Numerical Simulation of Skin Formation: Modeling of Scale Peeling

Shu Oba¹ and Katsuya Nagayama¹,*

¹Kyushu Institute of Technology Graduate School, 680-4, Kawazu, Iizuka, Fukuoka, 820-8502, Japan

* Corresponding Author: nagayama@mse.kyutech.ac.jp, Tel&Fax 81-948-29-7778

Abstract

Skin is formed by cell division, and the cells eventually mature into corneums and drop off. This process is known as turnover. With normal turnover, skin disease rarely occurs. However, the disturbance of turnover leads to skin inflammation and associated effects such as scale formation. The mechanisms that underpin scale formation are not fully understood. This study analyses the impact of scale formation in atopic dermatitis using a numerical simulation. The numerical simulation model of the skin was constructed by theoretically setting the main parameters i.e. transepidermal water loss (henceforth TEWL) of atopic dermatitis, thereby allowing the elucidation of the mechanism of scale formation. As a result, thick corneum and scale of atopic dermatitis were successfully modeled. In addition, the variation of desmosome distribution in stratum corneum was shown to be associated with scale formation.

1. Introduction

There is growing interest in the beauty field and skin disease regardless of gender. The prevalence of skin disease is rising and is associated with an increase in active research projects [1]. For example, atopic dermatitis is a disease whose cause and mechanism have not been completely elucidated. Besides, an established treatment that leads to the cure of the patient is unavailable; most strategies focus on coping therapies. There is an urgent need to address the clarifying of the mechanism.

Skin is formed by the proliferation and the differentiation of cells, which mature into corneum and drop off. The elucidation of the formation process would provide insights into numerous other phenomena related to skin. Despite the importance of observing the formation process inside the skin, there remains a paucity of evidence on skin formation.

The main aim of this study is to investigate the numerical simulation model of skin formation using a particle method. The research data in this thesis is drawn from the analysis method under a range of experimental conditions. In 2018, the analysis method made it possible to change corneum thickness according to skin environment (e.g., TEWL) [2]. In our study, the developed model (verified in the past [3], [4]) was used to elucidate the mechanism of scale formation in cases of atopic dermatitis.
2. Analysis target
Skin can be roughly divided into three layers: subcutaneous tissue, dermis, and epidermis. Figure 1 shows a cross-sectional view of the skin. The epidermis is used in the analysis and is composed of the basal layer, stratum spinosum, granular layer, and stratum corneum. Skin cell proliferation occurs daily in the basal layer, followed by migration through the stratum spinosum, granular layer, and stratum corneum. The cells eventually mature into corneum and drop off. This whole process is known as turnover.

3. Methods

3.1 Calculation model

3.1.1 Particle method [6]
Particle method was used in this model. This method does not depend on mesh because it does not use mesh and treats calculation point as a moving particle. Each particle was regarded as a single cell. Body and spring forces work between particles. The balance of these forces contributes to particle movement.

3.1.2 Free water and combined water
The skin is combined with two types of water: free water and combined water. The free water can move free in the skin. In contrast, the combined water cannot move freely in the skin because of the combination with corneum cells.

3.1.3 Water concentration and peeling calculations [2]
Water concentration and peeling calculations were introduced to each particle.

Skin water (distinguished from sweat) evaporates through stratum corneum; this phenomenon is called the transepidermal water loss (TEWL). It depends on skin condition (i.e., dry or moist). TEWL is given as follows:

\[ \text{TEWL} = \frac{c_0}{D} + \frac{1}{h(1-\mu)} \]

Figure 1. A sectional view of the skin [5].
$c_0$ is the free water concentration at the deepest level of the stratum corneum. $l$ is the corneum thickness. $D$ is the water diffusion coefficient. $h$ is the evaporation coefficient and $\mu$ is the humidity. Equation (1) was derived from the relationship between TEWL and corneum thickness by our lab in 2018, referring to the problem of one-dimensional steady heat transfer. The skin free water concentration is given as follows (see also equation 1).

$$\frac{dc}{dx} = -\frac{TEWL}{D}$$

(2)

In equation 2, $c$ is represented the free water concentration and $x$ is the position from the deepest level of the stratum corneum to the stratum corneum surface.

Corneum cells are attached by proteins called desmosome, which is generated simultaneously with cornification and must be degraded for peeling to occur. The activity of the enzyme that degrades desmosome are water-dependent [7]. As can be seen from the equation 2 above, the desmosome concentration can be given as follows.

$$\frac{d\text{Desmo}}{dt} = -\frac{2.04}{7}\left\{r_1 \left(\frac{c}{c_0}\right) + r_2\right\}$$

(3)

In equation 3, $\text{Desmo}$ presents the desmosome concentration. While $t$ is the time, and $r_1 (= c_0 / (1 \times 10^{-12}))$ is the free water concentration at the deepest level of the stratum corneum. And, $r_2$ is the combined water concentration.

3.1.4 Scale model [8], [9]

The mechanism of scale formation has not been clarified. The solution was then assayed for the mechanism of scale formation using the scale model for calculating scale formation method. As shown in Figure 2, desmosome concentration and variation were chosen in this study. In the case of atopic skin, corneum particles attached on the corneum particle that desmosome is completely degraded are peeled together because desmosomes are more likely to be distributed (see Figure 3 below).

![Figure 2](image)

* Desmosome production is set to 1.
* Initial desmosome concentration is uniform.

![Figure 3](image)

* Desmosome production is small.
* Initial desmosome concentration varies.

