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論文題目　Contribution of
Skin Mechanical Properties
to Human Tactile Sensitivity

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Contribution of Skin Mechanical Properties to Human Tactile Sensitivity
（ヒト触知覚における皮膚力学特性の寄与に関する研究）

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by

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Abstract

The sense of touch holds a wide range of importance in our lifelong experience. Delicate tactile sensitivity has a notable effect on motor function than muscle weakness in the elderly, contributes to the alleviation of psychological fear and pain, and trigger the establishment of positive and harmonious communication with others. Unfortunately, touch is a sensation that undergoes significant changes throughout a lifetime, and even individuals with a delicate tactile sensitivity may not necessarily retain it due to aging, lifestyle, and environmental factors. To maximize the value of touch, it is crucial to understand the factors contributing to variability in tactile sensitivity. Research has mainly focused on the state of the sensory nervous system, but there is insufficient emphasis on studying the direct influence of the skin mechanical properties. The mechanical properties of the skin, such as thickness and hardness, dramatically change with aging and UV exposure, and they can also be plastically altered by skincare products and skin massage. By focusing on the understudied the skin condition, a better understanding of individual differences in touch can be achieved, leading to the improvement of diminished tactile sensitivity through interventions targeting skin mechanical properties. This study aims to investigate the contribution of skin mechanical properties to human tactile sensitivity.

In Chapter 2, we found that the individual differences in skin extensibility can explain the variations in tactile sensitivity. In previous measurements of tactile sensitivity, the contributions of the mechanical properties of the skin to tactile sensitivity have been unclear, as they have been confounded by the effects of anisotropy, heterogeneity, and the layered structure of underlying tissues such as muscles and bones. Therefore, we have clearly identified the mechanical properties of the skin surface that contribute to tactile sensitivity by locally deforming the skin using suction pressure as a tactile stimulus. Furthermore, by simultaneously measuring skin deformation during tactile stimulation, we were able to directly compare the actual skin deformation with participants' tactile sensitivity. We measured tactile sensitivity in participants aged 20 to 79 with various skin characteristics using psychophysical methods. The results revealed several key findings. Firstly, even when the same amount of pressure stimulation is applied, the degree of skin deformation varies among individuals. Secondly, there was also intra- and interindividual variability of tactile sensitivity, although age alone was not sufficient to explain this variability. Finally, the amount of skin deformation can explain the variability in tactile sensitivity both intra- and interindividuals. In addition, a characteristic relationship was observed in which intra- and interindividual differences in tactile sensitivity were greater when the skin deformation was relatively small.

In Chapter 3, we clarified that higher compliance of the stratum corneum enhances tactile sensitivity. The effect of skin condition on tactile sensitivity has primarily been investigated through skin hydration intervention experiments. However, while the skin mechanical properties, particularly the stratum corneum, undergo significant changes in response to humidity and skincare, the specific properties that contribute to tactile sensitivity have not been identified. Therefore, we conducted a randomized comparative trial in which the intervention group had moisturizing cream applied to their cheeks, while the control group had purified water applied. We measured changes in the properties of the stratum corneum alongside changes in tactile sensitivity. We utilized suction as a suction stimulation to isolate the contribution of the skin surface properties and simultaneously measured the skin deformation during the stimulation. The results showed that after 10 minutes of hydration, the dynamic modulus of the stratum corneum decreased, leading to an increase in skin compliance

during suction stimulation. Furthermore, tactile sensitivity significantly improved only in group that applied the cream.

In Chapter 4, we clarified the effect of skin stiffness and viscoelasticity on touch propagation between skin layers. Given that mechanical quantities such as strain at the epidermis-dermis interface correlate with the recorded sensory afferent firing terminating at mechanoreceptors, simulating mechanical quantities within the skin is useful for investigating skin contribution to tactile sensitivity. Therefore, we evaluated the effect and trends of changes in skin stiffness and viscoelasticity on the propagation of mechanical quantities when the skin deforms in a history-dependent manner. Firstly, based on experimentally obtained human skin deformation during high-frequency vibrations of 10 Hz, we developed finite element models that replicated the measured human skin deformation. Secondly, we showed that not only stiffness but also viscoelasticity markedly affected mechanical stimuli propagation in the skin, and that the effect differed depending on the layer. Particularly, greater immediate responsiveness of the dermis contributed to greater propagation of mechanical stimulus. Furthermore, we observed the phenomenon of the accumulation of strain energy within the skin in response to vibrational stimuli.

