\|u_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}$  and integrating over  $[0, t]$  with  $t \in [0, T]$ , we deduce

$$\int_0^t ds \frac{d}{ds} \|u_m^\epsilon(s, \cdot)\|_{L^2(\Omega_\epsilon)} + d_m C_4 \int_0^t ds \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon|^2 dx \leq C_3 T \quad (75)$$

exploiting the boundedness of  $u_m^\epsilon(t, x)$  in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ . Hence

$$\|u_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)} + d_m C_4 \int_0^t ds \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon|^2 dx \leq C_5 \quad (76)$$

where  $C_4$  and  $C_5$  are positive constants independent of  $\epsilon$ . Then, the boundedness of  $\nabla_x u_m^\epsilon(t, x)$  in  $L^2([0, T] \times \Omega_\epsilon)$ , uniformly in  $\epsilon$ , follows immediately from (76).

□

**Lemma 4.7.** *Let  $u_M^\epsilon(t, x)$  be a classical solution of (13). Then*

$$\|u_M^\epsilon\|_{L^\infty(0, T; L^\infty(\Omega_\epsilon))} \leq K_M \quad (77)$$

*uniformly with respect to  $\epsilon$ , where*

$$K_M = e^T \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \quad (78)$$

with the constants  $K_j$  ( $1 < j < M$ ) given by (59).

*Proof.* Let us test the first equation of (13) with the function

$$\phi_M \equiv p (u_M^\epsilon)^{(p-1)} \quad p \geq 2.$$

The function  $\phi_M$  is strictly positive and continuously differentiable in  $[0, t] \times \bar{\Omega}$ , for all  $t > 0$ . Integrating, the divergence theorem yields

$$\begin{aligned} \int_0^t ds \int_{\Omega_\epsilon} \frac{\partial}{\partial s} (u_M^\epsilon)^p(s) dx &= -d_M p \int_0^t ds \int_{\Omega_\epsilon} \nabla_x u_M^\epsilon \cdot \nabla \left[ (u_M^\epsilon)^{(p-1)} \right] dx \\ &+ \frac{p}{2} \int_0^t ds \int_{\Omega_\epsilon} \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} u_j^\epsilon u_k^\epsilon (u_M^\epsilon)^{(p-1)} dx \end{aligned} \quad (79)$$

Hence

$$\begin{aligned} \int_{\Omega_\epsilon} (u_M^\epsilon)^p(t) dx + d_M p(p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla_x u_M^\epsilon|^2 (u_M^\epsilon)^{(p-2)} dx \\ = \frac{p}{2} \int_0^t ds \int_{\Omega_\epsilon} \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} u_j^\epsilon u_k^\epsilon (u_M^\epsilon)^{(p-1)} dx \end{aligned} \quad (80)$$

Taking into account the boundedness of  $u_j^\epsilon$  ( $1 \leq j < M$ ) in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$  we get

$$\begin{aligned} \int_{\Omega_\epsilon} (u_M^\epsilon)^p(t) dx + d_M p(p-1) \int_0^t ds \int_{\Omega_\epsilon} |\nabla_x u_M^\epsilon|^2 (u_M^\epsilon)^{(p-2)} dx \\ \leq p \int_0^t ds \int_{\Omega_\epsilon} \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right] (u_M^\epsilon)^{(p-1)} dx =: I_3 \end{aligned} \quad (81)$$

In order to estimate  $I_3$ , we use the Young inequality in the form (65):

$$\begin{aligned}
I_3 &\leq \int_0^t ds \int_{\Omega_\epsilon} p^p \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right]^p \eta^{1-p} dx + \int_0^t ds \int_{\Omega_\epsilon} \eta (u_M^\epsilon)^p dx \\
&\leq p^{p-1} \left( \frac{p}{p-1} \right)^{1-p} \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right]^p \eta^{1-p} |\Omega_\epsilon| t + \eta \int_0^t ds \int_{\Omega_\epsilon} (u_M^\epsilon)^p dx
\end{aligned} \tag{82}$$

Taking  $\eta = p$  yields

$$I_3 \leq \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right]^p |\Omega_\epsilon| t + p \int_0^t ds \int_{\Omega_\epsilon} (u_M^\epsilon)^p dx \tag{83}$$

Finally from (81) and (83) it follows that

$$\|u_M^\epsilon(t)\|_{L^p(\Omega_\epsilon)}^p \leq \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right]^p |\Omega_\epsilon| T + \int_0^t ds p \|u_M^\epsilon(s)\|_{L^p(\Omega_\epsilon)}^p \tag{84}$$

The Gronwall Lemma applied to (84) leads to the estimate

$$\|u_M^\epsilon(t)\|_{L^p(\Omega_\epsilon)}^p \leq \left[ \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k \right]^p |\Omega_\epsilon| T e^{pt} \tag{85}$$

Hence

$$\sup_{t \in [0, T]} \lim_{p \rightarrow \infty} \left[ \int_{\Omega_\epsilon} (u_M^\epsilon(t, x))^p dx \right]^{1/p} \leq \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} K_j K_k e^T \tag{86}$$

□

**Lemma 4.8.** *The sequence  $\nabla_x u_M^\epsilon$  is bounded in  $L^2([0, T] \times \Omega_\epsilon)$ , uniformly in  $\epsilon$ .*

The proof of Lemma 4.8 is achieved by applying exactly the same arguments considered in the proof of Lemma 4.6.

**Lemma 4.9.** *The sequence  $\partial_t u_j^\epsilon$  ( $1 \leq j \leq M$ ) is bounded in  $L^2([0, T] \times \Omega_\epsilon)$ , uniformly in  $\epsilon$ .*

*Proof.* Case  $j = 1$ : let us multiply the first equation in (10) by the function  $\partial_t u_1^\epsilon(t, x)$ .

