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# Particle Simulation on Human Epidermal Aging - Effect of Basal Layer and Cell Division Rate -

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***Abstract***

Wrinkles and freckles appear on people due to aging and, as such, affect their appearance. The epidermis is the outermost layer of a human's skin, and epidermal conditions can be diagnosed from it in order to provide appropriate care. Recently, those interested in anti-aging treatments have paid greater attention to the aging of the epidermal layer. The epidermis consists of four different layers. In particular, the basal layer, which is at the bottom of epidermis, has an undulating structure. This undulation is associated with aging: undulations in the basal layer become flat when the epidermis ages. However, the mechanisms between the aging process and the basal layer have not yet been made clear because it is difficult to directly observe the skin's basal layer. In order to investigate long-term skin formation, we created a model that simulates actual skin. Our model can analyze the epidermis while including undulations in the structure of the basal layer. In order to test this, we set conditions for the number of basal cells and the basal cell division rate so as to simulate aging and young epidermises. In the case of aging epidermises, the number of basal cells was fewer and the basal cell division rate was lower than for young skin. As a result of this analysis, the characteristics of aging skin were found.

***Keywords**:* Numerical Simulation, Particle Model, Aging, Basal Layer, Cell Division

## 1. Introduction

Wrinkles and freckles appear on people due to aging and, as such, affect their appearance. The epidermis is the outermost layer of a human's skin, and epidermal conditions can be diagnosed from it in order to provide appropriate care [1]. Recently, those interested in anti-aging treatments have paid greater attention to the aging of the epidermal layer.

The epidermis consists of four different layers. In particular, the basal layer, which is at the bottom of epidermis, has an undulating structure. This undulation is associated with aging: undulations in the basal layer become flat when the epidermis ages [2]. However, the mechanisms between the aging process and the basal layer have not yet been made clear because it is difficult to directly observe the skin's basal layer.

Computational simulations can be useful in further understanding the mechanisms underpinning the development of human skin, and several models have been proposed [3–6]. In this study, we propose a particle model that can handle complex biological phenomena, including cell interactions such as cell division, motion, deformation, and transition [7–9]. Furthermore, we believe that it is a suitable method for simulating skin formation.

In order to test this model, we developed an analytical method for the formation and turnover process of the skin, and we have also introduced multiple cell division patterns [10–14]. Our model can also analyze the epidermis while taking stock of the change in the basal layer structure. As a result, we could elucidate the relationship between cell division and the basal layer by using our model.

In this paper, we analyze a long-term skin formation process using this model. Furthermore, we also set the number of basal cells and the basal cell division rate, and simulated both an aging and young epidermis.

Our aim was to simulate how the epidermis ages in order to contribute to the development of medical skin treatments and cosmetics.

## 2. Analysis Object and Model Description

### 2.1 Analysis Object

Fig. 1 depicts a cross section of the skin [1], and the roles of each cell layer therein are described. The epidermis is the outermost layer of the skin and is primarily composed of cells called keratinocytes. The epidermis consists of four layers. The lowest layer of the epidermis, the basal layer, provides new cells each day by dividing. The dividing cells are called the prickle cell layer, and they are pushed and moved up toward the skin surface. This layer transforms into the granular layer and then the stratum corneum, which detaches itself from the surface of the skin. This is called the turnover process, and occurs approximately every four weeks. As a person ages, it becomes harder for the stratum corneum to detach from the surface, and as a result skin becomes thicker [2].

During this turnover process, skin cells change not only in their shape but also in their physical properties. However, the cycle of turnover is longer in an aging epidermis [2].

The dermis is located under the epidermis, and the two are separated by the basal layer. Capillaries in the dermis supply nutrition and oxygen to the basal cells. Therefore, it is considered that epidermis is influenced force interactions from the dermis and nutrition effects from capillaries.

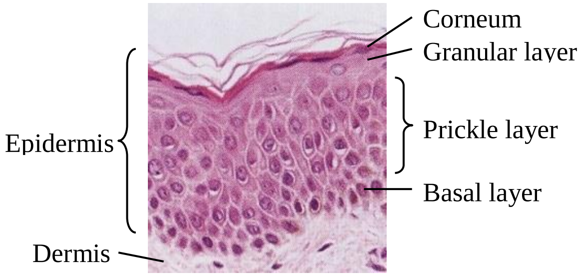


Fig. 1 Cross section of the skin [1]

### 2.2 Model Description

The particle model [7–9] is introduced into our analysis model so as to simulate the formation process of the epidermis [10–14]. The model considers the interaction between the particles and models the Langrangian motion of the particles. This method is suitable for analysis with large deformations or for when the number of calculation points are varied: *i.e.*, changing the generation, division, and disappearance of cells.

