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Multiscale Analysis of Thermoregulation in the Human Microvascular System

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Abstract

The bio-heat transfer equation is a macroscopic model for describing the heat transfer in microvascular tissue. So far the derivation of the Helmholtz term arising in the bio-heat transfer equation is not completely satisfactory. Here we use homogenization techniques to show that this term may be understood as asymptotic result of boundary value problems which provide a microscopic description for microvascular tissue. An appropriate scaling of so-called heat transfer coefficients in Robin boundary conditions on tissue-blood boundaries is seen to play the crucial role. In view of a future application of our new mathematical model for treatment planning in hyperthermia, we derive asymptotic estimates for the first order corrector.

Key words: bio-heat equation, hyperthermia, homogenization, correctors, heat transfer, Robin boundary conditions

Mathematics subject classification: 80A20, 35B27, 92C50

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Introduction

A detailed understanding of thermoregulation in the human vascular system is of utmost interest in a variety of applications in medical technology. The present paper emerges from problems arising in the patient-specific therapy planning for the cancer therapy *regional hyperthermia* – see [7, Chap. 1] for a general survey or [8] for details concerning applied adaptive multilevel methods. Up to now, the model of thermoregulation used therein is the quite popular *bio-heat transfer (BHT) equation*, a partial differential equation (PDE) model developed by the neurologist Pennes [15] already in 1948.

The aim of the present paper is to carefully revisit the original problem of thermoregulation on the micro/meso scale via mathematical homogenization.

The paper is organized as follows. In Section 1 we describe the problem setting in the framework of regional hyperthermia; the arguments underlying the existing derivations of the BHT equation are discussed together with their limitations. Next, in Section 2, we introduce a periodic model problem which is a usual first step within the homogenization approach – see, e.g., the research monograph [3]. This kind of model yields a slight variant of the BHT equation. More general scaling laws are discussed as well. However, as turns out, the more general approach does not lead to any further useful mathematical model. In Section 3, in view of a possible embedding of the microvascular model in a numerical multiscale model, we derive the first and second order corrector terms of our periodic model and prove error estimates for the first order corrector.

1 Thermoregulation Modeling Revisited

The investigations of this paper have been motivated by a long term interdisciplinary project in microwave regional hyperthermia, a rather recent cancer therapy. Its clinical setting at the Charité in Berlin is shown in Fig. 1, left. A prerequisite for mathematical therapy planning is the construction of a so-called virtual lab, which contains a 3D grid model of the real patient, the so-called virtual patient – see Fig. 1, right. The underlying medical and mathematical problem is to tune the microwave antennas optimally in such a way that heat is concentrated within the patient’s tumor, but nowhere else in healthy tissue.

For this purpose, the distribution of the temperature T within each individual human body must be quantitatively carefully modeled. Up to now, the rather simple so-called *bio-heat transfer (BHT) equation*

$$-\nabla\kappa\nabla T + \rho_t\rho_b c_b m(T - T_b) + S = 0 \quad (1.1)$$

is mostly used, where κ denotes the thermal conductivity, ρ_t/ρ_b the density of tissue/blood, c_b the specific heat capacity, m the perfusion, T_b the arterial temperature, and S some external thermal source – which in regional hyperthermia is the heating by microwave absorption. This elliptic PDE dates back to an early suggestion by the neurologist Pennes [15] from 1948 (actually he had treated the time dependent parabolic PDE). The construction of his model was based on

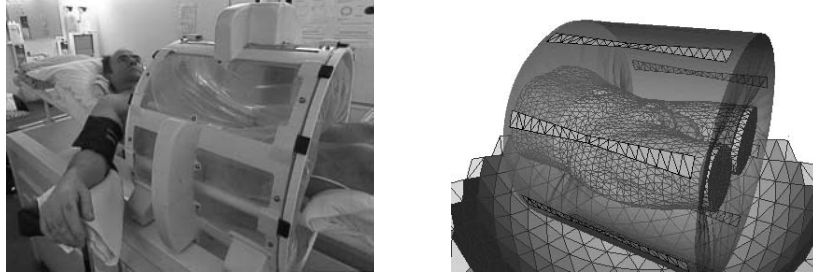


Figure 1: Regional hyperthermia: real patient (left, Charité), virtual patient (right, ZIB).

experimental observations which he tried to understand by an ingenious mixture of physical, physiological and mathematical arguments. His model was understood to apply to the whole resting human forearm. Multiscale considerations did not show up.

Not earlier than 1980 the two bioengineers Chen and Holmes [4] looked into this topic again in subtle detail. In their derivation the above Helmholtz term arises, when a “sufficiently large control volume” is considered, such that all further bifurcations from precapillary arterioles are contained. Moreover, they require the assumption that blood leaves the control volume at the solid tissue temperature. Upon carefully examining different heating effects by the blood flow, they arrive at the BHT equation with an additional convection term. In their summary, they draw the following main conclusions:

- The equilibration of blood temperature within solid tissue takes place between arterial branches and precapillary arterioles, not in the capillaries.
- The heat transfer from larger vessels should be calculated individually, and not collectively in a continuum formulation.

Obviously, these authors already envision a two-scale model – the BHT meso-level and the large vessel macro-level.

Later, in 1989, one of the present authors suggested another derivation of the Helmholtz term – see [17]. This derivation started from the above additional convection term and assumed some potential temperature flow – in the spirit of Darcy’s law as used in reservoir simulation. Following this line, Green’s theorem then helps to recover a Helmholtz term just as the one in the BHT equation. As is well-known, Darcy’s law has originally been based on experiments, whereas today it can be derived by homogenization arguments. First such derivations have used some periodic microstructure assumption [1, 9], more sophisticated later derivations could dispense of such a type of assumption [2].

Stepping back to the original problem, we are facing a true multiscale situation. As shown in Fig. 2, we will have to deal in parallel with large blood

vessels, medium size blood vessels, and small capillaries. Our computational concept for this situation is as follows:

- (a) Large blood vessels will be modeled as 3D spatial objects – compare also [12].
- (b) For the medium size blood vessels we might adopt a technique introduced by Quarteroni et al. [16] and model them as 1D spatial objects.
- (c) Finally, for the capillary heat distribution mechanism, we will need to derive some micromodel via homogenization – which is the topic of the present paper.

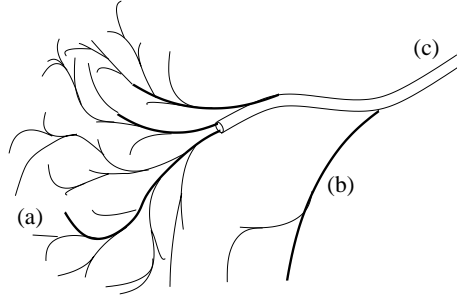


Figure 2: Multiscales in blood vessels: (a) capillaries, (b) medium size blood vessels, (c) large blood vessels.

2 Homogenization of a Periodic Model Problem

In this section, we consider the homogenization in periodic microstructures, a procedure which simplifies the presentation considerably and keeps the technical problems as few as possible. A generalization to a non-periodic setting will be given elsewhere.

Generally we use the notion $a \lesssim b$ to appreciate $a \leq Cb$ with some constant $C > 0$, $a \gtrsim b$ if $b \lesssim a$ and for $a \lesssim b \lesssim a$ we write $a \sim b$.