Integrating, the divergence theorem yields

$$\begin{aligned} \int_{\Omega_\epsilon} \left| \frac{\partial u_1^\epsilon(t, x)}{\partial t} \right|^2 dx + \frac{d_1}{2} \int_{\Omega_\epsilon} \frac{\partial}{\partial t} (|\nabla_x u_1^\epsilon(t, x)|^2) dx + \int_{\Omega_\epsilon} \left( \sum_{j=1}^M a_{1,j} u_1^\epsilon u_j^\epsilon \right) \frac{\partial u_1^\epsilon}{\partial t} dx \\ = \epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) \frac{\partial u_1^\epsilon}{\partial t} d\sigma_\epsilon(x) \end{aligned} \quad (87)$$

Define:  $w_1^\epsilon(t, x) := \sum_{j=1}^M a_{1,j} u_1^\epsilon u_j^\epsilon$ . Then, by using Hölder's and Young's inequalities, Eq. (87) can be rewritten as follows

$$\begin{aligned} \int_{\Omega_\epsilon} \left| \frac{\partial u_1^\epsilon}{\partial t} \right|^2 dx + d_1 \int_{\Omega_\epsilon} \frac{\partial}{\partial t} (|\nabla_x u_1^\epsilon|^2) dx \leq \|w_1^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2 \\ + 2\epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) \frac{\partial u_1^\epsilon}{\partial t} d\sigma_\epsilon(x) \end{aligned} \quad (88)$$

Exploiting the boundedness of  $u_j^\epsilon(t, x)$  ( $1 \leq j \leq M$ ) in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ , one get the estimate

$$\|w_1^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2 := \int_{\Omega_\epsilon} \left| \sum_{j=1}^M a_{1,j} u_1^\epsilon u_j^\epsilon \right|^2 dx \leq \sum_{j=1}^M a_{1,j}^2 \int_{\Omega_\epsilon} K_1^2 K_j^2 dx \leq C_1 \quad (89)$$

where  $C_1$  is a positive constant independent of  $\epsilon$ . Hence, (88) becomes

$$\int_{\Omega_\epsilon} \left| \frac{\partial u_1^\epsilon}{\partial t} \right|^2 dx + d_1 \frac{\partial}{\partial t} \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx \leq C_1 + 2\epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) \frac{\partial u_1^\epsilon}{\partial t} d\sigma_\epsilon(x) \quad (90)$$

Integrating over  $[0, t]$  with  $t \in [0, T]$ , we obtain

$$\begin{aligned} \int_0^t ds \int_{\Omega_\epsilon} \left| \frac{\partial u_1^\epsilon}{\partial s} \right|^2 dx + d_1 \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon(t, x)|^2 dx \leq C_1 T \\ + 2\epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) u_1^\epsilon(t, x) d\sigma_\epsilon(x) \\ - 2\epsilon d_1 \int_0^t ds \int_{\Gamma_\epsilon} \frac{\partial}{\partial s} \psi \left( s, x, \frac{x}{\epsilon} \right) u_1^\epsilon(s, x) d\sigma_\epsilon(x) \end{aligned} \quad (91)$$

since  $\psi \left( t = 0, x, \frac{x}{\epsilon} \right) \equiv 0$ . Now we estimate the last two terms on the right-hand side of (91). Taking into account the inequalities (53)-(54) and Lemma A.1, we find

$$\begin{aligned}
2 \epsilon d_1 \int_{\Gamma_\epsilon} \psi \left( t, x, \frac{x}{\epsilon} \right) u_1^\epsilon(t, x) d\sigma_\epsilon(x) &\leq \epsilon d_1 \|\psi(t, \cdot, \frac{\cdot}{\epsilon})\|_{L^2(\Gamma_\epsilon)}^2 + \epsilon d_1 \|u_1^\epsilon(t, \cdot)\|_{L^2(\Gamma_\epsilon)}^2 \\
&\leq d_1 C_2 \|\psi(t)\|_B^2 + C_3 d_1 \int_{\Omega_\epsilon} |u_1^\epsilon|^2 dx + C_3 d_1 \epsilon^2 \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx \\
&\leq C_4 + \epsilon^2 d_1 C_3 \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx
\end{aligned} \tag{92}$$

where  $C_4 \geq 0$  is a constant independent of  $\epsilon$  since  $\psi \in L^\infty(0, T; B)$  and  $u_1^\epsilon$  is bounded in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ . Analogously, we get the following inequality

$$\begin{aligned}
2 \epsilon d_1 \int_0^t ds \int_{\Gamma_\epsilon} \frac{\partial}{\partial s} \psi \left( s, x, \frac{x}{\epsilon} \right) u_1^\epsilon(s, x) d\sigma_\epsilon(x) \\
\leq \epsilon d_1 \int_0^t ds \left\| \frac{\partial \psi(s)}{\partial s} \right\|_{L^2(\Gamma_\epsilon)}^2 + \epsilon d_1 \int_0^t ds \|u_1^\epsilon(s)\|_{L^2(\Gamma_\epsilon)}^2 \\
\leq C_5 d_1 T + C_6 d_1 \int_0^t ds \|u_1^\epsilon(s)\|_{L^2(\Omega_\epsilon)}^2 + \epsilon^2 C_6 d_1 \int_0^t ds \|\nabla_x u_1^\epsilon(s)\|_{L^2(\Omega_\epsilon)}^2 \leq C_7
\end{aligned} \tag{93}$$

where  $C_7 \geq 0$  is a constant independent of  $\epsilon$ , since  $u_1^\epsilon$  is bounded in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ ,  $\nabla_x u_1^\epsilon$  is bounded in  $L^2(0, T; L^2(\Omega_\epsilon))$  and

$$\epsilon \int_{\Gamma_\epsilon} \left| \partial_t \psi \left( t, x, \frac{x}{\epsilon} \right) \right|^2 d\sigma_\epsilon(x) \leq \tilde{C} \|\partial_t \psi(t)\|_B^2 \leq C_5$$

with  $\tilde{C}$  and  $C_5$  independent of  $\epsilon$ . Combining the estimates (92) and (93) with (91) we obtain that

$$\int_0^t ds \int_{\Omega_\epsilon} \left| \frac{\partial u_1^\epsilon}{\partial s} \right|^2 dx + d_1 (1 - \epsilon^2 C_3) \int_{\Omega_\epsilon} |\nabla_x u_1^\epsilon|^2 dx \leq C_1 T + C_4 + C_7 \tag{94}$$

For a sequence  $\epsilon$  of positive numbers going to zero:  $(1 - \epsilon^2 C_3) \geq 0$ . Then, the second term on the left-hand side of (94) is non-negative, and one has

$$\|\partial_t u_1^\epsilon\|_{L^2(0, T; L^2(\Omega_\epsilon))}^2 \leq C \tag{95}$$

where  $C \geq 0$  is a constant independent of  $\epsilon$ .

