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Numerical Simulations of Skin Formation: Convergence of Moisture Transport and Stratum Corneum Thickness

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Abstract. As the epidermis adapts to different environments, desquamation of keratinocytes is affected by the water content in the epidermis. The thickness of the outermost layer of skin is determined by the interaction between exfoliation and moisture evaporation. The balance between these processes is the key to healthy skin, but has not been studied. The present study constructs a qualitative numerical model of stratum corneum thickness based on the interaction between exfoliation and evaporation processes.

1. Introduction

The dermatological mechanisms behind the smoothness of human skin are of great interest to the health and beauty industry. However, because most experiments that target human subjects are generally precluded by ethical constraints, the internal developmental mechanism behind skin roughness is understood only superficially from the data collected by noninvasive measurements. This study reports a numerical study of the formation of epidermis that uncovers insight about how skin develops.

The stratum corneum is the outermost layer of the human skin, and is also where new cells keratinize. This ‘horny layer’ is kept fresh by the sloughing of old keratin and replenishment with new cells. This peeling–regeneration cycle, called *turnover*, is known to be related to the moisture content in the stratum corneum [1]. For example, if the water content of the stratum corneum reduces the desmosomes that hold keratinocytes together degrade, and the stratum corneum becomes thicker than usual. The thickening of the outer layer suppresses the evaporation of moisture from the skin thereby enhancing water retention. In contrast, a high-humidity environment promotes desquamation. Therefore, epidermis turnover adjusts dynamically to different environments. Dry climates exert a remarkable aging effect on skin. Aging reportedly results from the decreased activity of the enzyme that degrades desmosomes in addition to the surrounding climate [1]. Many diseases are the result of maladaptation to the environment because epidermal turnover has failed.

Several computational models have been proposed for developing understanding of the mechanisms behind the development of human skin [2–5]. This article proposes a particle model that can handle complex biological phenomena, including cell interactions such as cell division, motion, deformation, and transition [6–8]. The method is suitable for simulating skin formation.

Assuming a healthy epidermis, the next sections analyze the process by which human skin converges to a constant thickness through the competing processes of water volatilization and exfoliation.

2. Methods

2.1. *Analysis flow*

Figure 1 is a flowchart of the present analysis. The simulation study period was 200 days. Transepidermal water loss assumed to be constant in our earlier study [9] was set as a variable in the present model to investigate epidermal turnover. The models in this study therefore use different values for the "water calculation", "desquamation calculation", and "update parameters" steps.

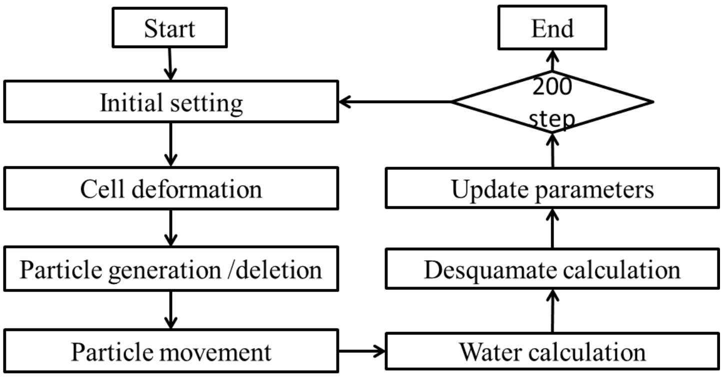

Figure 1. Analytic flow of the present study

2.2 *Initial setting*

To initialize the model, dermal layer and basal layer particles were placed in the calculation area ($300 \times 300 \times 300$ μ^3 grid), and keratinocytes were divided from the basal layer. The division frequency of the keratinocytes was set as a constant.

Epidermal cells are classified into four groups, depending on the progress of keratinization. Figure 2 shows the shapes of various particle types. Stem cells located closest to the body are called basal cells from which the spinal cells differentiate. Cells then differentiate further into granule cells, and eventually become outer layer horny cells. In the numerical simulation we differentiate the particles by thickness. In each step of the analysis, the thickness of each particle is decreased, and the number of particles that reach a certain thickness are updated.

Each particle moves to a position that balances the spring forces between particles [10]. New particles differentiated from the basal layer shift the neighboring particles, moving the whole mass upward. Periodic boundary conditions were assumed in our calculations.

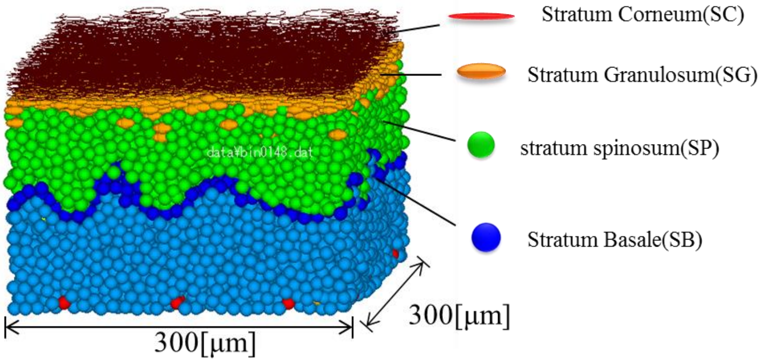

Figure 2. Particle model of keratinization

2.3 *Desquamation calculation*

Since the decomposition of desmosomes is proportional to the amount of skin moisture [1] desmosomes in the stratum corneum (SC) are decomposed by moisture. In the present model, each horny cell has its own desmosome content, which is updated after each water calculation step. The degree of reduction in desmosomes is determined by the moisture content of horny cells. Particles with desmosome content below the threshold are removed from the calculation area as extinct cells.