Let $\Omega \subset \mathbb{R}^3$, be a bounded domain. For $y_i > 0$, $i = 1, 2, 3$, we set $Y := \prod_{i=1}^3 (0, y_i)$ and for a bounded domain Q with $\overline{Q} \subset Y$ we define $Y^* := Y \setminus \overline{Q}$. The boundary of Q is assumed to be polygonal or, alternatively, at least C^2 . For $\epsilon > 0$ let $\tau(\epsilon Q) := \cup_{k \in \mathbb{Z}^3} \epsilon(k + Q)$. We always assume that $\partial\Omega \cap \tau(\epsilon Q) = \emptyset$ and write $Q_\epsilon := \Omega \cap \tau(\epsilon Q)$ as well as $\Omega_\epsilon := \Omega \setminus \overline{Q_\epsilon}$.

With respect to our underlying problem of heat-transfer in microvascular tissue we think of Q_ϵ as small regions of blood of certain temperature. The domains Ω_ϵ describe solid tissue parts where heat-transfer by conduction takes place. For simplicity, we assume that heat transfer in the solid tissue is described

by thermal conductivity with conductivity coefficient equal to 1. Taking into account some external thermal sources S_ϵ the temperature distribution is then modeled by the diffusion equations $-\Delta T_\epsilon = S_\epsilon$. Furthermore, we shall assume that on the inner boundaries ∂Q_ϵ the transition between blood regions and solid tissue is governed by Newton's cooling law with respect to an ϵ dependent heat transfer coefficient.

More precisely speaking, we consider for appropriate $\epsilon > 0$ and $\alpha > 0$ the boundary value problems

$$\begin{cases} -\Delta T_\epsilon = S_\epsilon & \text{in } \Omega_\epsilon, \\ T_\epsilon = 0 & \text{on } \partial\Omega, \\ \frac{\partial T_\epsilon}{\partial n} = \epsilon\alpha(T_b^\epsilon - T_\epsilon) & \text{on } \partial Q_\epsilon, \end{cases} \quad (2.2)$$

for given thermal sources S_ϵ and given blood temperatures T_b^ϵ .

For $V_\epsilon := \{u \in H^1(\Omega_\epsilon) \mid u|_{\partial\Omega} = 0\}$ and $S_\epsilon \in V'_\epsilon$, $T_b^\epsilon \in L^2(\partial Q_\epsilon)$ the variational formulation of the boundary value problem reads as follows: Find $T_\epsilon \in V_\epsilon$ such that

$$\int_{\Omega_\epsilon} \nabla T_\epsilon \cdot \nabla v \, dx = \langle S_\epsilon, v \rangle_{V'_\epsilon, V_\epsilon} - \alpha\epsilon \int_{\partial Q_\epsilon} T_\epsilon v \, d\sigma + \epsilon\alpha \int_{\partial Q_\epsilon} T_b^\epsilon v \, d\sigma \quad \text{for } v \in V_\epsilon. \quad (2.3)$$

Clearly, the variational problems (2.3) possess unique solutions $T_\epsilon \in V_\epsilon$.

Our results in this section will show that the ϵ -scaling of the heat transfer coefficient on ∂Q_ϵ is the correct scaling law. From a physical point of view, one may motivate the ϵ scaling by the following arguments: Let us assume that $T_b = 0$ and $S_\epsilon := S$ is a real thermal source, i.e., $T_\epsilon > 0$ in Ω_ϵ and in the limit for $\epsilon \rightarrow 0$ holds $T^* := \lim_{\epsilon \rightarrow 0} T_\epsilon > 0$ as well as on $\Omega_\delta := \Omega \setminus \{x \in \Omega \mid \text{dist}(x, \partial\Omega) < \delta\}$ for some small $\delta > 0$ it is $T^* \gtrsim 1$. Therefore, for ϵ small enough, one also has $T_\epsilon|_{\partial Q_\epsilon \cap \Omega^\delta} \gtrsim 1$. Upon applying on ∂Q_ϵ the boundary conditions

$$\frac{\partial T_\epsilon}{\partial n} + h_\epsilon T_\epsilon = 0$$

for $h_\epsilon > 0$, the variational formulation

$$\int_{\Omega_\epsilon} \nabla T_\epsilon \nabla v \, dx = \langle S_\epsilon, v \rangle_{V'_\epsilon, V_\epsilon} - h_\epsilon \int_{\partial Q_\epsilon} T_\epsilon v \, d\sigma, \quad v \in V_\epsilon,$$

gives for $v = T_\epsilon$

$$h_\epsilon \int_{\partial Q_\epsilon} |T_\epsilon|^2 \, d\sigma + \int_{\Omega_\epsilon} |\nabla T_\epsilon|^2 \, dx = \langle S, T_\epsilon \rangle_{V'_\epsilon, V_\epsilon} \lesssim \|T_\epsilon\|_{V_\epsilon}.$$

From this, applying the Poincaré inequality, see (2.6), we arrive at

$$h_\epsilon \int_{\partial Q_\epsilon} |T_\epsilon|^2 \, d\sigma \lesssim 1. \quad (2.4)$$

Since

$$\int_{\partial Q_\epsilon} |T_\epsilon|^2 d\sigma \geq \int_{\partial Q_\epsilon \cap \Omega^\delta} |T_\epsilon|^2 d\sigma \gtrsim |\partial Q_\epsilon \cap \Omega^\delta| \gtrsim \epsilon^{-1},$$

the inequality (2.4) implies, for sufficiently small $\epsilon > 0$, that

$$h_\epsilon \lesssim \epsilon.$$

In the final part of this section we will see that for constant $T_b > 0$ and $S_\epsilon = 0$ the Robin boundary condition $\frac{\partial T_\epsilon}{\partial n} + h_\epsilon T_\epsilon = 0$ with $h_\epsilon \sim \epsilon^\gamma$ for $\gamma > 1$ implies $\|\epsilon^{1-\gamma} T_\epsilon\|_{V_\epsilon} \lesssim 1$, hence $\|T_\epsilon\|_{V_\epsilon} \lesssim \epsilon^{\gamma-1}$ and finally $\|T_\epsilon\|_{V_\epsilon} \rightarrow 0$ for $\epsilon \rightarrow 0$. Therefore one should have

$$h_\epsilon \sim \epsilon.$$

In the following we make use of the existence of extension operators $P^\epsilon \in \mathcal{L}(V_\epsilon, H_0^1(\Omega))$ such that

$$\|\nabla P^\epsilon(v)\|_{[L^2(\Omega)]^3} \leq C \|\nabla v\|_{[L^2(\Omega_\epsilon)]^3}, \quad v \in V_\epsilon \quad (2.5)$$

with $C > 0$ independent of $\epsilon > 0$. Clearly, (2.5) implies the Poincaré inequality on Ω_ϵ , i.e., there exist a constant $C > 0$ such that for appropriate $\epsilon > 0$ holds

$$\|w\|_{L^2(\Omega_\epsilon)} \leq C \|\nabla w\|_{[L^2(\Omega_\epsilon)]^3}, \quad w \in V_\epsilon. \quad (2.6)$$

Theorem 1 *If $S_\epsilon \rightarrow S$ in $L^2(\Omega)$ and $T_b^\epsilon \rightarrow T_b$ in $H_0^1(\Omega)$, then*

$$P^\epsilon(T_\epsilon) \rightharpoonup T^* \quad \text{in } H^1(\Omega)$$

where T^* is the solution of the boundary value problem

$$\begin{cases} -\operatorname{div}(\mathcal{A} \nabla T^*) + \alpha \frac{|\partial Q|}{|Y|} (T^* - T_b) = \frac{|Y^*|}{|Y|} S & \text{in } \Omega, \\ T^* = 0 & \text{on } \partial\Omega. \end{cases} \quad (2.7)$$