Case  $1 < j < M$ : let us multiply the first equation in (12) by the function  $\partial_t u_m^\epsilon(t, x)$ . Integrating, the divergence theorem yields

$$\begin{aligned}
& \int_{\Omega_\epsilon} \left| \frac{\partial u_m^\epsilon(t, x)}{\partial t} \right|^2 dx + \frac{d_m}{2} \int_{\Omega_\epsilon} \frac{\partial}{\partial t} (|\nabla_x u_m^\epsilon(t, x)|^2) dx + \int_{\Omega_\epsilon} \left( \sum_{j=1}^M a_{m,j} u_m^\epsilon u_j^\epsilon \right) \frac{\partial u_m^\epsilon}{\partial t} dx \\
&= \frac{1}{2} \int_{\Omega_\epsilon} \left( \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon \right) \frac{\partial u_m^\epsilon}{\partial t} dx
\end{aligned} \tag{96}$$

Define

$$w_m^\epsilon(t, x) := \sum_{j=1}^M a_{m,j} u_m^\epsilon u_j^\epsilon$$

and

$$s_m^\epsilon(t, x) := \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon.$$

Then, by using Hölder's and Young's inequalities, Eq. (96) can be rewritten as follows

$$\begin{aligned}
& \int_{\Omega_\epsilon} \left| \frac{\partial u_m^\epsilon}{\partial t} \right|^2 dx + 2 d_m \int_{\Omega_\epsilon} \frac{\partial}{\partial t} (|\nabla_x u_m^\epsilon|^2) dx \leq 2 \|w_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2 \\
& \quad + \|s_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2
\end{aligned} \tag{97}$$

Exploiting the boundedness of  $u_j^\epsilon(t, x)$  ( $1 \leq j \leq M$ ) in  $L^\infty(0, T; L^\infty(\Omega_\epsilon))$ , one get the estimate

$$\|w_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2 := \int_{\Omega_\epsilon} \left| \sum_{j=1}^M a_{m,j} u_m^\epsilon u_j^\epsilon \right|^2 dx \leq \sum_{j=1}^M a_{m,j}^2 \int_{\Omega_\epsilon} K_m^2 K_j^2 dx \leq C_1 \tag{98}$$

where  $C_1$  is a positive constant independent of  $\epsilon$ . Similarly, we have

$$\|s_m^\epsilon(t, \cdot)\|_{L^2(\Omega_\epsilon)}^2 =: \int_{\Omega_\epsilon} \left| \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon \right|^2 dx \leq \sum_{j=1}^{m-1} a_{j,m-j}^2 \int_{\Omega_\epsilon} K_j^2 K_{m-j}^2 dx \leq C_2 \tag{99}$$

where  $C_2$  is a positive constant independent of  $\epsilon$ . Hence, (97) becomes

$$\int_{\Omega_\epsilon} \left| \frac{\partial u_m^\epsilon}{\partial t} \right|^2 dx + 2 d_m \frac{\partial}{\partial t} \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon|^2 dx \leq 2 C_1 + C_2 \tag{100}$$

Integrating over  $[0, t]$  with  $t \in [0, T]$ , we obtain

$$\int_0^t ds \int_{\Omega_\epsilon} \left| \frac{\partial u_m^\epsilon}{\partial s} \right|^2 dx + 2 d_m \int_{\Omega_\epsilon} |\nabla_x u_m^\epsilon(t, x)|^2 dx \leq C_3 T \quad (101)$$

Since the second term on the left-hand side of (101) is non-negative, we conclude that

$$\|\partial_t u_m^\epsilon\|_{L^2(0, T; L^2(\Omega_\epsilon))}^2 \leq C \quad (102)$$

where  $C \geq 0$  is a constant independent of  $\epsilon$ .

By applying exactly the same arguments considered in proving the boundedness of  $\partial_t u_j^\epsilon(t, x)$  ( $1 < j < M$ ) in  $L^2(0, T; L^2(\Omega_\epsilon))$ , one can derive also the following estimate

$$\|\partial_t u_M^\epsilon\|_{L^2(0, T; L^2(\Omega_\epsilon))}^2 \leq C \quad (103)$$

where  $C \geq 0$  is a constant independent of  $\epsilon$ .

□

## 5 Homogenization of the Smoluchowski equation

### 5.1 Two-scale convergence method

Let us introduce some definitions and results on two-scale convergence from [3], [4], [40], slightly modified to allow for homogenization with a parameter (the time  $t$ ) [18], [31], [38].

**Definition 5.1.** *A sequence of functions  $v^\epsilon$  in  $L^2([0, T] \times \Omega)$  two-scale converges to  $v_0 \in L^2([0, T] \times \Omega \times Y)$  if*

$$\lim_{\epsilon \rightarrow 0} \int_0^T \int_{\Omega} v^\epsilon(t, x) \phi\left(t, x, \frac{x}{\epsilon}\right) dt dx = \int_0^T \int_{\Omega} \int_Y v_0(t, x, y) \phi(t, x, y) dt dx dy \quad (104)$$

for all  $\phi \in C^1([0, T] \times \bar{\Omega}; C^\infty_\#(Y))$ .

The notion of 'two-scale convergence' makes sense because of the next compactness theorem.

**Theorem 5.1.** *If  $v^\epsilon$  is a bounded sequence in  $L^2([0, T] \times \Omega)$ , then there exists a function  $v_0(t, x, y)$  in  $L^2([0, T] \times \Omega \times Y)$  such that, up to a subsequence,  $v^\epsilon$  two-scale converges to  $v_0$ .*

The following theorem is useful in obtaining the limit of the product of two two-scale convergent sequences.