The cellular particles move in response to inter-particle forces, such as the volume conservation force and the spring force. These relationships are shown in Eqs. (1)–(3) [13, 14].

The volume conservation force, F, in Eq. (1) maintains the distance between the particles. Due to the repulsive force, particles eventually move to a stable distance. In this equation, k is a coefficient, ddr is the distance between two particles, dr0 is the standard distance (10.0 µm in this case), dr1 is the maximum distance for which the volume conservation force can act; dr1 is larger than dr0.

The basal layer maintains shape of monolayer, which includes its undulating structure. In order to introduce this monolayer into our model, we use the spring force shown in Eq. (2). Here k' is the coefficient of an elastic spring. The distance at which the spring force acts upon varies with the number density of the basal layer because it can fill the gaps generated by the basal layer. In addition, the spring force is also introduced to the stratum corneum and the granular layer in order to introduce strong cell junction.

By summing up the forces from the surrounding particles, the particles gradually move to the position of the force balance, as shown by Eq. (3). x and x' are the positions before and after the movement by these forces. α is a coefficient, and its value is 0.003.

Here states the methodology to solve equations which find the position of the force balance in detail. As shown in Eq. (3), each particle move according to the sum of volume conservation force and spring force. At this time, the particles repulse toward the position where the forces are weakened. Therefore, each particle gradually moves and converges at the position of the force balance by repeating the repulsion. Our model determines the positions by calculating 2,500 times per day.

$$\vec{F} = k \cdot \left(1 - \frac{ddr}{1.106 \times dr0}\right) \cdot \left(1 - \frac{ddr}{dr1}\right) \cdot \frac{dd\vec{r}}{ddr} \tag{1}$$

$$\vec{f} = k' \cdot \left(1 - \frac{ddr}{1.106 \times dr0}\right) \cdot \frac{dd\vec{r}}{ddr} \tag{2}$$

$$\vec{x}' = \vec{x} + \alpha \cdot \left(\sum \vec{F} + \sum \vec{f}\right) \tag{3}$$

Though the volume conservation force acts on the particles in the dermis and the prickle layer, the spring force is also added to the particles of other layers so as to increase the connections between the particles.

In addition, each basal cell is a stem cell and can divide into two daughter cells. This division has three patterns, as shown in Fig. 2. Pattern 1 is where both cells become basal cells, and Pattern 2 is where one cell remains a basal cell while the other becomes a prickle cell. In Pattern 3, meanwhile, both cells change into prickle cells. Each basal cell follows one of these three patterns at random.

The basal layer is affected a change in these cell division patterns, and as a result undulations form on the basal layer [13]. For example, when the number of basal cells increases, they press against other cells. Conversely, when the number of basal cells decreases, the surrounding basal cells fill the gap and keep the shape of monolayer.

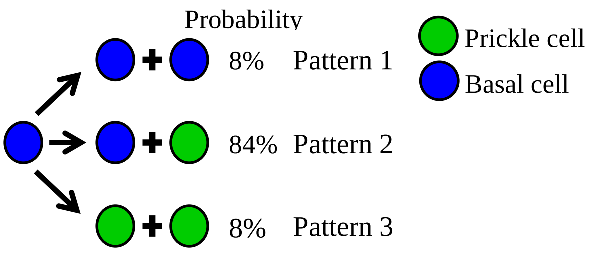


Fig. 2 Cell division of a basal layer cell [15, 16]

## 3. Calculation Conditions

### 3.1 Base Model

The initial configuration shown in Fig. 3 only consists of the dermis (light blue), capillary (red), and basal layer (blue). Cell particles in this model are represented by a spherical shape with a 10 µm diameter. The shape becomes thinner in the granular layer, changing with time, and adopts an elliptical shape that extends in the transverse direction by approximately 1 µm in thickness in the stratum corneum.