The coefficients of the constant and positive definite matrix $\mathcal{A} = (a_{ij})_{ij}$ are given by

$$a_{ij} = \frac{|Y^*|}{|Y|} \delta_{ij} - \frac{1}{|Y|} \int_{Y^*} \frac{\partial \chi^j}{\partial y_i} dy \quad (2.8)$$

where the functions χ^j are solutions to

$$\begin{cases} -\Delta \chi^j = 0 & \text{in } Y^* \\ \frac{\partial(\chi^j - y_j)}{\partial n} = 0 & \text{on } \partial Q, \\ \chi^j \text{ } Y\text{-periodic} \end{cases} \quad (2.9)$$

Proof. The proof of the theorem is essentially based on considerations in [5]. Therefore we only sketch the necessary modifications. In order to relate our Robin boundary value problems (2.2) here to the Neumann problems studied there, we set $u_\epsilon := \epsilon^{-1}T_\epsilon$ and $f_\epsilon := \epsilon^{-1}S_\epsilon$, which leads to

$$\begin{cases} -\Delta u_\epsilon = f_\epsilon & \text{in } \Omega_\epsilon, \\ u_\epsilon = 0 & \text{on } \partial\Omega, \\ \frac{\partial u_\epsilon}{\partial n} + \epsilon\alpha u_\epsilon = \alpha T_b^\epsilon & \text{on } \partial Q_\epsilon. \end{cases} \quad (2.10)$$

Note that $f_\epsilon = \epsilon^{-1}S_\epsilon$ need not and will not fulfil the uniform estimate $\|f_\epsilon\|_{V'_\epsilon} \lesssim 1$ assumed in [5]. The boundary value problems (2.10) are interpreted as variational problems, i.e., $u_\epsilon \in V_\epsilon$ have to satisfy for $v \in V_\epsilon$

$$\int_{\Omega_\epsilon} \nabla u_\epsilon \cdot \nabla v \, dx = \langle f_\epsilon, v \rangle_{V'_\epsilon, V_\epsilon} - \alpha\epsilon \int_{\partial Q_\epsilon} u_\epsilon v \, d\sigma + \alpha \int_{\partial Q_\epsilon} T_b^\epsilon v \, d\sigma. \quad (2.11)$$

We notice that Corollaire 3.4 (b) in [5] implies for $\mu^\epsilon \in W^{-1,\infty}(\Omega)$ defined by

$$\langle \mu^\epsilon, \varphi \rangle := \epsilon \int_{\partial Q_\epsilon} \varphi \, d\sigma, \quad \varphi \in W_0^{1,1}(\Omega),$$

and $\mu \in W^{-1,\infty}(\Omega)$ defined by

$$\langle \mu, \varphi \rangle := \frac{|\partial Q|}{|Y|} \int_{\Omega} \varphi \, dx, \quad \varphi \in W_0^{1,1}(\Omega),$$

that in $W^{-1,\infty}(\Omega)$ holds $\mu^\epsilon \rightarrow \mu$ for $\epsilon \rightarrow 0$, which provides in particular a constant $C_\mu > 0$ with

$$\|\mu^\epsilon\|_{W^{-1,\infty}(\Omega)} \leq C_\mu \quad (2.12)$$

for $\epsilon > 0$. Applying (2.12) and $\|T_b^\epsilon\|_{H^1(\Omega)} \leq C$, which follows from $T_b^\epsilon \rightarrow T_b$ in $H^1(\Omega)$, we obtain

$$\left| \int_{\partial Q_\epsilon} T_b^\epsilon u_\epsilon \, d\sigma \right| = \epsilon^{-1} |\langle \mu^\epsilon, T_b^\epsilon u_\epsilon \rangle| \leq \frac{C_\mu}{\epsilon} \int_{\Omega_\epsilon} |\nabla(u_\epsilon T_b^\epsilon)| \, dx \leq \frac{C_\mu \cdot C}{\epsilon} \left(\int_{\Omega_\epsilon} |\nabla u_\epsilon|^2 \, dx \right)^{1/2}.$$

Therefore, (2.11) for $v = u_\epsilon$ gives

$$\begin{aligned} \int_{\Omega_\epsilon} |\nabla u_\epsilon|^2 \, dx &= \langle f_\epsilon, u_\epsilon \rangle_{V'_\epsilon, V_\epsilon} - \alpha\epsilon \int_{\partial Q_\epsilon} |u_\epsilon|^2 \, d\sigma + \alpha \int_{\partial Q_\epsilon} T_b^\epsilon u_\epsilon \, d\sigma \\ &\leq \epsilon^{-1} |\langle S_\epsilon, u_\epsilon \rangle_{V'_\epsilon, V_\epsilon}| + \frac{\alpha C_\mu \cdot C}{\epsilon} \left(\int_{\Omega_\epsilon} |\nabla u_\epsilon|^2 \, dx \right)^{1/2}. \end{aligned}$$

In other words, there exists some constant $C > 0$ such that

$$\|\epsilon u_\epsilon\|_{H_0^1(\Omega_\epsilon)} \leq C \quad \text{for } \epsilon > 0.$$

Selecting a suitable subsequence, there is $u^* \in H_0^1(\Omega)$ with

$$P^\epsilon(\epsilon u_\epsilon) \rightharpoonup u^* \quad \text{in } H_0^1(\Omega).$$

Now we proceed analogously to the proof of Théorème 4.7 in [5]: Setting $\xi_\epsilon :=$

$$\nabla(\epsilon u_\epsilon) \text{ in } \Omega_\epsilon \text{ and } \tilde{\xi}_\epsilon := \begin{cases} 0 & \text{in } Q_\epsilon \\ \xi_\epsilon & \text{in } \Omega_\epsilon \end{cases}, \text{ we obtain for } \varphi \in C_0^\infty(\Omega)$$

$$\int_{\Omega} \tilde{\xi}_\epsilon \cdot \nabla \varphi \, dx = \langle \chi_{\Omega_\epsilon} S_\epsilon, \varphi \rangle_{V'_\epsilon, V_\epsilon} - \alpha \langle \mu^\epsilon, \epsilon u_\epsilon \varphi \rangle + \alpha \langle \mu^\epsilon, T_b^\epsilon \varphi \rangle,$$

hence for $\xi^* \in [L^2(\Omega)]^3$ with $\tilde{\xi}_\epsilon \rightharpoonup \xi^*$ for $\epsilon \rightarrow 0$

$$\int_{\Omega} \xi^* \cdot \nabla \varphi \, dx = \frac{|Y^*|}{|Y|} \langle S, \varphi \rangle_{H^{-1}(\Omega), H_0^1(\Omega)} - \alpha \langle \mu, u^* \varphi \rangle + \alpha \langle \mu, T_b \varphi \rangle,$$

i.e., in Ω holds

$$-\operatorname{div} \xi^* = \frac{|Y^*|}{|Y|} S + \alpha \frac{|\partial Q|}{|Y|} (T_b - u^*).$$

Furthermore, following the proof of Théorème 4.7 in [5] step by step and applying again $\epsilon f_\epsilon = S_\epsilon$, we end up with

$$\xi^* = \mathcal{A} \nabla u^* \quad \text{in } \Omega,$$

where the coefficients a_{ij} of the matrix $\mathcal{A} = (a_{ij})_{ij}$ are given in (2.8). Finally, remember that $T_\epsilon = \epsilon u_\epsilon$ and denote u^* by T^* , which completes the proof. ■

At this point, some remarks on the boundary value problems (2.9) and their solutions χ^j may be in order: If Q has a C^2 -boundary, $f \in L^2(Y^*)$ and $g \in H^{1/2}(\partial Q)$, then the inhomogeneous problem

$$\begin{cases} -\Delta \theta = f & \text{in } Y^* \\ \frac{\partial \theta}{\partial n} = g & \text{on } \partial Q, \\ \theta \text{ } Y\text{-periodic} \end{cases}$$

has a unique solution $\theta \in H^2(Y^*)/\mathbb{R}$ iff

$$\int_{Y^*} f \, dx = - \int_{\partial Q} g \, d\sigma.$$

Furthermore, if f and g are constant functions, one has $\theta \in W^{1,\infty}(Y^*)$, see [10].