**Theorem 5.2.** *Let  $v^\epsilon$  be a sequence of functions in  $L^2([0, T] \times \Omega)$  which two-scale converges to a limit  $v_0 \in L^2([0, T] \times \Omega \times Y)$ . Suppose furthermore that*

$$\lim_{\epsilon \rightarrow 0} \int_0^T \int_{\Omega} |v^\epsilon(t, x)|^2 dt dx = \int_0^T \int_{\Omega} \int_Y |v_0(t, x, y)|^2 dt dx dy \quad (105)$$

*Then, for any sequence  $w^\epsilon$  in  $L^2([0, T] \times \Omega)$  that two-scale converges to a limit  $w_0 \in L^2([0, T] \times \Omega \times Y)$ , we have*

$$\begin{aligned} \lim_{\epsilon \rightarrow 0} \int_0^T \int_{\Omega} v^\epsilon(t, x) w^\epsilon(t, x) \phi\left(t, x, \frac{x}{\epsilon}\right) dt dx \\ = \int_0^T \int_{\Omega} \int_Y v_0(t, x, y) w_0(t, x, y) \phi(t, x, y) dt dx dy \end{aligned} \quad (106)$$

for all  $\phi \in C^1([0, T] \times \bar{\Omega}; C^\infty_\#(Y))$ .

The next theorems yield a characterization of the two-scale limit of the gradients of bounded sequences  $v^\epsilon$ . This result is crucial for applications to homogenization problems.

We identify  $H^1(\Omega) = W^{1,2}(\Omega)$ , where the Sobolev space  $W^{1,p}(\Omega)$  is defined by

$$W^{1,p}(\Omega) = \left\{ u \mid u \in L^p(\Omega), \frac{\partial u}{\partial x_i} \in L^p(\Omega), i = 1, \dots, N \right\}$$

and we denote by  $H^1_\#(Y)$  the closure of  $C^\infty_\#(Y)$  for the  $H^1$ -norm.

**Theorem 5.3.** *Let  $v^\epsilon$  be a bounded sequence in  $L^2(0, T; H^1(\Omega))$  that converges weakly to a limit  $v(t, x)$  in  $L^2(0, T; H^1(\Omega))$ . Then,  $v^\epsilon$  two-scale converges to  $v(t, x)$ , and there exists a function  $v_1(t, x, y)$  in  $L^2([0, T] \times \Omega; H^1_\#(Y)/\mathbb{R})$  such that, up to a subsequence,  $\nabla v^\epsilon$  two-scale converges to  $\nabla_x v(t, x) + \nabla_y v_1(t, x, y)$ .*

**Theorem 5.4.** *Let  $v^\epsilon$  and  $\epsilon \nabla v^\epsilon$  be two bounded sequences in  $L^2([0, T] \times \Omega)$ . Then, there exists a function  $v_1(t, x, y)$  in  $L^2([0, T] \times \Omega; H^1_\#(Y)/\mathbb{R})$  such that, up to a subsequence,  $v^\epsilon$  and  $\epsilon \nabla v^\epsilon$  two-scale converge to  $v_1(t, x, y)$  and  $\nabla_y v_1(t, x, y)$ , respectively.*

The main result of two-scale convergence can be generalized to the case of sequences defined in  $L^2([0, T] \times \Gamma_\epsilon)$ .

**Theorem 5.5.** *Let  $v^\epsilon$  be a sequence in  $L^2([0, T] \times \Gamma_\epsilon)$  such that*

$$\epsilon \int_0^T \int_{\Gamma_\epsilon} |v^\epsilon(t, x)|^2 dt d\sigma_\epsilon(x) \leq C \quad (107)$$

where  $C$  is a positive constant, independent of  $\epsilon$ . There exist a subsequence (still denoted by  $\epsilon$ ) and a two-scale limit  $v_0(t, x, y) \in L^2([0, T] \times \Omega; L^2(\Gamma))$  such that  $v^\epsilon(t, x)$  two-scale converges to  $v_0(t, x, y)$  in the sense that

$$\lim_{\epsilon \rightarrow 0} \epsilon \int_0^T \int_{\Gamma_\epsilon} v^\epsilon(t, x) \phi\left(t, x, \frac{x}{\epsilon}\right) dt d\sigma_\epsilon(x) = \int_0^T \int_\Omega \int_\Gamma v_0(t, x, y) \phi(t, x, y) dt dx d\sigma(y) \quad (108)$$

for any function  $\phi \in C^1([0, T] \times \bar{\Omega}; C^\infty_\#(Y))$ .

The proof of Theorem 5.5 is very similar to the usual two-scale convergence theorem [3]. It relies on the following lemma [4]:

**Lemma 5.1.** *Let  $B = C[\bar{\Omega}; C^\infty_\#(Y)]$  be the space of continuous functions  $\phi(x, y)$  on  $\bar{\Omega} \times Y$  which are  $Y$ -periodic in  $y$ . Then,  $B$  is a separable Banach space which is dense in  $L^2(\Omega; L^2(\Gamma))$ , and such that any function  $\phi(x, y) \in B$  satisfies*

$$\epsilon \int_{\Gamma_\epsilon} \left| \phi\left(x, \frac{x}{\epsilon}\right) \right|^2 d\sigma_\epsilon(x) \leq C \|\phi\|_B^2, \quad (109)$$

and

$$\lim_{\epsilon \rightarrow 0} \epsilon \int_{\Gamma_\epsilon} \left| \phi\left(x, \frac{x}{\epsilon}\right) \right|^2 d\sigma_\epsilon(x) = \int_\Omega \int_\Gamma |\phi(x, y)|^2 dx d\sigma(y). \quad (110)$$

## 5.2 Presentation of the main results

**Theorem 5.6.** *Let  $u_m^\epsilon(t, x)$  ( $1 \leq m \leq M$ ) be a family of classical solutions to problems (10)-(13). The sequences  $\widetilde{u}_m^\epsilon$  and  $\widetilde{\nabla}_x u_m^\epsilon$  ( $1 \leq m \leq M$ ) two-scale converge to:  $[\chi(y) u_m(t, x)]$  and  $[\chi(y)(\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y))]$  ( $1 \leq m \leq M$ ), respectively, where tilde denotes the extension by zero outside  $\Omega_\epsilon$  and  $\chi(y)$  represents the characteristic function of  $Y^*$ . The limiting functions  $(u_m(t, x), u_m^1(t, x, y))$  ( $1 \leq m \leq M$ )*

are the unique solutions in  $L^2(0, T; H^1(\Omega)) \times L^2([0, T] \times \Omega; H_{\#}^1(Y)/\mathbb{R})$  of the following two-scale homogenized systems:

If  $m = 1$  we have:

$$\left\{ \begin{array}{l} \theta \frac{\partial u_1}{\partial t}(t, x) - \operatorname{div}_x \left[ d_1 A \nabla_x u_1(t, x) \right] + \theta u_1(t, x) \sum_{j=1}^M a_{1,j} u_j(t, x) \\ = d_1 \int_{\Gamma} \psi(t, x, y) d\sigma(y) \\ [A \nabla_x u_1(t, x)] \cdot n = 0 \\ u_1(0, x) = U_1 \end{array} \right. \begin{array}{l} \text{in } [0, T] \times \Omega \\ \\ \text{on } [0, T] \times \partial\Omega \\ \text{in } \Omega \end{array} \quad (111)$$

if  $1 < m < M$  we have

$$\left\{ \begin{array}{l} \theta \frac{\partial u_m}{\partial t}(t, x) - \operatorname{div}_x \left[ d_m A \nabla_x u_m(t, x) \right] + \theta u_m(t, x) \sum_{j=1}^M a_{m,j} u_j(t, x) \\ = \frac{\theta}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j(t, x) u_{m-j}(t, x) \\ [A \nabla_x u_m(t, x)] \cdot n = 0 \\ u_m(0, x) = 0 \end{array} \right. \begin{array}{l} \text{in } [0, T] \times \Omega \\ \\ \text{on } [0, T] \times \partial\Omega \\ \text{in } \Omega \end{array} \quad (112)$$

if  $m = M$  we have:

$$\left\{ \begin{array}{l} \theta \frac{\partial u_M}{\partial t}(t, x) - \operatorname{div}_x \left[ d_M A \nabla_x u_M(t, x) \right] \\ = \frac{\theta}{2} \sum_{\substack{j+k \geq M \\ k < M \\ j < M}} a_{j,k} u_j(t, x) u_k(t, x) \\ [A \nabla_x u_M(t, x)] \cdot n = 0 \\ u_M(0, x) = 0 \end{array} \right. \begin{array}{l} \text{in } [0, T] \times \Omega \\ \\ \text{on } [0, T] \times \partial\Omega \\ \text{in } \Omega \end{array} \quad (113)$$

where

$$u_m^1(t, x, y) = \sum_{i=1}^N w_i(y) \frac{\partial u_m}{\partial x_i}(t, x) \quad (1 \leq m \leq M),$$

$$\theta = \int_Y \chi(y) dy = |Y^*|$$

is the volume fraction of material, and  $A$  is a matrix with constant coefficients defined by

$$A_{ij} = \int_{Y^*} (\nabla_y w_i + \hat{e}_i) \cdot (\nabla_y w_j + \hat{e}_j) dy$$

with  $\hat{e}_i$  being the  $i$ -th unit vector in  $\mathbb{R}^N$ , and  $(w_i)_{1 \leq i \leq N}$  the family of solutions of the cell problem

$$\begin{cases} -\operatorname{div}_y[\nabla_y w_i + \hat{e}_i] = 0 & \text{in } Y^* \\ (\nabla_y w_i + \hat{e}_i) \cdot n = 0 & \text{on } \Gamma \\ y \rightarrow w_i(y) \quad Y\text{-periodic} \end{cases} \quad (114)$$

*Proof.* In view of Lemmas 4.1-4.2 and 4.4-4.8 the sequences  $\widetilde{u_m^\epsilon}$  and  $\widetilde{\nabla_x u_m^\epsilon}$  ( $1 \leq m \leq M$ ) are bounded in  $L^2([0, T] \times \Omega)$ , and by application of Theorem 5.1 and Theorem 5.3 they two-scale converge, up to a subsequence, to:  $[\chi(y) u_m(t, x)]$  and  $[\chi(y)(\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y))]$  ( $1 \leq m \leq M$ ). Similarly, in view of Lemma 4.9, it is possible to prove that the sequence  $\left(\frac{\partial \widetilde{u_m^\epsilon}}{\partial t}\right)$  ( $1 \leq m \leq M$ ) two-scale converges to:  $\left[\chi(y) \frac{\partial u_m}{\partial t}(t, x)\right]$  ( $1 \leq m \leq M$ ).

We can now find the homogenized equations satisfied by  $u_m(t, x)$  and  $u_m^1(t, x, y)$  ( $1 \leq m \leq M$ ).

In the case  $m = 1$ , let us multiply the first equation of (10) by the test function

$$\phi_\epsilon \equiv \phi(t, x) + \epsilon \phi_1\left(t, x, \frac{x}{\epsilon}\right)$$

where  $\phi \in C^1([0, T] \times \overline{\Omega})$  and  $\phi_1 \in C^1([0, T] \times \overline{\Omega}; C_\#^\infty(Y))$ . Integrating, the divergence theorem yields

$$\begin{aligned}
& \int_0^T \int_{\Omega_\epsilon} \frac{\partial u_1^\epsilon}{\partial t} \phi_\epsilon(t, x, \frac{x}{\epsilon}) dt dx + d_1 \int_0^T \int_{\Omega_\epsilon} \nabla_x u_1^\epsilon \cdot \nabla \phi_\epsilon dt dx \\
& + \int_0^T \int_{\Omega_\epsilon} u_1^\epsilon \sum_{j=1}^M a_{1,j} u_j^\epsilon \phi_\epsilon dt dx = \epsilon d_1 \int_0^T \int_{\Gamma_\epsilon} \psi\left(t, x, \frac{x}{\epsilon}\right) \phi_\epsilon dt d\sigma_\epsilon(x)
\end{aligned} \tag{115}$$