2.4 Trans-epidermal water loss

Skin roughness results from disturbances to the structure of the SC that reduce its water retention. Therefore, trans-epidermal water loss (TEWL) is a key indicator when evaluating the barrier function of the skin as well as the shape of the outer layer. Equations (1)~(3) describe moisture diffusion using Fick's law, a one-dimensional diffusion equation. Note that we defined C_0 as a constant assuming that the dermis provides a constant moisture supply.

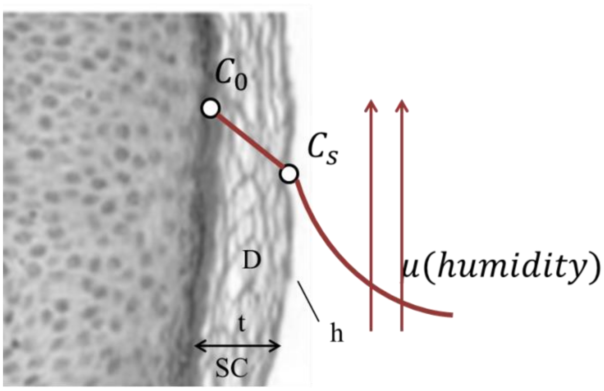

Figure 3
C_0 and C_s are water contents on the inside and outside of the SC, respectively. μ is humidity in the environment. D is the diffusion coefficient of water in the stratum corneum, h is a proportional constant, and t is the thickness of the SC.

Equation (1) determines the amount of water diffused from the SC to the surface. As the SC grows thicker less moisture evaporates. Assuming this phenomenon, we defined an inverse proportional relationship between TEWL and the SC thickness t. Equation (2) computes the amount of water that evaporates from the keratinous surface into the atmosphere. We introduced h as a parameter to describe the surface conditions such as the quality of the sebum barrier or the shape of the horny layer, which have some influence on evaporation rates. Equation (3) is derived by solving Equations (1) and

(2) for C_s and rearranging. This equation states the inverse proportionality between TEWL and SC thickness.

$$\mathrm{TEWL}_1 = -\mathrm{D}\frac{\mathrm{C_s - C_0}}{\mathrm{t}} \quad (1)$$

$$\mathrm{TEWL}_2 = \mathrm{h}C_s(1-\mu) \quad (2)$$

$$\mathrm{TEWL} = \frac{C_0}{\frac{t}{D}+\frac{1}{h(1-\mu)}} \quad (3)$$

3. Results and Discussion

In the simulation runs, the SC thickness increased and decreased in cycles, and eventually settled at a constant value. Figure 4(a) shows the placement of each kind of particle at different time periods in the analysis, and Figure 4(b) shows the water content of the particles at the same points.

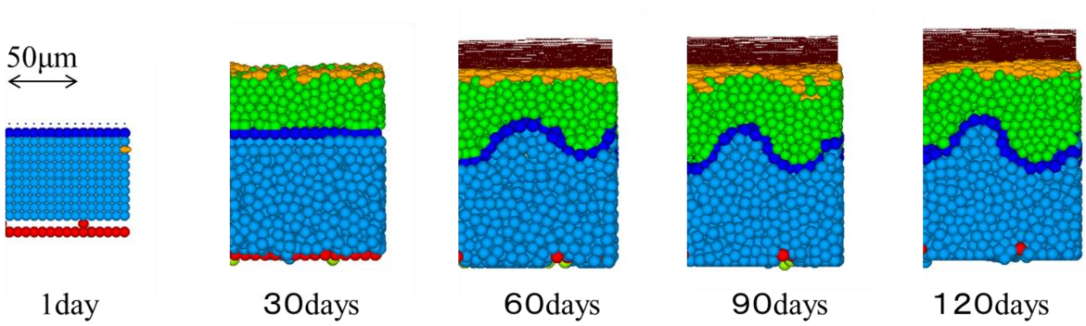

Figure 4(a). Placements of the various particle types at different times.