It is near by hand to ask for the resulting limit equation when the heat-transfer coefficients on the inner boundaries ∂Q_ϵ are scaled in any other way. In particular we are interested in the case $h_\epsilon \sim \epsilon^\gamma$ for $\gamma > 1$, since our remarks in the beginning of this section already suggest $h_\epsilon \lesssim \epsilon$.

Theorem 2 If $\gamma > 1$, $\epsilon^{1-\gamma}S_\epsilon \rightarrow S$ in $L^2(\Omega)$ and $T_b^\epsilon \rightharpoonup T_b$ in $H^1(\Omega)$, the solutions $T_\epsilon \in V_\epsilon$ to

$$\begin{cases} -\Delta T_\epsilon = S_\epsilon & \text{in } \Omega_\epsilon, \\ T_\epsilon = 0 & \text{on } \partial\Omega, \\ \frac{\partial T_\epsilon}{\partial n} = \epsilon^\gamma \alpha(T_b^\epsilon - T_\epsilon) & \text{on } \partial Q_\epsilon. \end{cases}$$

satisfy

$$P^\epsilon(\epsilon^{1-\gamma}T_\epsilon) \rightharpoonup T^* \quad \text{in } H_0^1(\Omega) \quad (2.13)$$

with

$$-\operatorname{div}(\mathcal{A}\nabla T^*) + \alpha \frac{|\partial Q|}{|Y|}(T^* - T_b) = \frac{|Y^*|}{|Y|}S.$$

Proof. We set $u_\epsilon := \epsilon^{-\gamma}T_\epsilon$, such that

$$\begin{cases} -\Delta u_\epsilon = \epsilon^{-\gamma}S_\epsilon & \text{in } \Omega_\epsilon, \\ u_\epsilon = 0 & \text{on } \partial\Omega, \\ \frac{\partial u_\epsilon}{\partial n} + \epsilon^\gamma \alpha u_\epsilon = \alpha T_b^\epsilon & \text{on } \partial\Omega_\epsilon. \end{cases}$$

We follow the proof for $\gamma = 1$, i.e. Theorem 1, which leads us to

$$\int_{\Omega_\epsilon} |\nabla u_\epsilon|^2 dx \leq \epsilon^{-\gamma} |\langle S_\epsilon, u_\epsilon \rangle_{V'_\epsilon, V_\epsilon}| + \frac{\alpha C_\mu \cdot C}{\epsilon} \left(\int_{\Omega_\epsilon} |\nabla u_\epsilon|^2 \right)^{1/2}.$$

Thus, $\epsilon^{1-\gamma} \|S_\epsilon\|_{V'_\epsilon} \leq C$ for $\epsilon > 0$ implies $\|\epsilon u_\epsilon\|_{H^1(\Omega_\epsilon)} \leq C$ for $\epsilon > 0$, which gives

$$P^\epsilon(\epsilon u_\epsilon) \rightharpoonup u^* \quad \text{in } H_0^1(\Omega).$$

Next, $\epsilon^{1-\gamma}S_\epsilon \rightarrow S$ in $L^2(\Omega)$ for $\epsilon \rightarrow 0$ implies

$$-\operatorname{div} \mathcal{A} \nabla u^* = \frac{|Y^*|}{|Y|}S + \alpha \frac{|\partial Q|}{|Y|}(T_b - u^*).$$

Since $u_\epsilon = \epsilon^{-\gamma}T_\epsilon$, we have

$$P^\epsilon(\epsilon^{1-\gamma}T_\epsilon) \rightharpoonup u^* \quad \text{in } H_0^1(\Omega).$$

Setting $T^* := u^*$ gives the result. ■

Finally, let us shortly discuss the case when the heat transfer coefficients are independent of ϵ : Considering on ∂Q_ϵ the Robin boundary condition

$$\frac{\partial T_\epsilon}{\partial n} = \alpha(T_b^\epsilon - T_\epsilon),$$

we obtain, under appropriate assumptions on S_ϵ ,

$$P^\epsilon(\epsilon^{1/2}T_\epsilon) \rightharpoonup 0 \quad \text{in } H_0^1(\Omega).$$

This means that the solutions T_ϵ to the periodic microscale problems need the scaling factor $\epsilon^{1/2}$ to become uniformly bounded in $H_0^1(\Omega_\epsilon)$.

3 First and Second Order Correctors

It is well-known from general homogenization theory that the solution to the homogenized equation is not the strong, but only the weak limit of the solutions to the periodic problems. Therefore correctors are introduced, i.e. ϵ -dependent functions, such that the sum of the solutions to the periodic problems and those corrector functions converge strongly. Moreover, for many periodic problems it could be shown that the convergence is of some order ϵ^s for $s > 0$ with respect to appropriate norms.

Generally, correctors can be understood as smoothing operators, because they suppress the fast oscillations in the gradient of $T_\epsilon - T^*$. Thus, in view of an efficient numerical approximation to the problems under consideration, corrector results are of particular interest. For the role of correctors in numerical homogenization see [11].

We shall prove two corrector results: Theorem 3 provides an asymptotic estimate for the “classical” first order corrector, cf. [3, 6, 13]. With respect to additional boundary correction terms an asymptotically better result is presented in Theorem 4.

In the following we assume that

$$\text{dist}(\partial\Omega, \partial Q_\epsilon) \gtrsim \epsilon \quad \text{for } \epsilon > 0,$$

which implies $\text{dist}(\partial\Omega, \partial Q_\epsilon) \geq \frac{\epsilon}{C_\Omega}$ with some ϵ independent $C_\Omega > 0$. Furthermore, we assume that the domain Ω possesses a C^∞ -boundary $\partial\Omega$, the boundary of Q is at least C^2 and for the data $S_\epsilon = S \in C^\infty(\bar{\Omega})$ and $T_b^\epsilon = T_b \in C^\infty(\bar{\Omega})$.