Passing to the two-scale limit we get

$$\begin{aligned}
& \int_0^T \int_{\Omega} \int_{Y^*} \frac{\partial u_1}{\partial t}(t, x) \phi(t, x) dt dx dy \\
& + d_1 \int_0^T \int_{\Omega} \int_{Y^*} [\nabla_x u_1(t, x) + \nabla_y u_1^1(t, x, y)] \cdot [\nabla_x \phi(t, x) + \nabla_y \phi_1(t, x, y)] dt dx dy \\
& + \int_0^T \int_{\Omega} \int_{Y^*} u_1(t, x) \sum_{j=1}^M a_{1,j} u_j(t, x) \phi(t, x) dt dx dy \\
& = d_1 \int_0^T \int_{\Omega} \int_{\Gamma} \psi(t, x, y) \phi(t, x) dt dx d\sigma(y).
\end{aligned} \tag{116}$$

The last term on the left-hand side of (116) has been obtained by using Theorem 5.2, while the term on the right-hand side has been attained by application of Theorem 5.5. An integration by parts shows that (116) is a variational formulation associated to the following homogenized system:

$$-div_y[d_1(\nabla_x u_1(t, x) + \nabla_y u_1^1(t, x, y))] = 0 \quad \text{in } [0, T] \times \Omega \times Y^* \tag{117}$$

$$[\nabla_x u_1(t, x) + \nabla_y u_1^1(t, x, y)] \cdot n = 0 \quad \text{on } [0, T] \times \Omega \times \Gamma \tag{118}$$

$$\begin{aligned}
& \theta \frac{\partial u_1}{\partial t}(t, x) - div_x \left[ d_1 \int_{Y^*} (\nabla_x u_1(t, x) + \nabla_y u_1^1(t, x, y)) dy \right] \\
& + \theta u_1(t, x) \sum_{j=1}^M a_{1,j} u_j(t, x) - d_1 \int_{\Gamma} \psi(t, x, y) d\sigma(y) = 0 \quad \text{in } [0, T] \times \Omega
\end{aligned} \tag{119}$$

$$\left[ \int_{Y^*} (\nabla_x u_1(t, x) + \nabla_y u_1^1(t, x, y)) dy \right] \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \tag{120}$$

where

$$\theta = \int_Y \chi(y) dy = |Y^*|$$

is the volume fraction of material. To conclude, by continuity, we have that

$$u_1(0, x) = U_1 \quad \text{in } \Omega.$$

Taking advantage of the constancy of the diffusion coefficient  $d_1$ , Eqs. (117) and (118) can be reexpressed as follows

$$\Delta_y u_1^1(t, x, y) = 0 \quad \text{in } [0, T] \times \Omega \times Y^* \quad (121)$$

$$\nabla_y u_1^1(t, x, y) \cdot n = -\nabla_x u_1(t, x) \cdot n \quad \text{on } [0, T] \times \Omega \times \Gamma \quad (122)$$

Then,  $u_1^1(t, x, y)$  satisfying (121)-(122) can be written as

$$u_1^1(t, x, y) = \sum_{i=1}^N w_i(y) \frac{\partial u_1}{\partial x_i}(t, x) \quad (123)$$

where  $(w_i)_{1 \leq i \leq N}$  is the family of solutions of the cell problem

$$\begin{cases} -\operatorname{div}_y[\nabla_y w_i + \hat{e}_i] = 0 & \text{in } Y^* \\ (\nabla_y w_i + \hat{e}_i) \cdot n = 0 & \text{on } \Gamma \\ y \rightarrow w_i(y) \quad Y\text{-periodic} \end{cases} \quad (124)$$

By using the relation (123) in Eqs. (119) and (120) we get

$$\begin{aligned} \theta \frac{\partial u_1}{\partial t}(t, x) - \operatorname{div}_x \left[ d_1 A \nabla_x u_1(t, x) \right] + \theta u_1(t, x) \sum_{j=1}^M a_{1,j} u_j(t, x) \\ - d_1 \int_{\Gamma} \psi(t, x, y) d\sigma(y) = 0 \quad \text{in } [0, T] \times \Omega \end{aligned} \quad (125)$$

$$[A \nabla_x u_1(t, x)] \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \quad (126)$$

where  $A$  is a matrix with constant coefficients defined by

$$A_{ij} = \int_{Y^*} (\nabla_y w_i + \hat{e}_i) \cdot (\nabla_y w_j + \hat{e}_j) dy.$$

In the case  $1 < m < M$ , let us multiply the first equation of (12) by the test function

$$\phi_\epsilon \equiv \phi(t, x) + \epsilon \phi_1 \left( t, x, \frac{x}{\epsilon} \right)$$

where  $\phi \in C^1([0, T] \times \bar{\Omega})$  and  $\phi_1 \in C^1([0, T] \times \bar{\Omega}; C^\infty_\#(Y))$ . Integrating, the divergence theorem yields

$$\begin{aligned} & \int_0^T \int_{\Omega_\epsilon} \frac{\partial u_m^\epsilon}{\partial t} \phi_\epsilon(t, x, \frac{x}{\epsilon}) dt dx + d_m \int_0^T \int_{\Omega_\epsilon} \nabla_x u_m^\epsilon \cdot \nabla \phi_\epsilon dt dx \\ & + \int_0^T \int_{\Omega_\epsilon} u_m^\epsilon \sum_{j=1}^M a_{m,j} u_j^\epsilon \phi_\epsilon dt dx = \frac{1}{2} \int_0^T \int_{\Omega_\epsilon} \sum_{j=1}^{m-1} a_{j,m-j} u_j^\epsilon u_{m-j}^\epsilon \phi_\epsilon dt dx \end{aligned} \quad (127)$$

Passing to the two-scale limit we get

$$\begin{aligned} & \int_0^T \int_{\Omega} \int_{Y^*} \frac{\partial u_m}{\partial t}(t, x) \phi(t, x) dt dx dy \\ & + d_m \int_0^T \int_{\Omega} \int_{Y^*} [\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y)] \cdot [\nabla_x \phi(t, x) + \nabla_y \phi_1(t, x, y)] dt dx dy \\ & + \int_0^T \int_{\Omega} \int_{Y^*} u_m(t, x) \sum_{j=1}^M a_{m,j} u_j(t, x) \phi(t, x) dt dx dy \\ & = \frac{1}{2} \int_0^T \int_{\Omega} \int_{Y^*} \sum_{j=1}^{m-1} a_{j,m-j} u_j(t, x) u_{m-j}(t, x) \phi(t, x) dt dx dy. \end{aligned} \quad (128)$$