The contribution of the present study can be summarized as follows. Firstly, by applying localized stimuli to the skin using suction pressure, we elucidated the relevance of skin extensibility to tactile sensitivity while eliminating the influence of skin complexity. Secondly, through limited interventions and detailed dermatological evaluations, we clarified the extent of the influence of the stratum corneum on tactile sensitivity. Finally, we provided a mechanical interpretation of how changes in skin stiffness and viscoelasticity affect the information received by mechanoreceptors by developing sophisticated models that reproduce history-dependent skin deformation. We quantified the previously unexplored impact of skin viscoelasticity, thus demonstrating the high importance of skin's mechanical properties in the tactile perception pathway. These findings provide a universal interpretation of the contributions of skin mechanical properties to touch and valuable insights for effectively regulating the skin condition and evoking a fine tactile sensation.

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Chapter 1

Introduction

1.1 Significance of touch

This section presents the value and significance of touch experiences that go beyond sensing the external and internal environments, highlighting their relevance to everyday life.

Humans perceive various external stimuli such as pressure, vibration, and temperature through the skin to obtain sensory information such as the shape and texture of objects that come into contact with the skin. Furthermore, we make judgments, remember, learn, and move based on such sensory information input to the brain. Tactile sensation is not only to generate pain sensation and warnings for biological defense, but is also essential for us to realize appropriate communication with objects, self, others (Hertenstein et al., 2009; McGlone, Wessberg, and Olausson, 2014). The importance of tactile sensation is reviewed below from the viewpoints of motor function, cognition, physical physiology, and sociality (Figure 1.1).

Tactile sensation contributes to proper motor function. In order for the elderly to continue to live independently, it is important to prevent the decline of physical functions necessary for independent living. It has been reported that hand motor function is an important factor in the decline of activities of daily living, affecting eating, dressing, and writing (Shiffman, 1992). Then, in an experiment to measure hand motor function in elderly females certified in need of low level of care, tactile sensitivity and reaction time were found to be more correlated than hand muscle strength such as grip strength (Yasuda, Murata, and Murata, 2010).

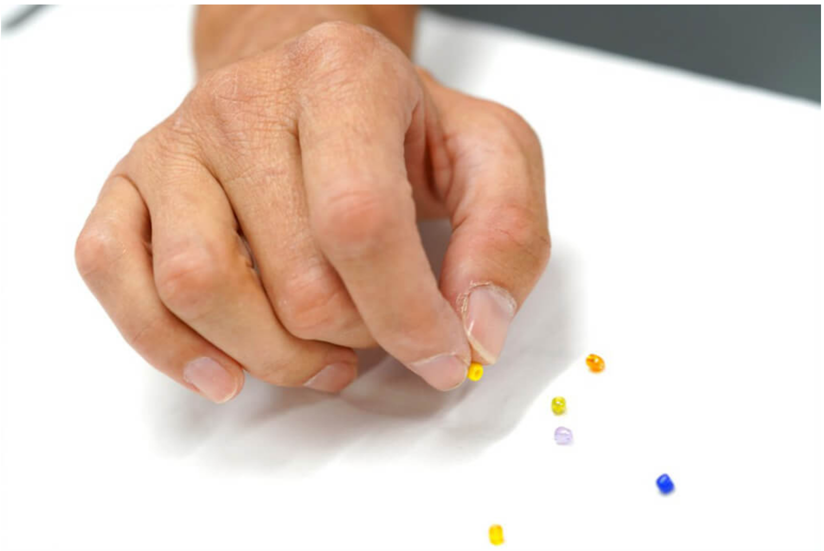
Tactile sensation also influences the cognition of external stimuli. There are surface roughness properties that we find pleasant when we touch the texture of a material (Verrillo, Bolanowski, and McGlone, 1999), and neuroscientific research approaches have experimentally demonstrated that tactile stimulation with gentle stroking at a certain speed induce pleasant sensations (Löken et al., 2009), and that the deep pressure produced during hugging and massaging is also perceived as pleasant and calming (Case et al., 2021). Highly empathic participants evaluated human social touch as inducing more pleasant emotions (Peled-Avron et al., 2016). Furthermore, as a function of emotional response regulation in the face of stressors, the brain neural activation to the threat of electric shock was shown to be attenuated when the hand is held by the spouse (Coan, Schaefer, and Davidson, 2006). Comforting touch involving distress-alleviating behaviors of an observer towards the suffering of a target is also known (Inui, Tsuji, and Kakigi, 2006; Fleisher et al., 2014; Goldstein et al., 2016; Shamay-Tsoory and Eisenberger, 2021).

Tactile sensations affect not only our emotions, but also our objective physiological state. The role of tactile affection on physiological variables such as blood pressure and heart rate was investigated. For example, individuals who received pre-stress partner contact with their partners before stress demonstrated significantly lower systolic and diastolic blood pressure (Grewen et al., 2003) or lower cortisol than the no contact group. Women who received physical partner contact before stress exhibited significantly lower cortisol and heart rate responses to stress (Ditzen et al., 2007). Warm touch also changes hormone status and contributes to appropriate control of depressive symptoms (Holt-Lunstad, Birmingham, and Light, 2008; Holt-Lunstad, Birmingham, and Light, 2011). Given such results, it seems plausible to conclude that affectional physical behavior contributes to lower reactivity to stressful life events.