For the formal derivation of first and second order correctors we follow the standard approach, cf. [13]: Starting point is the asymptotic ansatz

$$T_\epsilon(x) = T_0(x, y) + \epsilon T_1(x, y) + \epsilon^2 T_2(x, y) + \dots,$$

with $y = x/\epsilon$ and where T_i are Y -periodic functions defined on $\Omega \times Y^*$. Then, applying

$$\Delta = \epsilon^{-2} \Delta_y + 2\epsilon^{-1} \Delta_{xy} + \Delta_x,$$

where $\Delta_y = \sum_{i=1}^3 \frac{\partial^2}{\partial y_i^2}$, $\Delta_{xy} = \sum_{i=1}^3 \frac{\partial^2}{\partial x_i \partial y_i}$, $\Delta_x = \sum_{i=1}^3 \frac{\partial^2}{\partial x_i^2}$, as well as

$$\frac{\partial}{\partial n} = \epsilon^{-1} \frac{\partial}{\partial n(y)} + n(y) \cdot \nabla_x,$$

we obtain in Ω_ϵ

$$\begin{aligned} -\Delta T_\epsilon &= -\epsilon^2 \Delta_y T_0 - \epsilon^{-1} (\Delta_y T_1 + 2\Delta_{xy} T_0) - (\Delta_x T_0 + 2\Delta_{xy} T_1 + \Delta_y T_2) + \dots \\ &= S, \end{aligned} \tag{3.14}$$

and on ∂Q_ϵ

$$\begin{aligned} \frac{\partial T_\epsilon}{\partial n} &= \epsilon^{-1} \frac{\partial}{\partial n(y)} T_0 + \frac{\partial}{\partial n(y)} T_1 + n(y) \cdot \nabla_x T_0 + \epsilon \left(\frac{\partial}{\partial n(y)} T_2 + n(y) \cdot \nabla_x T_1 \right) + \dots \\ &= \epsilon \alpha (T_b - T_0) - \epsilon^2 \alpha T_1 - \dots \end{aligned} \tag{3.15}$$

Comparing the coefficients to ϵ^{-2} in (3.14) and ϵ^{-1} in (3.15), respectively, leads to

$$\begin{cases} -\Delta_y T_0 = 0 & \text{in } Y^*, \\ \frac{\partial T_0(x, y)}{\partial n(y)} = 0 & \text{on } \partial Q, \\ T_0 \text{ } Y\text{-periodic.} \end{cases} \quad (3.16)$$

The only solutions to problem (3.16) are constants, i.e., T_0 is independent of y . Therefore, considering x as parameter, we get

$$T_0(x, y) = T_0(x)$$

with some x dependent function T_0 .

Next, comparing the coefficients to ϵ^{-1} in (3.14) and ϵ^0 in (3.15), respectively, yields

$$\begin{cases} -\Delta_y T_1 = 0 & \text{in } Y^*, \\ \frac{\partial T_1(x, y)}{\partial n(y)} = -n(y) \cdot \nabla_x T_0(x) & \text{on } \partial Q, \\ T_1 \text{ } Y\text{-periodic.} \end{cases} \quad (3.17)$$

Again, the variable x might be considered as parameter. Furthermore, applying the functions χ^j from (2.9) we obtain

$$T_1(x, y) = - \sum_{j=1}^3 \chi^j(y) \frac{\partial}{\partial x_j} T_0(x) + \tilde{T}_1(x),$$

with some function \tilde{T}_1 only depending on x . We choose $\tilde{T}_1(x) = 0$.

Finally, the coefficients to ϵ^0 in (3.14) and ϵ in (3.15), respectively, supply

$$\begin{cases} -\Delta_y T_2(x, y) = S + \Delta_x T_0(x) - 2 \sum_{i,j=1}^3 \frac{\partial \chi^j}{\partial y_i}(y) \frac{\partial^2}{\partial x_i \partial x_j} T_0(x) & \text{in } Y^*, \\ \frac{\partial T_2(x, y)}{\partial n(y)} = \alpha(T_b - T_0) + \sum_{i=1}^3 n_i(y) \left(\sum_{j=1}^3 \chi^j(y) \frac{\partial^2}{\partial x_i \partial x_j} T_0(x) \right) & \text{on } \partial Q, \\ T_2 \text{ } Y\text{-periodic.} \end{cases} \quad (3.18)$$

There exists a solution T_2 to (3.18), if and only if

$$-|Y^*| \Delta_x T_0 + \sum_{i,j=1}^3 \left(\int_{Y^*} \frac{\partial \chi^j}{\partial y_i}(y) dy \right) \frac{\partial^2 T_0}{\partial x_i \partial x_j} + \alpha |\partial Q| (T_0 - T_b) = |Y^*| S \quad \text{in } \Omega,$$

which is equation (2.7). Therefore, we set $T_0 := T^*$,

$$T_1(x, y) := - \sum_{j=1}^3 \chi^j(y) \frac{\partial}{\partial x_j} T^*(x)$$

and obtain in Y^*

$$-\Delta_y T_2 = -\alpha \frac{|\partial Q|}{|Y^*|} (T_b - T_0) + \sum_{i,j=1}^3 \left[\frac{1}{|Y^*|} \left(\int_{Y^*} \frac{\partial \chi^j}{\partial y_i}(y) dy \right) - 2 \frac{\partial \chi^j}{\partial y_i} \right] \frac{\partial^2 T^*}{\partial x_i \partial x_j}.$$

Introducing the functions $\chi \in H^1(Y^*)$ as the solutions to

$$\begin{cases} -\Delta_y \chi = -\frac{|\partial Q|}{|Y^*|} & \text{in } Y^*, \\ \frac{\partial \chi}{\partial n(y)} = 1 & \text{on } \partial Q, \\ \chi \text{ } Y\text{-periodic} \end{cases} \quad (3.19)$$

and the functions $\chi^{ij} \in H^1(Y^*)$ as the solutions to

$$\begin{cases} -\Delta_y \chi^{ij} = \frac{1}{|Y^*|} \left(\int_{Y^*} \frac{\partial \chi^j}{\partial y_i}(y) dy \right) - 2 \frac{\partial \chi^j}{\partial y_i} & \text{in } Y^*, \\ \frac{\partial \chi^{ij}}{\partial n(y)} = n_i(y) \chi^j(y) & \text{on } \partial Q, \\ \chi^{ij} \text{ } Y\text{-periodic}, \end{cases} \quad (3.20)$$

the function T_2 is given by

$$T_2(x, y) = \alpha \chi(y) (T_b(x) - T^*(x)) + \sum_{i,j=1}^3 \chi^{ij}(y) \frac{\partial^2 T^*(x)}{\partial x_i \partial x_j} + \tilde{T}_2(x).$$

Again we set $\tilde{T}_2(x) = 0$. The boundary value problem (3.19) is uniquely solvable, since $\int_{\partial Q} 1 d\sigma = \int_{Y^*} \frac{|\partial Q|}{|Y^*|} dy$, and the boundary value problems (3.20) are uniquely solvable, since

$$\begin{aligned} \int_{\partial Q} n_i(y) \chi^j(y) d\sigma &= \int_{Y^*} \frac{\partial \chi^j}{\partial y_i}(y) dy \\ &= - \int_{Y^*} \left[\frac{1}{|Y^*|} \left(\int_{Y^*} \frac{\partial \chi^j}{\partial y_i}(y) dy \right) - 2 \frac{\partial \chi^j}{\partial y_i} \right] dy. \end{aligned}$$

Now we are prepared to formulate the following theorem for the first order corrector.