**Figure 2.** Comparation of normal skin and atopic skin.

**Figure 3.** Scale formation method.
4. Analysis conditions

4.1 Initial setting

It can be seen from the data in Figure 4 that the analysis area is $300 \times 300 \times 300 \, \mu m^3$. The initial placement consists of blood vessels; dermis and basal layer from the bottom (see Figure 4). The boundary condition is a periodic boundary condition. Each particle is spherical, with a diameter of 10 $\mu m$. The shape of the particles changes in the layer above stratum spinosum; their thickness decreases, $c_0$, $r_1$, $r_2$ and $\mu$ are set to $0.4 \times 10^{-12} \, g/\mu m^3$, 0.4, 0.2 and 0.6, respectively.

![Figure 4. The initial placement of the analysis model.](image)

4.2 Parameters

In this analysis, the patterns of both atopic skin and normal skin were modeled and compared. Table 1 summarizes the parameters of the two skin conditions. The basal cells of atopic skin divide at twice the rate of those of normal skin [10]. Water diffusion coefficient $D$ in atopic skin is 10 times larger than that in normal skin because of the defect in skin barrier function. Evaporation coefficient $h$ in atopic skin is larger than that in normal skin because of dry skin. For these reasons, we have set out $D$ and $h$ properly. Initial desmosome concentration [8] and variation [9] in atopic skin are less and larger than those in normal skin respectively. The results of the analysis are summarised based on the following conditions in Table 1.

|                        | Normal skin | Atopic skin |
|------------------------|-------------|-------------|
| Division frequency [/day]| 0.2         | 0.4         |
| Water diffusion coefficient $D$ $[\mu m^2/s]$ | 0.1         | 1.0         |
| Evaporation coefficient $h \times 10^{-4}$ $[\mu m/s]$ | 0.268       | 3.95        |
| Initial desmosome concentration | 1           | 0.5 ~ 0.8   |

5. Results of analysis, and discussion

Figure 5 confirms that a thick stratum corneum is formed and sections of corneums are scattered (referred to as scale).
Figure 5. Analysis image of atopic skin.

Figure 6 confirms that more water is lost from atopic skin than normal skin due to the former’s drier property. Also, the results obtained from the analysis revealed that stratum corneum is thicker in atopic skin than normal skin. Atopic skin is lack of ceramide, which is an inter-keratinocyte lipid with a role in water retention. It is apparent from the figure that low levels of this lipid interfere with skin barrier function, leading to water loss and dry skin in individuals with atopic skin. This phenomenon corresponds to the results shown in Figure 6 below.

As can be seen in Figure 6, the plot of water loss versus time is undulating because the skin is repeatedly drying and wetting. It also shows an inverse relationship to the thickness of the stratum corneum, as shown in Figure 7. There is an interaction between the skin condition (dry or wet) and the corneum thickness and is well-documented. The balance of the skin can be maintained by adjusting the barrier function according to the external environment. As such, the results of this analysis are consistent with the real skin phenomenon.

The results, as shown in Figure 8, indicate that there is a relationship between the variation of desmosome distribution in stratum corneum and scale formation. It also demonstrates that the greater the variation of desmosome distribution in stratum corneum is, the higher the appearance rate of thick scale increases. From the obtained results, we can see that the skin is peeled easily. It is interesting to note that the variation of desmosome distribution is related to scale formation.
**Figure 6.** Transepidermal water loss (TEWL).

**Figure 7.** Corneum thickness.

**Figure 8.** Relationship between the variation of desmosome distribution and scale formation.
6. Conclusion

In this investigation, the aim was to model atopic dermatitis with a particle method. Regarding the analysis of the skin, the free water, combined water, water concentration calculation and peeling calculation were introduced in this study. The scale model (constructed by the relationship between desmosome concentration and variation) were introduced in the analysis model of atopic dermatitis. Suitable parameters for normal skin and atopic skin analyses were theoretically set.

The evidence from this study suggests that the introduction of free water and combined water can be contributed to the analysis of real skin which is closely related to real skin. Water concentration and peeling calculations brought the real skin turnover phenomenon. These data suggest that it was possible to reproduce the formation of thick stratum corneum and scale. The findings of this investigation on comparison of atopic skin and normal skin (e.g., TEWL or corneum thickness) show the degree of dryness of atopic skin. These findings have significant implications for the understanding of how the variation of desmosome distribution in stratum and corneum scale formation are associated.

References

[1] Nagayama M A 2004 Physica D Nonlinear Phenomena 194(3-4) 151-165
[2] Shobuda K and Nagayama K 2018 Proc. 9th TSME Int. Conf. on Mechanical Engineering (Phuket)
[3] Nagayama K Uehara T Amano Y and Tanahashi M 2015 J. Biosciences and Medicines 3 45
[4] Nagayama K Matsuoka S Morisaki N and Taguchi H 2015 J. Biosciences and Medicines 4 1
[5] Saita T 2009 Introduction to dermatopathology diagnosis, 2nd edition (Japan:Nankodo) 2
[6] Kurihara T and Nagayama K 2016 Proc. 7th TSME Int. Conf. on Mechanical Engineering (Chiang Mai)
[7] Koyama J 1999 J. SCCJ. 33 16
[8] Lee U H Kim B E Kim D J Cho Y G Ye Y M and Leung D Y M 2017 Br. J. Dermatol. 176 537
[9] Igawa S Kishibe M Honma M Murakami M Mizuno Y Suga Y Seishima M Ohguchi Y Akiyama M Hirose K Yamamoto A I and Iizuka H 2013 J Dermatol Sci. 72 54
[10] Watanabe M Tagami H Horii I Takahashi M and Kligman A M 1999 Arch. Dermatol. 127 1689