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Effective diffusivity in membranes with tetrakaidekahedral cells and implications for the permeability of human stratum corneum

Ivo Muha[1], Arne Naegel[1], Sabine Stichel[1], Alfio Grillo, Michael Heisig, Gabriel Wittum*

Goethe-University, Goethe-Center for Scientific Computing, Kettenhofweg 139, 60325 Frankfurt a.M., Germany

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ABSTRACT

The stratum corneum, the outermost layer of the skin, acts as the main barrier of human skin. This membrane consists of flat and thin corneocyte cells which are embedded into an intercellular lipid matrix. A previous study elucidated how tetrakaidekahedral-shaped cells influence the barrier properties of the membrane. It remained an open question whether the mathematical tools from homogenization theory can be applied to this case. We show (i) how the method of asymptotic expansion can be used to homogenize membranes consisting of tetrakaidekahedral-shaped cells and calculate the effective diffusivity. Furthermore, numerical results confirm that (ii) the resulting tensor is of diagonal shape, and (iii) the transversal and lateral diffusivity can be described uniformly with different coefficients.

1. Introduction

The stratum corneum (SC), the outermost layer of the skin, is a biphasic membrane and typically about 10–20 μm thick [1]. It consists of flattened and keratinized corneocyte cells embedded in the intercellular lipid matrix. Due to the different properties of these phases they build a repellent layer and, therefore, the stratum corneum provides the main part of the barrier function of the skin against the environment.

The three-dimensional shape of cells in the SC can be well described by tetrakaidekahedra (TKD) [2–6]. This cell type has an almost optimal surface-to-volume ratio and provides a barrier, in which a minimal amount of mass is used very effectively. This shape has been confirmed in newer microscopic investigations [7–11] and has since been used in [12,13] to simulate diffusion processes in human SC. Note, that this model geometry is still an approximation, as, e.g., hair follicles, sweat glands and morphological variabilities are not considered.

Previous studies often approximated the structure of SC by a two-dimensional brick-and-mortar model geometry [14–16]. A straightforward generalization of this model to 3D can be found, e.g., in [17–20] and consists of cuboids. Differences between several two- and three-dimensional models with respect to permeability have been evaluated in [13]. The study proved that the shape of the cells has an important impact on the permeability of the membrane. The brick-and-mortar models yield lower permeabilities than the corresponding cuboid models, but are unrealistic due to the neglected dimension. Yet the TKD models with staggered corneocytes provide a barrier with similar favorable properties in 3D.

Due to the complexity of the geometry and the difference in length scales involved in its microstructure, solving the diffusion equation directly on the detailed microstructure involves high computational costs. Effective diffusivities are given, e.g., by the minimized domain method [21], and in [18,19] by applying the method of asymptotic expansion [22,23] for brick-and-mortar structures. In this work we show how the method of asymptotic expansion can be applied to membranes with tetrakaidekahedral-shaped base cells. By using homogenization theory the computational cost of modeling transdermal diffusion through SC is significantly reduced because there is no need to solve the model equations in a three-dimensional highly heterogeneous microstructure.

This work is organized as follows: In Section 2 we describe the model geometry and the associated equations. Elementary techniques from homogenization theory and the computational methods are summarized briefly as well. In Section 3 we present numerical results by studying the influence of overlap ω, height h and number of layers N with varying diffusion and partition coeffi-

* Corresponding author. Tel.: +49 69 798 25259.
E-mail address: wittum@gcsc.uni-frankfurt.de (G. Wittum).
[1] These authors contributed equally to this work.

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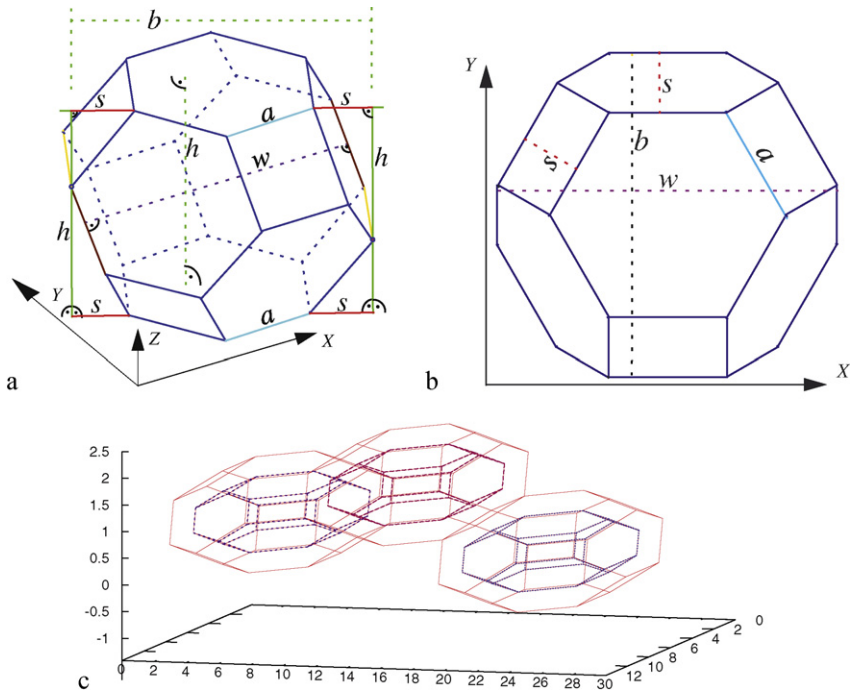