Theorem 3 *If $\chi, \chi^j, \chi^{ij} \in W^{1,\infty}(Y^*)$, there is a constant $C > 0$ independent of $\epsilon > 0$ such that*

$$\|\nabla(T_\epsilon - (T^* - \epsilon \sum_{j=1}^3 \chi^j(\frac{\cdot}{\epsilon}) \frac{\partial T^*}{\partial x_j}))\|_{[L^2(\Omega_\epsilon)]^3} \leq C \epsilon^{1/2}.$$

Proof. Setting $R_\epsilon := T_\epsilon - T^* - \epsilon T_1$ and $H_\epsilon := R_\epsilon - \epsilon^2 T_2$, we get

$$-\Delta R_\epsilon = S + \Delta_x T^* + 2\Delta_{xy} T_1 + \epsilon \Delta_x T_1$$

and

$$-\Delta H_\epsilon = \epsilon(\Delta_x T_1 + 2\Delta_{xy} T_2) + \epsilon^2 \Delta_x T_2.$$

By our assumptions on $\partial\Omega$, S and T_b , the solution T^* to (2.7) satisfies $T^* \in C^\infty(\overline{\Omega})$. Since $\chi, \chi^{ij} \in W^{1,\infty}(Y^*)$ we have $\Delta_x T_1, \Delta_{xy} T_2, \Delta_x T_2 \in L^2(\Omega_\epsilon)$ with

$$\|\Delta_x T_1\|_{L^2(\Omega_\epsilon)} + \|\Delta_{xy} T_2\|_{L^2(\Omega_\epsilon)} + \|\Delta_x T_2\|_{L^2(\Omega_\epsilon)} \lesssim 1.$$

The boundary $\partial\Omega_\epsilon$ splits into the two parts $\partial\Omega$ and ∂Q_ϵ . On $\partial\Omega$ the functions T_ϵ and T^* vanish by definition. Thus we have

$$H_\epsilon|_{\partial\Omega} = -\epsilon T_1|_{\partial\Omega} - \epsilon^2 T_2|_{\partial\Omega} \quad \text{with} \quad \|T_1\|_{L^2(\partial\Omega)} + \|T_2\|_{L^2(\partial\Omega)} \lesssim 1.$$

On ∂Q_ϵ we have

$$\frac{\partial T_\epsilon}{\partial n} = \epsilon \alpha(T_b - T_\epsilon)$$

and, see (3.17),

$$\frac{\partial(T^* + \epsilon T_1)}{\partial n} = n(y) \cdot \nabla_x T^* + \frac{\partial}{\partial n(y)} T_1 + \epsilon n(y) \cdot \nabla_x T_1 = \epsilon n(y) \cdot \nabla_x T_1,$$

i.e., it is

$$\frac{\partial R_\epsilon}{\partial n} = \epsilon[\alpha(T_b - T_\epsilon) - n(y) \cdot \nabla_x T_1]$$

as well as, see (3.18),

$$\frac{\partial H_\epsilon}{\partial n} = \frac{\partial R_\epsilon}{\partial n} - \epsilon^2 \frac{\partial T_2}{\partial n} = \epsilon \alpha(T^* - T_\epsilon) - \epsilon^2 n(y) \cdot \nabla_x T_2.$$

Thus, we obtain on ∂Q_ϵ with $Z_\epsilon := -\alpha T_1 - n(y) \cdot \nabla_x T_2 - \epsilon \alpha T_2$ that

$$\frac{\partial H_\epsilon}{\partial n} + \epsilon \alpha H_\epsilon = \epsilon^2 Z_\epsilon. \quad (3.21)$$

Integration by parts gives

$$\|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 = - \int_{\Omega_\epsilon} \Delta H_\epsilon H_\epsilon dx + \int_{\partial Q_\epsilon} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma + \int_{\partial\Omega} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma. \quad (3.22)$$

In what follows we need to estimate the three terms on the right side of (3.22).

First term: We notice that the Poincaré inequality implies

$$\begin{aligned} \|H_\epsilon\|_{L^2(\Omega_\epsilon)} &\leq \|T_\epsilon - T^*\|_{L^2(\Omega_\epsilon)} + \epsilon \|T_1\|_{L^2(\Omega_\epsilon)} + \epsilon^2 \|T_2\|_{L^2(\Omega_\epsilon)} \\ &\lesssim \|\nabla(T_\epsilon - T^*)\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon \\ &\lesssim 1. \end{aligned}$$

Thus we get

$$\left| \int_{\Omega_\epsilon} \Delta H_\epsilon H_\epsilon dx \right| \leq \|\Delta H_\epsilon\|_{L^2(\Omega_\epsilon)} \|H_\epsilon\|_{L^2(\Omega_\epsilon)} \lesssim \epsilon.$$

Second term: Applying the identity (3.21) we get

$$\int_{\partial Q_\epsilon} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma = -\epsilon \alpha \int_{\partial Q_\epsilon} H_\epsilon^2 + \epsilon^2 \int_{\partial Q_\epsilon} H_\epsilon Z_\epsilon d\sigma \leq \epsilon^2 \|H_\epsilon\|_{L^2(\partial Q_\epsilon)} \|Z_\epsilon\|_{L^2(\partial Q_\epsilon)}. \quad (3.23)$$

Next we prove

$$\|H_\epsilon\|_{L^2(\partial Q_\epsilon)} \lesssim \epsilon^{-1/2} :$$

To this end we introduce Y -periodic functions $q_j \in C^1(\bar{Y})$ with

$$q_j(y) = \begin{cases} n_j(y) & y \in \partial Q, \\ 0 & \text{near } \partial Y, \end{cases}$$

i.e., it is $n^2 = \sum_{j=1}^3 q_j^2(y) = 1$ on ∂Q . Green then gives

$$\begin{aligned} \int_{\partial Q_\epsilon} H_\epsilon^2(x) d\sigma &= \sum_{j=1}^3 \int_{\partial Q_\epsilon} H_\epsilon^2(x) q_j(x/\epsilon) n_j(x) d\sigma \\ &= - \sum_{j=1}^3 \int_{\partial \Omega} H_\epsilon^2(x) q_j(x/\epsilon) n_j(x) d\sigma + \sum_{j=1}^3 \int_{\Omega_\epsilon} q_j(x/\epsilon) \frac{\partial(H_\epsilon^2(x))}{\partial x_j} dx \\ &\quad + \epsilon^{-1} \sum_{j=1}^3 \int_{\Omega_\epsilon} \frac{\partial q_j}{\partial y_j}(x/\epsilon) H_\epsilon^2(x) dx \\ &\lesssim \|H_\epsilon\|_{L^2(\partial \Omega)}^2 + \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 + \epsilon^{-1} \|H_\epsilon\|_{L^2(\Omega_\epsilon)}^2 \\ &\lesssim \epsilon^{-1}, \end{aligned}$$

i.e.,

$$\|H_\epsilon\|_{L^2(\partial Q_\epsilon)} \lesssim \epsilon^{-1/2}. \quad (3.24)$$

For Z_ϵ we have to refine this argument: First we get

$$\int_{\partial Q_\epsilon} Z_\epsilon^2(x) d\sigma \lesssim \|Z_\epsilon\|_{L^2(\partial \Omega)}^2 + \epsilon^{-1} \|Z_\epsilon\|_{L^2(\Omega_\epsilon)}^2 + \sum_{j=1}^3 \int_{\Omega_\epsilon} q_j(x/\epsilon) \frac{\partial(Z_\epsilon^2(x))}{\partial x_j} dx.$$

Inserting the definition of Z_ϵ in the first both terms on the right hand side and considering each part of Z_ϵ separately gives $\|Z_\epsilon\|_{L^2(\partial \Omega)}^2 \lesssim 1$ and $\|Z_\epsilon\|_{L^2(\Omega_\epsilon)}^2 \lesssim 1$. For estimating the third term we notice that

$$\int_{\Omega_\epsilon} q_j(x/\epsilon) \frac{\partial(Z_\epsilon^2(x))}{\partial x_j} dx = 2 \int_{\Omega_\epsilon} q_j(x/\epsilon) \cdot Z_\epsilon(x) \cdot \frac{\partial Z_\epsilon(x)}{\partial x_j} dx.$$