The effect through tactile sensation is not limited to the self, but spreads to the relationship with humans and even society at large. A review by gallace summarizes well that interpersonal tactile stimulation is an effective means of influencing people's social behavior (Gallace and Spence, 2010). For example, in a supermarket, when customers are touched by an experimenter posing as a clerk, they are far more likely to respond positively to requests to sample and purchase food than when no one touches them (Hornik, 1992). Students' evaluations of the library were found to be more favorable when the librarian made physical contact with the student by placing his or her hand directly on the student's palm when returning the student's library card. Interestingly, this effect occurred even though none of the students remembered being touched by the librarian (Fisher, Rytting, and Heslin, 1976). Tactile sensation can also directly transmit emotions. Participants could decode anger, fear, disgust, love, gratitude, and sympathy via touch at much-better-than-chance levels and accurately decode distinct emotions by merely watching others communicate via touch (Hertenstein et al., 2006). Emotional touch, for example, can be a remarkable medium to intuitively close the distance with a romantic partner, thereby increasing intimacy and supporting the partner (Chatel-Goldman et al., 2014). Also, neuroscience research has shown that the somatosensory cortex, a brain region classically thought to be responsible for body surface touch, contributes to the ability to empathize with pain (Singer et al., 2004; Bufalari et al., 2007) and non-painful touch (Keysers et al., 2004; Schaefer, Heinze, and Rotte, 2012). In fact, tactile acuity from two-point discrimination was also found to be positively correlated with empathy (Schaefer, Joch, and Rother, 2021; Schaefer et al., 2022). A link to tactile sensation has also been shown with respect to individual behavioral characteristics. It has been hypothesized that introverts have persistently higher cortical arousal than extroverts, and that as a result, introverts should have lower sensory thresholds in the ascending reticular activating system due to intrinsic impulses that facilitate the potentials evoked by sensory system stimulation (Eysenck, 1963). Interestingly, it has been shown that introverts actually have lower auditory and tactile thresholds (Edman, Schalling, and Rissler, 1979).

The significance of touch has been revealed through subjective reports and objective measurements in various scenarios. It has become evident that touch, which directly interacts with the skin, can provide unique experiences in terms of motor function, cognition, physical physiology, and sociality. While vision tends to dominate in terms of information processing, touch supports fundamental human activities. In recent years, quantitative associations have begun to emerge between touch and factors that may not seem directly related to skin, such as personality and sociability. It is conceivable that the scope of the contribution of touch to human life is immeasurably vast.

A further aspect to contemplate is the individual variability in the benefits derived from touch. Human beings exhibit a remarkable diversity, with individuals of different ages, lifestyles, and cultural backgrounds potentially possessing distinct sensory processing systems. It is widely acknowledged that the effects of touch can vary significantly based on the context of the stimulus and the specific individual receiving it (Coan, Schaefer, and Davidson, 2006; Saarinen et al., 2021). It is important to understand that sensory structures associated with touch, which are closely related to individual preferences, are highly complex. Additionally, there may be a relationship between an individual's perception of external stimuli and their personality traits. Regarding the connection between touch and sociability mentioned earlier, it has been reported that the activity level of central regions involved in individual information processing, such as the somatosensory cortex, is related to individual differences in empathy (Gazzola, Aziz-Zadeh, and Keysers, 2006; Schaefer, Heinze, and Rotte, 2012). Based on the above, in the era of an aging society and diversity, it is important to discuss individuals' sensory experiences while understanding their unique backgrounds because these experiences are not visible. This approach may gain attention as a valuable avenue for research.



Fine motor functions (e.g., training to pick up small beads) are greatly supported by tactile input information. Image adapted from (Inanici et al., 2021).

Affective touch (e.g., holding hands, tender stroke, and hug) provides health and social benefits. Image adapted from (Cohut, 2018).

FIGURE 1.1: Tactile sensations that underpin daily life.

Touch, which directly interacts with the skin, can provide unique experiences and values in terms of motor function, cognition, physical physiology, and sociality.

1.2 Sensory pathway of touch

This section focuses on the mechanism of touch and the sensory pathway through which it occurs, specifically emphasizing the sensations that arise on the superficial layers of the skin.

The perceptual pathway through which humans process mechanical stimuli given to the skin as tactile sensations is composed of multiple elements (Biga et al., 2023) (Figure 1.2). Regarding the perceptual pathway, it can be divided into three phases: the detection phase, the transduction phase, and the integration phase.