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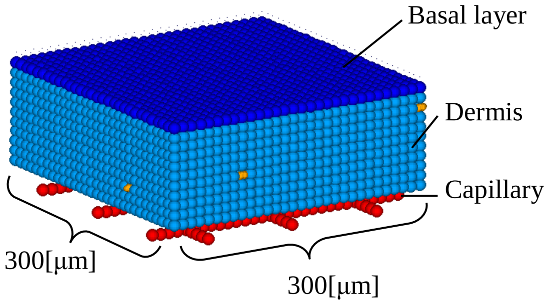


Fig. 3 Perspective view

Each basal cell divides once every five days of analysis time (0.2 times per day), and the two daughter cells take one of three patterns shown in Fig. 2 at random. The divided prickle cells freely move under a force in order to keep the volume constant until they reach the granular layer. The spring force begins to gradually occur from the granular layer to the stratum corneum and connects it to each particle to make the continuum. Consequently, migrations reduce and the structure becomes fixed.

Although there are no layers above the basal layer initially, a flat epidermis is formed in the analysis model in 45 days due to basal cell division; the basal cells only divide through Pattern 2 in this period. The basal layer has 900 cells (in a 30 by 30 particle square) initially, and the number of basal cells increases to 1,080 after 45 days—this is an increase of 20 %. The base model was analyzed under these conditions.

### 3.2 Aging Model

When human skin ages, the number of basal cells reduces and the cell division rate of the basal cells decreases [2]. In this paper, we simulate changing these two conditions for both aging and young epidermises.

Table 1 shows the analysis conditions. The model simulates aging as it changes from Case 1 to Case 3.

Table. 1 Analysis conditions of the number of basal cells and the cell division rate

| | Number of basal cells | Cell division rate [time/day] |
|---|---|---|
| Case 1 | 1260 | 0.2 |
| Case 2 | 900 | 0.2 |
| Case 3 | 900 | 0.1 |

The number of basal cells between two conditions, 1,260 and 900 cells, are compared. The fewer basal cells there are, the older the epidermis is indicated to be.

The cell division rate of the basal cells also uses two conditions; 0.2 and 0.1 cell divisions per day. The basal cell division rate of a normal epidermis is 0.2 time per day, while it is half that for an aging epidermis [2].

We analyzed the model for up to 100 days under these analysis conditions.

## 4. Results and Discussion

Fig. 4 shows the time variation of the base model (45, 60, and 100 days). From the results, undulations formed on the basal layer, and the undulations move and change in shape with time. In addition, the basal layer maintained shape of monolayer and separated the prickle layer and the dermis. Introducing the spring force enabled the base model to get these results. Besides, undulations formed by functions of each cell division pattern shown in Fig. 2 [13].

We compared the Fig. 4 results with the actual skin shown in Fig. 5 to verify the base model. As a result, the height of the undulations, the distance between the undulations, and thickness of epidermis of the model qualitatively corresponded to Fig. 5. Thus, the results of the model were similar to the actual epidermis. However, this paper did not consider the thickness of the stratum corneum because we will introduce a detachment model for it into the model in future work.

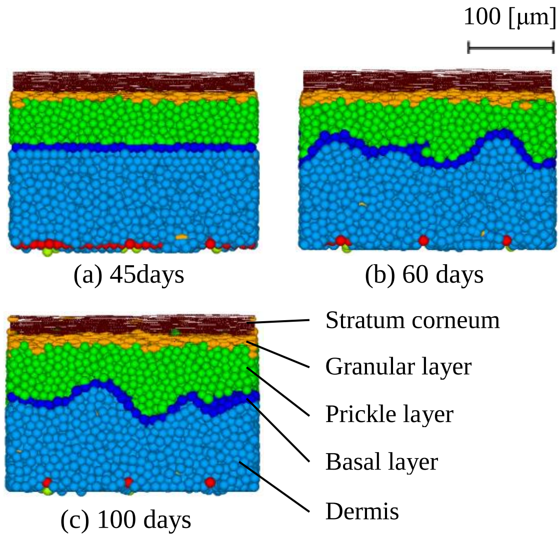


Fig. 4 Time variation of the analysis model

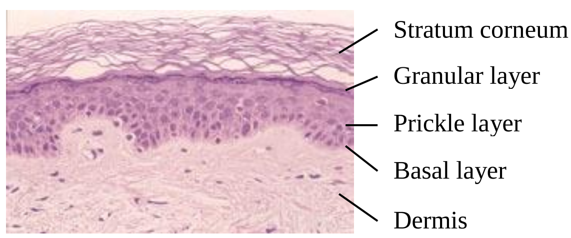


Fig. 5 Cross-section of the actual skin [17]

Subsequently, Fig. 6 shows the simulation results of aging and young epidermis. Case 1 indicates young epidermis, Case 2 and Case 3 mean aging epidermis.