Again we have to insert the definition of Z_ϵ and to check each arising term separately. Let us exemplarily consider $\int_{\Omega_\epsilon} q_j(x/\epsilon) \cdot T_1(x) \cdot \frac{\partial T_1(x)}{\partial x_j} dx$: It is

$$\begin{aligned}
& \left| \int_{\Omega_\epsilon} q_j(x/\epsilon) \cdot T_1(x) \cdot \frac{\partial T_1(x)}{\partial x_j} dx \right| \\
&= \left| \int_{\Omega_\epsilon} q_j(x/\epsilon) \left(\sum_{i=1}^3 \chi^i(x/\epsilon) \frac{\partial T^*(x)}{\partial x_i} \right) \left(\sum_{k=1}^3 \epsilon^{-1} \frac{\partial \chi^k}{\partial y_j}(x/\epsilon) \frac{\partial T^*(x)}{\partial x_k} + \chi^k(x/\epsilon) \frac{\partial^2 T^*(x)}{\partial x_k \partial x_j} \right) dx \right| \\
&= \left| \sum_{i,k=1}^3 \int_{\Omega_\epsilon} q_j(x/\epsilon) \chi^i(x/\epsilon) \frac{\partial T^*(x)}{\partial x_i} \left(\epsilon^{-1} \frac{\partial \chi^k}{\partial y_j}(x/\epsilon) \frac{\partial T^*(x)}{\partial x_k} + \chi^k(x/\epsilon) \frac{\partial^2 T^*(x)}{\partial x_k \partial x_j} \right) dx \right| \\
&\lesssim \sum_{i,k=1}^3 \int_{\Omega_\epsilon} \left| \frac{\partial T^*(x)}{\partial x_i} \right| \left(\epsilon^{-1} \left| \frac{\partial T^*(x)}{\partial x_k} \right| + \left| \frac{\partial^2 T^*(x)}{\partial x_k \partial x_j} \right| \right) dx \\
&\lesssim \epsilon^{-1}.
\end{aligned}$$

Checking analogously the other terms yields

$$\left| \int_{\Omega_\epsilon} q_j(x/\epsilon) \frac{\partial (Z_\epsilon^2(x))}{\partial x_j} dx \right| \lesssim \epsilon^{-1}$$

and

$$\|Z_\epsilon\|_{L^2(\partial Q_\epsilon)} \lesssim \epsilon^{-1/2}. \quad (3.25)$$

Thus we obtain by (3.23) and (3.24)

$$\int_{\partial Q_\epsilon} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma \lesssim \epsilon.$$

Third term: Inserting $H_\epsilon|_{\partial\Omega} = -\epsilon T_1|_{\partial\Omega} - \epsilon^2 T_2|_{\partial\Omega}$ leads to

$$\left| \int_{\partial\Omega} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma \right| \leq \epsilon \left| \int_{\partial\Omega} T_1 \frac{\partial H_\epsilon}{\partial n} d\sigma \right| + \epsilon^2 \left| \int_{\partial\Omega} T_2 \frac{\partial H_\epsilon}{\partial n} d\sigma \right|. \quad (3.26)$$

Following an idea in [6], we take $m_\epsilon \in C_0^\infty(\mathbb{R}^3)$ with

$$m_\epsilon(x) = \begin{cases} 1 & \text{if } \text{dist}(x, \partial\Omega) \leq \epsilon/4C_\Omega, \\ 0 & \text{if } \text{dist}(x, \partial\Omega) \geq \epsilon/2C_\Omega, \end{cases} \text{ and transition such that } \|\nabla m_\epsilon\|_{L^\infty(\Omega)} \lesssim \epsilon^{-1}.$$

We set $U_\epsilon := \{x \in \Omega \mid \text{dist}(x, \partial\Omega) \leq \epsilon/2C_\Omega\}$. Now,

$$\begin{aligned} \frac{\partial}{\partial x_k}(m_\epsilon(x)T_1(x)) &= \frac{\partial m_\epsilon}{\partial x_k}T_1(x) + m_\epsilon(x)\frac{\partial T_1(x)}{\partial x_k} \\ &= -\frac{\partial m_\epsilon}{\partial x_k}\sum_{j=1}^3\chi^j(y)\frac{\partial T^*(x)}{\partial x_j} - m_\epsilon(x)\sum_{j=1}^3\epsilon^{-1}\frac{\partial \chi^j}{\partial y_k}(x/\epsilon)\frac{\partial T^*(x)}{\partial x_j} \\ &\quad - m_\epsilon(x)\sum_{j=1}^3\chi^j(y)\frac{\partial^2 T^*(x)}{\partial x_k\partial x_j}. \end{aligned}$$

Thus, we obtain

$$\|\nabla(m_\epsilon T_1)\|_{[L^2(U_\epsilon)]^3} \lesssim \epsilon^{-1}\|\nabla T^*\|_{[L^2(U_\epsilon)]^3} + 1.$$

Moreover, with

$$\|\nabla T^*\|_{[L^2(U_\epsilon)]^3} \lesssim \epsilon^{1/2}\|\nabla T^*\|_{[H^1(\Omega)]^3},$$

see [14], we conclude that

$$\|\nabla(m_\epsilon T_1)\|_{[L^2(U_\epsilon)]^3} \lesssim \epsilon^{-1/2}.$$

Next, the identity $m_\epsilon|_{\partial\Omega} = 1$ gives

$$\begin{aligned} \left| \int_{\partial\Omega} T_1 \frac{\partial H_\epsilon}{\partial n} d\sigma \right| &= \left| \int_{\partial\Omega} m_\epsilon T_1 \frac{\partial H_\epsilon}{\partial n} d\sigma \right| \\ &\leq \left| \int_{\Omega_\epsilon} m_\epsilon T_1 \Delta H_\epsilon dx \right| + \left| \int_{\Omega_\epsilon} \nabla(m_\epsilon T_1) \nabla H_\epsilon dx \right| \\ &\lesssim \epsilon + \|\nabla(m_\epsilon T_1)\|_{[L^2(U_\epsilon)]^3} \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \\ &\lesssim \epsilon + \epsilon^{-1/2} \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}. \end{aligned}$$

Since analogously to above holds

$$\|\nabla(m_\epsilon T_2)\|_{[L^2(U_\epsilon)]^3} \lesssim \epsilon^{-1/2},$$

we also get

$$\left| \int_{\partial\Omega} T_2 \frac{\partial H_\epsilon}{\partial n} d\sigma \right| \lesssim \epsilon + \epsilon^{-1/2} \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}.$$

Thus, we obtain by (3.26)

$$\left| \int_{\partial\Omega} H_\epsilon \frac{\partial H_\epsilon}{\partial n} d\sigma \right| \lesssim \epsilon^2 + \epsilon^{1/2} \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}.$$

Term collection: Combining the estimates, we are led to

$$\begin{aligned}\|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 &\lesssim \epsilon + \epsilon^{1/2}\|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \\ &\lesssim \max\{\epsilon, \epsilon^{1/2}\|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}\},\end{aligned}$$

which implies

$$\|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \lesssim \epsilon^{1/2}.$$

Finally, we get

$$\|\nabla R_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \leq \|\nabla H_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^2\|\nabla T_2\|_{[L^2(\Omega_\epsilon)]^3} \lesssim \epsilon^{1/2} + \epsilon \lesssim \epsilon^{1/2}.$$