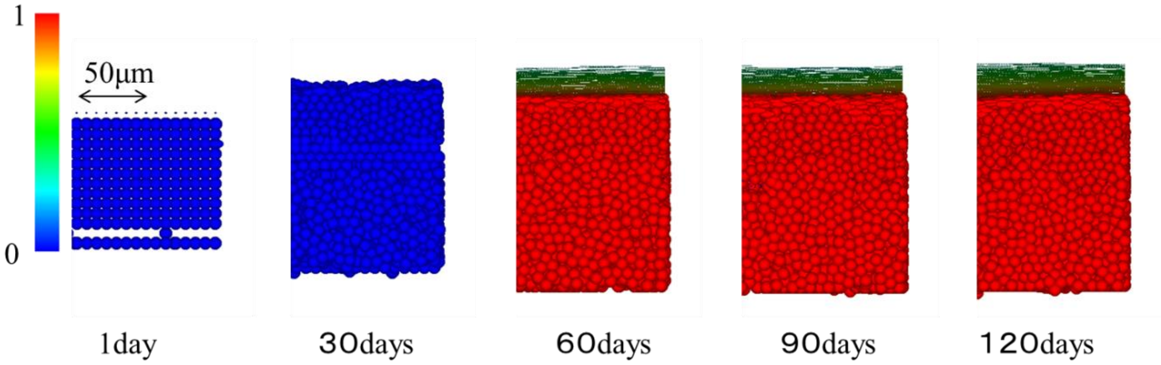

Figure 4(b). Water content of the particles at different times.

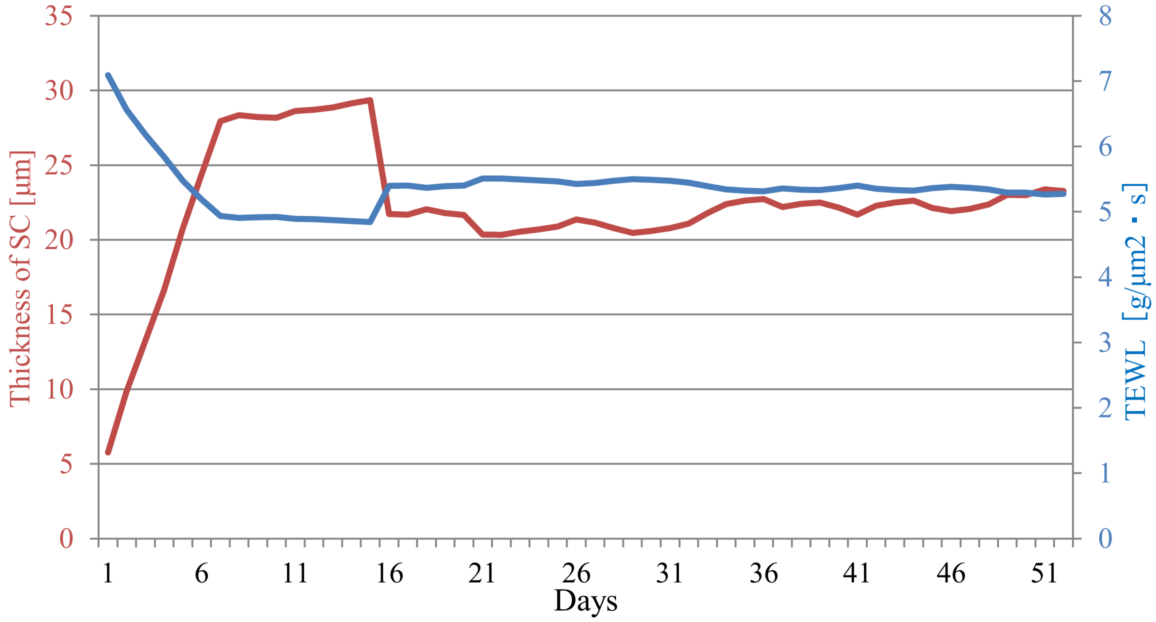

Figure 5. Convergence of turnover.

In Figure 5, the thickness of the SC and TEWL are plotted with day 1 as the step in which the first moisture calculation was performed. The thickness of SC gradually increases due to the increase of keratinous particles, and peeling began on day 7. SC thickness decreased more from days 14 to 16 than it did before and after because the horny cells were generated and peeled off before the moisture calculation step.

4. Conclusion

Healthy turnover is indispensable for the maintenance of healthy skin. During the turnover process, thickness of the SC is adjusted to the environment through the interaction between the water retention of the SC and the exfoliation rate, and the latter of which is determined by humidity in the environment. Many skin diseases follow the collapse of this mechanism due to keratin dysplasia and peeling. This article is built upon the model of moisture diffusion and exfoliation which we proposed in a previously published report. The model qualitatively reproduced the SC's water retention function by defining an inverse proportional relation between the SC thickness and TEWL. We modeled the relationship between peeling and water transport as linear. In our previous study, an upper limit was set on the number of SC cells, and any surplus was erased. However, this model yielded a constant thickness SC and became regardless of the environmental humidity. Therefore, we also altered the peeling model so the effects of moisture conditions in the SC on exfoliation rates could be studied. The revised model showed a convergence of SC thickness over time to a thickness determined by the model parameters. In the future, we plan to include a mechanism that describes excessive drying and peeling to consider the influence of inflammation and aging on the turnover mechanism.

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