Fig. 1. Illustration of a TKD corneocyte cell in side view (a) and top view (b). Redrawn from [24,13]. (c) Corneocyte cells T_{cor} (inner TKD, blue) are embedded in a lipid matrix T_{lip}. In this example an agglomeration of three cells T (outer TKD, red) is obtained. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

cients on the effective diffusion tensor. The last section is devoted to conclusions.

2. Theory and methods

This section introduces the basic properties of the investigated cell geometry. Furthermore, we explain the model equations and give a short overview of the homogenization method used to calculate an effective diffusion tensor.

2.1. Geometry model

The model geometry of the corneocyte cells is built by tetrakaidekahedra (TKD) [3–6]. The concept of this model is based on the idea of densest packing and minimal interface area and can be dated back to a work by Lord Kelvin in the nineteenth century [2]. A detailed description of this model can be found in [12,24].

A single cell T_{cor} representing a corneocyte is given by a TKD, which is characterized by the parameters: vertical height h, edge length a of the basic hexagon and distance w of two corresponding edges between hexagons on the sides (Fig. 1). For the sake of convenience, we may also define the projected distance b and the length of shift s, their relation to our actual model parameters w and a is given in [12]. The corneocyte cell T_{cor} is embedded into another slightly larger TKD T both having the same center of mass. The surrounding lipid matrix is then given by

$$T_{lip} = T \setminus T_{cor}. \tag{1}$$

Since we want to expand the geometry periodically, the distance of T_{cor} to its boundary ∂T is chosen as $d/2$, where d is the thickness of the lipid channel.

For simplicity we denote a TKD T with variable corneocyte edge length a and corneocyte height h by TKD(a, h). In our computations we always choose the corneocyte width $w = 30\,\mu m$. For the lipid channel a thickness $d = 0.1\,\mu m$ is used. These values are consistent with literature [13]. The horizontal overlap between TKD cells T is then given by the ratio

$$\omega = \frac{s_T}{b_T} = \frac{w_T - 2a_T}{2w_T - a_T} \tag{2}$$

with $0 < \omega < 0.5$. The subscript T indicates the quantities corresponding to the cell T, whereas the quantities without subscript are defined for the cell T_{cor}.

Agglomerates of TKD structures obviously provide a dense packing of the space. As illustrated in Fig. 2, the resulting geometric structures can locally be represented by a reference cell Y. By identifying two parallel faces of the cuboid Y, a torus, i.e., an infinite

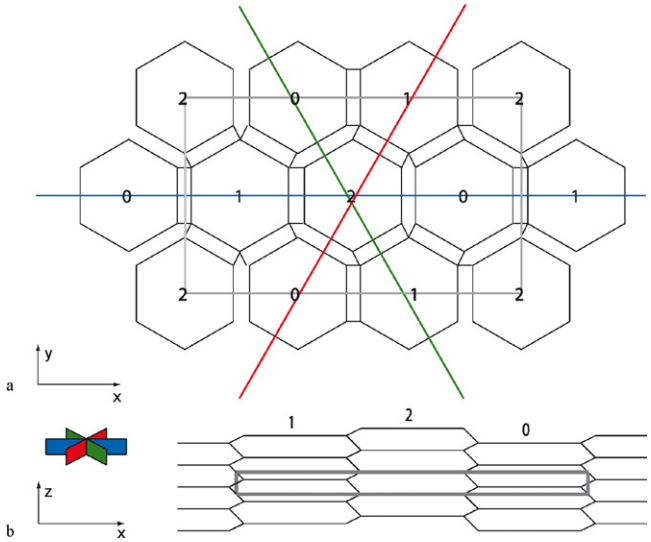

Fig. 2. Reference cell Y for TKD membrane is shown as a grey box in an ensemble of cells providing a dense packing of space. (a) Top view x–y plane. (b) Cross section z–x plane. The numbers {0,1,2} indicate the three different heights of the top face of a TKD, as it can be seen in (b).