■

The order $\frac{1}{2}$ in the asymptotic estimate for the first order corrector results essentially from $T_1|_{\partial\Omega} \neq 0$. In fact, appropriate additional correction terms with respect to the boundary $\partial\Omega$ give the order 1 uniformly in ϵ . The following theorem shows, that such correction terms are given by the solutions $\Theta_\epsilon \in H^1(\Omega_\epsilon)$ of the boundary value problems

$$\begin{cases} -\Delta\Theta_\epsilon = 0 & \text{in } \Omega_\epsilon, \\ \Theta_\epsilon = T_1 & \text{on } \partial\Omega, \\ \frac{\partial\Theta_\epsilon}{\partial n} = -\epsilon\alpha\Theta_\epsilon & \text{on } \partial Q_\epsilon. \end{cases}$$

Theorem 4 *If $\chi, \chi^j, \chi^{ij} \in W^{1,\infty}(Y^*)$, there is a constant $C > 0$ independent of $\epsilon > 0$ such that*

$$\|\nabla(T_\epsilon - (T^* - \epsilon(\sum_{j=1}^3 \chi^j(\frac{\cdot}{\epsilon})\frac{\partial T^*}{\partial x_j} + \Theta_\epsilon)))\|_{[L^2(\Omega_\epsilon)]^3} \leq C\epsilon.$$

Proof. We define $\tilde{R}_\epsilon := R_\epsilon + \epsilon\Theta_\epsilon$ and $\tilde{H}_\epsilon := \tilde{R}_\epsilon - \epsilon^2 T_2$. In Ω_ϵ holds

$$-\Delta\tilde{H}_\epsilon = -\Delta H_\epsilon = \epsilon(\Delta_x T_1 + 2\Delta_{xy} T_2) + \epsilon^2 \Delta_x T_2.$$

On $\partial\Omega$ we have

$$\tilde{H}_\epsilon = -\epsilon^2 T_2,$$

and on ∂Q_ϵ it is

$$\frac{\partial\tilde{H}_\epsilon}{\partial n} + \epsilon\alpha\tilde{H}_\epsilon = \epsilon^2 Z_\epsilon.$$

We proceed analogously to the proof of Theorem 3 and observe first that

$$\|\nabla\tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 = -\int_{\Omega_\epsilon} \Delta\tilde{H}_\epsilon \tilde{H}_\epsilon dx + \int_{\partial Q_\epsilon} \tilde{H}_\epsilon \frac{\partial\tilde{H}_\epsilon}{\partial n} d\sigma + \int_{\partial\Omega} \tilde{H}_\epsilon \frac{\partial\tilde{H}_\epsilon}{\partial n} d\sigma.$$

Again we need to estimate the three terms on the right side.

First term: The Poincaré inequality yields

$$\begin{aligned}
\|\tilde{H}_\epsilon\|_{L^2(\Omega_\epsilon)} &\leq \|T_\epsilon - T^* - \epsilon(T_1 - \Theta_\epsilon)\|_{L^2(\Omega_\epsilon)} + \epsilon^2\|T_2\|_{L^2(\Omega_\epsilon)} \\
&\lesssim \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^2(\|\nabla T_2\|_{[L^2(\Omega_\epsilon)]^3} + \|T_2\|_{L^2(\Omega_\epsilon)}) \\
&\lesssim \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon,
\end{aligned}$$

such that

$$\left| \int_{\Omega_\epsilon} \Delta \tilde{H}_\epsilon \tilde{H}_\epsilon \, dx \right| \leq \|\Delta \tilde{H}_\epsilon\|_{L^2(\Omega_\epsilon)} \|\tilde{H}_\epsilon\|_{L^2(\Omega_\epsilon)} \lesssim \epsilon \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^2.$$

Second term: First we obtain by (3.25)

$$\int_{\partial Q_\epsilon} \tilde{H}_\epsilon \frac{\partial \tilde{H}_\epsilon}{\partial n} \, d\sigma = -\epsilon\alpha \int_{\partial Q_\epsilon} \tilde{H}_\epsilon^2 + \epsilon^2 \int_{\partial Q_\epsilon} \tilde{H}_\epsilon Z_\epsilon \, d\sigma \leq \epsilon^2 \|\tilde{H}_\epsilon\|_{L^2(\partial Q_\epsilon)} \|Z_\epsilon\|_{L^2(\partial Q_\epsilon)} \lesssim \epsilon^{3/2} \|\tilde{H}_\epsilon\|_{L^2(\partial Q_\epsilon)}. \quad (3.27)$$

Next, applying the Y -periodic functions $q_j \in C^1(\bar{Y})$, we get

$$\begin{aligned}
\int_{\partial Q_\epsilon} \tilde{H}_\epsilon^2(x) \, d\sigma &= - \sum_{j=1}^3 \int_{\partial\Omega} \tilde{H}_\epsilon^2(x) q_j(x/\epsilon) n_j(x) \, d\sigma + \sum_{j=1}^3 \int_{\Omega_\epsilon} q_j(x/\epsilon) \frac{\partial(\tilde{H}_\epsilon^2(x))}{\partial x_j} \, dx \\
&\quad + \epsilon^{-1} \sum_{j=1}^3 \int_{\Omega_\epsilon} \frac{\partial q_j}{\partial y_j}(x/\epsilon) \tilde{H}_\epsilon^2(x) \, dx \\
&\lesssim \epsilon^4 + \|\tilde{H}_\epsilon\|_{L^2(\Omega_\epsilon)} \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^{-1} \|\tilde{H}_\epsilon\|_{L^2(\Omega_\epsilon)}^2 \\
&\lesssim \epsilon^{-1} \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 + \epsilon.
\end{aligned}$$

Thus, the inequality (3.27) yields

$$\int_{\partial Q_\epsilon} \tilde{H}_\epsilon \frac{\partial \tilde{H}_\epsilon}{\partial n} \, d\sigma \lesssim \epsilon \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^2.$$

Third term: We apply again the functions $m_\epsilon \in C_0^\infty(\mathbb{R}^3)$ and get

$$\begin{aligned}
\left| \int_{\partial\Omega} \tilde{H}_\epsilon \frac{\partial \tilde{H}_\epsilon}{\partial n} \, d\sigma \right| &= \epsilon^2 \left| \int_{\partial\Omega} m_\epsilon T_2 \frac{\partial \tilde{H}_\epsilon}{\partial n} \, d\sigma \right| \\
&\leq \epsilon^2 \left(\left| \int_{\Omega_\epsilon} m_\epsilon T_2 \Delta \tilde{H}_\epsilon \, dx \right| + \left| \int_{\Omega_\epsilon} \nabla(m_\epsilon T_2) \nabla \tilde{H}_\epsilon \, dx \right| \right) \\
&\lesssim \epsilon^3 + \epsilon^{3/2} \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}.
\end{aligned}$$

Term collection: We obtain

$$\begin{aligned}\|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}^2 &\lesssim \epsilon^2 + \epsilon \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \\ &\lesssim \max\{\epsilon^2, \epsilon \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3}\},\end{aligned}$$

which implies

$$\|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \lesssim \epsilon.$$

As the final result, we then get

$$\|\nabla \tilde{R}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} \leq \|\nabla \tilde{H}_\epsilon\|_{[L^2(\Omega_\epsilon)]^3} + \epsilon^2 \|\nabla T_2\|_{[L^2(\Omega_\epsilon)]^3} \lesssim \epsilon.$$

■

Conclusion

We have studied the important medical modeling question of microvascular thermoregulation from the mathematical scratch using homogenization techniques. As a result we obtain an elliptic PDE similar to, but slightly different from the traditional bio-heat transfer (BHT) equation. In future numerical modeling – such as therapy planning in the cancer therapy hyperthermia – we want to integrate our new model into a three-scale vascular model. For this reason, we additionally derived the first order corrector together with uniform asymptotic estimates.

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