The last term on the left-hand side of (128) and the term on the right-hand side have been obtained by using Theorem 5.2. An integration by parts shows that (128) is a variational formulation associated to the following homogenized system:

$$-div_y [d_m (\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y))] = 0 \quad \text{in } [0, T] \times \Omega \times Y^* \quad (129)$$

$$[\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y)] \cdot n = 0 \quad \text{on } [0, T] \times \Omega \times \Gamma \quad (130)$$

$$\begin{aligned}
& \theta \frac{\partial u_m}{\partial t}(t, x) - \operatorname{div}_x \left[ d_m \int_{Y^*} (\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y)) dy \right] \\
& + \theta u_m(t, x) \sum_{j=1}^M a_{m,j} u_j(t, x) - \frac{\theta}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j(t, x) u_{m-j}(t, x) = 0 \quad \text{in } [0, T] \times \Omega
\end{aligned} \tag{131}$$

$$\left[ \int_{Y^*} (\nabla_x u_m(t, x) + \nabla_y u_m^1(t, x, y)) dy \right] \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \tag{132}$$

where

$$\theta = \int_Y \chi(y) dy = |Y^*|$$

is the volume fraction of material. Moreover, by continuity

$$u_m(0, x) = 0 \quad \text{in } \Omega.$$

Taking advantage of the constancy of the diffusion coefficient  $d_m$ , Eqs. (129) and (130) can be reexpressed as follows

$$\Delta_y u_m^1(t, x, y) = 0 \quad \text{in } [0, T] \times \Omega \times Y^* \tag{133}$$

$$\nabla_y u_m^1(t, x, y) \cdot n = -\nabla_x u_m(t, x) \cdot n \quad \text{on } [0, T] \times \Omega \times \Gamma \tag{134}$$

Then,  $u_m^1(t, x, y)$  satisfying (133)-(134) can be written as

$$u_m^1(t, x, y) = \sum_{i=1}^N w_i(y) \frac{\partial u_m}{\partial x_i}(t, x) \tag{135}$$

where  $(w_i)_{1 \leq i \leq N}$  is the family of solutions of the cell problem

$$\begin{cases} -\operatorname{div}_y [\nabla_y w_i + \hat{e}_i] = 0 & \text{in } Y^* \\ (\nabla_y w_i + \hat{e}_i) \cdot n = 0 & \text{on } \Gamma \\ y \rightarrow w_i(y) \quad Y\text{-periodic} \end{cases} \tag{136}$$

By using the relation (135) in Eqs. (131) and (132) we get

$$\begin{aligned} & \theta \frac{\partial u_m}{\partial t}(t, x) - \operatorname{div}_x \left[ d_m A \nabla_x u_m(t, x) \right] + \theta u_m(t, x) \sum_{j=1}^M a_{m,j} u_j(t, x) \\ & - \frac{\theta}{2} \sum_{j=1}^{m-1} a_{j,m-j} u_j(t, x) u_{m-j}(t, x) = 0 \quad \text{in } [0, T] \times \Omega \end{aligned} \quad (137)$$

$$[A \nabla_x u_m(t, x)] \cdot n = 0 \quad \text{on } [0, T] \times \partial\Omega \quad (138)$$

where  $A$  is a matrix with constant coefficients defined by

$$A_{ij} = \int_{Y^*} (\nabla_y w_i + \hat{e}_i) \cdot (\nabla_y w_j + \hat{e}_j) dy.$$

The proof for the case  $m = M$  is achieved by applying exactly the same arguments considered when  $1 < m < M$ .

□

Theorem 5.6 shows that the macroscale (homogenized) model, obtained from Eqs. (10)-(13) as  $\epsilon \rightarrow 0$ , is asymptotically consistent with the original model and resolves both the coarse and the small scale. The information given on the micro-scale, by the non-homogeneous Neumann boundary condition in (10), is transferred into the source term in the first equation of (111), describing the limit model. Furthermore, on the macro-scale, the geometric structure of the perforated domain induces a correction in that the scalar diffusion coefficients  $d_i$  ( $1 \leq i \leq M$ ), defined at the microscale, are replaced by a tensorial quantity with constant coefficients.

## A Appendix A

**Lemma A.1.** *The following estimate holds: if  $v \in \operatorname{Lip}(\Omega_\epsilon)$ , then*

$$\|v\|_{L^2(\Gamma_\epsilon)}^2 \leq C_1 \left[ \epsilon^{-1} \int_{\Omega_\epsilon} |v|^2 dx + \epsilon \int_{\Omega_\epsilon} |\nabla_x v|^2 dx \right] \quad (139)$$

where  $C_1$  is a constant which does not depend on  $\epsilon$ .

The inequality (139) can be easily obtained from the standard trace theorem by means of a scaling argument [4], [14], [15].

**Lemma A.2.** *Suppose that the domain  $\Omega_\epsilon$  is such that assumption (8) is satisfied. Then there exists a family of linear continuous extension operators*

$$P_\epsilon : W^{1,p}(\Omega_\epsilon) \rightarrow W^{1,p}(\Omega)$$

and a constant  $C > 0$  independent of  $\epsilon$  such that

$$P_\epsilon u = u \quad \text{in } \Omega_\epsilon$$

and

$$\int_{\Omega} |P_\epsilon u|^p dx \leq C \int_{\Omega_\epsilon} |u|^p dx, \quad (140)$$

$$\int_{\Omega} |\nabla(P_\epsilon u)|^p dx \leq C \int_{\Omega_\epsilon} |\nabla u|^p dx \quad (141)$$

for each  $u \in W^{1,p}(\Omega_\epsilon)$  and for any  $p \in (1, +\infty)$ .

For the proof of this Lemma see for instance [14].