The results changed in the thickness of the epidermis and the height of undulations from the base model. In contrast, the granular layer and the stratum corneum maintained a flat shape in spite of the height of the undulations. The shape was caused by the spring force in these layers simulating the strong cell junction.

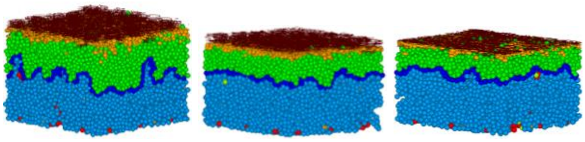


Fig. 6 Simulations of the aging and young epidermises

Fig. 7 shows the bottom view of the Fig. 6 results to give clear height and shape of undulations of model's internal. The red color indicates that the particle is moving upward, light green indicates it is stationary, and blue indicates it is moving downward.

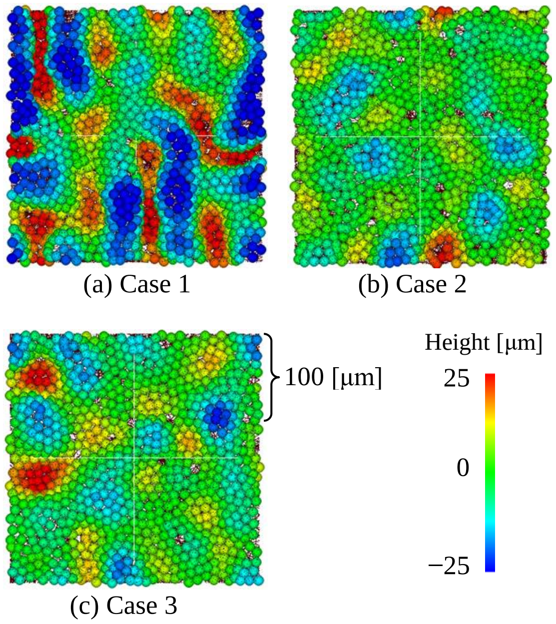


Fig. 7 Bottom view of the simulation results

The undulations in the basal layer structure became smaller and the epidermis thinned as the model adopted the aging conditions (from Case 1 to Case 3) in Figs. 6 and 7.

These characteristics agree well with what is observed in actual aging epidermises [2]. Moreover, the characteristics also appeared in actual abdominal skin shown in Fig. 8 [18]: (a) indicates young skin and (b) presents aging skin. For this reason, we could verify that the aging model qualitatively corresponded to the actual aging. In particular, the model was accurate with regards to the conditions set for the reduction in the number of basal cells and cell division rate.

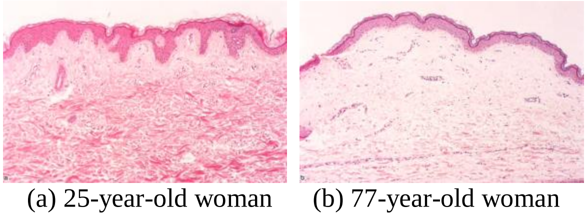


Fig. 8 Cross-section of abdominal skin [18]

The surface area of the basal layer became small due to the reduction in the number of basal cells. In other words, we consider that the undulations in cases 2 and 3 became small as there were not enough basal cells through which the undulations could form. In addition, the basal cells generate epidermal cells above the basal layer: as a result, these cells were fewer, thus creating a thinner epidermis.

Furthermore, in the cases where the basal cell division rate was low, the number of times that the basal cells generated epidermal cells also reduced. Undulations in the basal layer therefore became small and the epidermis became thin.

## 5. Conclusions

In this study, we introduced aging conditions into our model of the epidermis. Additionally, we also simulated and compared aging and young epidermises. In particular, we reduced the number of basal cells and the cell division rate of basal cells so as to simulate aging. As a result, the characteristics of an aging epidermis are demonstrated; smaller undulations in the basal layer were observed, and the epidermis became thinner.

Reducing the number of basal cells resulted in a smaller surface area for the basal layer as well as fewer epidermal cells generated. Furthermore, we consider that reducing the number of times that the basal cells generate epidermal cells to also be a factor in the reduction of the basal cell division rate.

When skin ages, the stratum corneum becomes thicker [2]. In future, we will look to examine the relationship between aging and the stratum corneum by introducing a detachment model for the stratum corneum into our model.

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