As a consequence of the existence of extension operators one can derive the Sobolev inequalities in  $W^{1,p}(\Omega_\epsilon)$  with a constant independent of  $\epsilon$ .

**Lemma A.3** (Anisotropic Sobolev inequalities in perforated domains).

(i) *For arbitrary  $u \in H^1(0, T; L^2(\Omega_\epsilon)) \cap L^2(0, T; H^1(\Omega_\epsilon))$  and  $q_1$  and  $r_1$  satisfying the conditions*

$$\begin{cases} \frac{1}{r_1} + \frac{N}{2q_1} = \frac{N}{4} \\ r_1 \in [2, \infty], q_1 \in [2, \frac{2N}{N-2}] \quad \text{for } N > 2 \end{cases} \quad (142)$$

the following estimate holds

$$\|u\|_{L^{r_1}(0, T; L^{q_1}(\Omega_\epsilon))} \leq c \|u\|_{Q_\epsilon(T)} \quad (143)$$

where  $c$  is a positive constant independent of  $\epsilon$  and

$$\|u\|_{Q_\epsilon(T)}^2 := \sup_{0 \leq t \leq T} \int_{\Omega_\epsilon} |u(t)|^2 dx + \int_0^T dt \int_{\Omega_\epsilon} |\nabla u(t)|^2 dx \quad (144)$$

(ii) For arbitrary  $u \in H^1(0, T; L^2(\Omega_\epsilon)) \cap L^2(0, T; H^1(\Omega_\epsilon))$  and  $q_2$  and  $r_2$  satisfying the conditions

$$\begin{cases} \frac{1}{r_2} + \frac{(N-1)}{2q_2} = \frac{N}{4} \\ r_2 \in [2, \infty], q_2 \in [2, \frac{2(N-1)}{(N-2)}] \text{ for } N \geq 3 \end{cases} \quad (145)$$

the following estimate holds

$$\|u\|_{L^{r_2}(0, T; L^{q_2}(\Gamma_\epsilon))} \leq c \epsilon^{-\frac{N}{2} - \frac{(1-N)}{q_2}} \|u\|_{Q_\epsilon(T)} \quad (146)$$

where  $c$  is a positive constant independent of  $\epsilon$  and the norm  $\|u\|_{Q_\epsilon(T)}$  is defined as in (144).

*Proof.*

(i) The extension Lemma A.2 ensures the well-definiteness of a linear continuous extension operator  $P_\epsilon$  which satisfies (140) and (141). By the classical multiplicative Sobolev inequalities valid in  $\Omega$  (see [33] and [41]), we have that

$$\|P_\epsilon u\|_{L^{r_1}(0, T; L^{q_1}(\Omega))} \leq c_1 \|P_\epsilon u\|_{Q(T)} \quad (147)$$

where  $c_1 \geq 0$  depends only on  $\Omega$ ,  $r_1$ ,  $q_1$ , with  $r_1$  and  $q_1$  satisfying the conditions (142) and

$$\|P_\epsilon u\|_{Q(T)}^2 := \sup_{0 \leq t \leq T} \int_\Omega |P_\epsilon u(t)|^2 dx + \int_0^T dt \int_\Omega |\nabla(P_\epsilon u(t))|^2 dx \quad (148)$$

By using (140), (141) and (147), we conclude that

$$\begin{aligned} \|u\|_{L^{r_1}(0, T; L^{q_1}(\Omega_\epsilon))} &\leq C' \|P_\epsilon u\|_{L^{r_1}(0, T; L^{q_1}(\Omega))} \\ &\leq C' c_1 \|P_\epsilon u\|_{Q(T)} \leq C' c_1 C \|u\|_{Q_\epsilon(T)} \end{aligned} \quad (149)$$

where  $c := C' c_1 C$  is independent of  $\epsilon$ .

(ii) Let us rewrite the anisotropic Sobolev inequality valid on  $\partial\Omega$  (see [33] and [41]):

$$\begin{aligned} &\left[ \int_0^T dt \left[ \int_{\partial\Omega} |u(t)|^{q_2} d\mathcal{H}^{N-1} \right]^{\frac{r_2}{q_2}} \right]^{\frac{1}{r_2}} \\ &\leq c_1 \left[ \sup_{0 \leq t \leq T} \int_\Omega |u(t)|^2 dy + \int_0^T dt \int_\Omega |\nabla u(t)|^2 dy \right]^{1/2} \end{aligned} \quad (150)$$

where  $c_1 \geq 0$  depends only on  $r_2$ ,  $q_2$  and on local properties of the surface  $\partial\Omega$  (which is assumed to be piecewise smooth) with  $r_2$  and  $q_2$  satisfying the conditions (145). By performing the change of variable  $y = \frac{x}{\epsilon}$ , it is easy to obtain the corresponding re-scaled estimates:

$$\begin{aligned} & \epsilon^{\frac{(1-N)}{q_2}} \left[ \int_0^T dt \left[ \int_{\Gamma_\epsilon} |u(t)|^{q_2} d\mathcal{H}^{N-1} \right]^{\frac{r_2}{q_2}} \right]^{\frac{1}{r_2}} \\ & \leq c_1 \epsilon^{-\frac{N}{2}} \left[ \sup_{0 \leq t \leq T} \int_{\Omega_\epsilon} |u(t)|^2 dx + \epsilon^2 \int_0^T dt \int_{\Omega_\epsilon} |\nabla u(t)|^2 dx \right]^{1/2} \end{aligned} \quad (151)$$

$$\begin{aligned} & \left[ \int_0^T dt \left[ \int_{\Gamma_\epsilon} |u(t)|^{q_2} d\mathcal{H}^{N-1} \right]^{\frac{r_2}{q_2}} \right]^{\frac{1}{r_2}} \\ & \leq c \epsilon^{-\frac{N}{2} - \frac{(1-N)}{q_2}} \left[ \sup_{0 \leq t \leq T} \int_{\Omega_\epsilon} |u(t)|^2 dx + \int_0^T dt \int_{\Omega_\epsilon} |\nabla u(t)|^2 dx \right]^{1/2} \end{aligned} \quad (152)$$

where  $c$  is a positive constant independent of  $\epsilon$ .

□

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