Firstly, in the detection phase, mechanoreceptors and sensory nerves in the skin detect stimuli from the environment. The skin has a structure consisting of four layers in order from the surface of the body: the stratum corneum, epidermis, dermis, and subcutaneous tissue (Figure 1.4). Sensory nerve endings generally project to the dermis layer, extending in a fibrous bundle-like manner or branching out. Mechanoreceptors and nerve terminals that directly receive mechanical stimuli via the skin have very distinctive functions and morphologies, and contribute to the characteristic neural responses. The long peripheral axon that transmit tactile sensation include Aβ fibers innervates specialised end organs (Merkel, Ruffini, Meissner, and Pacinian types) and C fibers that end in free nerve endings in the dermis and epidermis. Mechanical stimuli given to the skin are received by mechanoreceptors, converted into electrochemical signals in connected sensory nerves, a process that has recently been elucidated at the molecular and cellular levels (Lumpkin and Caterina, 2007; Hao et al., 2015; Handler and Ginty, 2021; Maksimovic et al., 2014; Nikolaev et al., 2020; Neubarth et al., 2020). The relationship between the neural responses and the mechanical quantities generated inside the skin has been investigated to find out what exactly are the mechanical stimuli that skin mechanoreceptors receive. In general, skin mechanoreceptors are observed to be more sensitive to various strain patterns than to stress distributions (Phillips and Johnson, 1981; LaMotte and Srinivasan, 1987a; LaMotte and Srinivasan, 1987b; Srinivasan and LaMotte, 1987; Srinivasan and Dandekar, 1996; Edin and Johansson, 1995). Furthermore, these mechanoreceptors are located in the skin at positions that are structurally sensitive to such mechanical quantities (Maeno, Kobayashi, and Yamazaki, 1997; Maeno, Kobayashi, and Yamazaki, 1998; Shinoda, 2002). The mechanical quantities that propagate in the skin contributes to tactile sensation, especially as they relate to skin stretching, indicating that skin mechanical properties and tactile sensation are closely related.

Secondly, in transduction phase, the electrochemical signal transmitted from the mechanoreceptors triggers nerve firing in the connected sensory nerves, which are then conveyed as electrical impulses through the dorsal root ganglia to the spinal cord. There are various patterns of nerve firing associated with the different types of mechanoreceptors (Johnson, 2001), and these patterns can vary based on the frequency response characteristics (Gescheider, Bolanowski, and Hardick, 2001) and the size of the receptive fields (Johansson and Vallbo, 1983). The specialised endings serve to mechanically magnify or filter the forces imposed on the skin. What elementary sensations humans experience have been investigated by inserting tungsten microelectrodes into the median and ulnar nerve bundles supplying the skin of the fingers and performing intra-neural microstimulation (Ochoa and Torebjörk, 1983; Ochoa and Torebjörk, 1989). For example, intermittent tapping was elicited in rapidly adapting nerves terminating in Meissner corpuscles, vibration and tickling in immediate-adapted nerves terminating in Pachinian corpuscles, and compression in slowly adapting nerves connected to Merkel cells.

Finally, in the integration phase, the electrical signals transmitted along sensory nerves are processed and integrated. The neural axons enter the spinal cord and then enter the posterior column nuclei, where they are relayed and processed by intermediate neurons. They ascend through the brainstem and input to the thalamus. From here, they reach the primary somatosensory cortex in the cerebral cortex where information processing occurs. Furthermore, they are then transmitted to the adjacent secondary somatosensory cortex where higher-level feature extraction and sensory integration take place. The spinal cord is known to involve information processing, such as the gate control theory (Melzack and Wall, 1965), in which sensory information transmitted from Aβ fibers and C fibers to the spinal cord is regulated. It has been found that stroking the skin can alleviate pain on the skin, and scratching the skin can suppress itching, revealing their effects and mechanisms (Yosipovitch et al., 2007; Dong and Dong, 2018; Cevikbas and Lerner, 2020). In addition, there seem to be higher-order stages of processing, such as cortical excitations, which may play a role. Cognitive psychology research has shown that the presence or absence of visual attention can influence the two-point discrimination threshold (Kennett, Taylor-Clarke, and Haggard, 2001). The timing of cardiac and respiratory cycles has been reported to impact sensory threshold for weak electrical currents (Motyka et al., 2019; Al et al., 2020; Grund et al., 2022; Galvez-Pol et al., 2022).

1.3 Lifetime change in touch

This section summarizes the changes that occur in tactile sensation itself, as well as the skin and sensory nervous system that comprises the sensory pathway of touch, in response to daily environmental factors and throughout a person's lifetime.

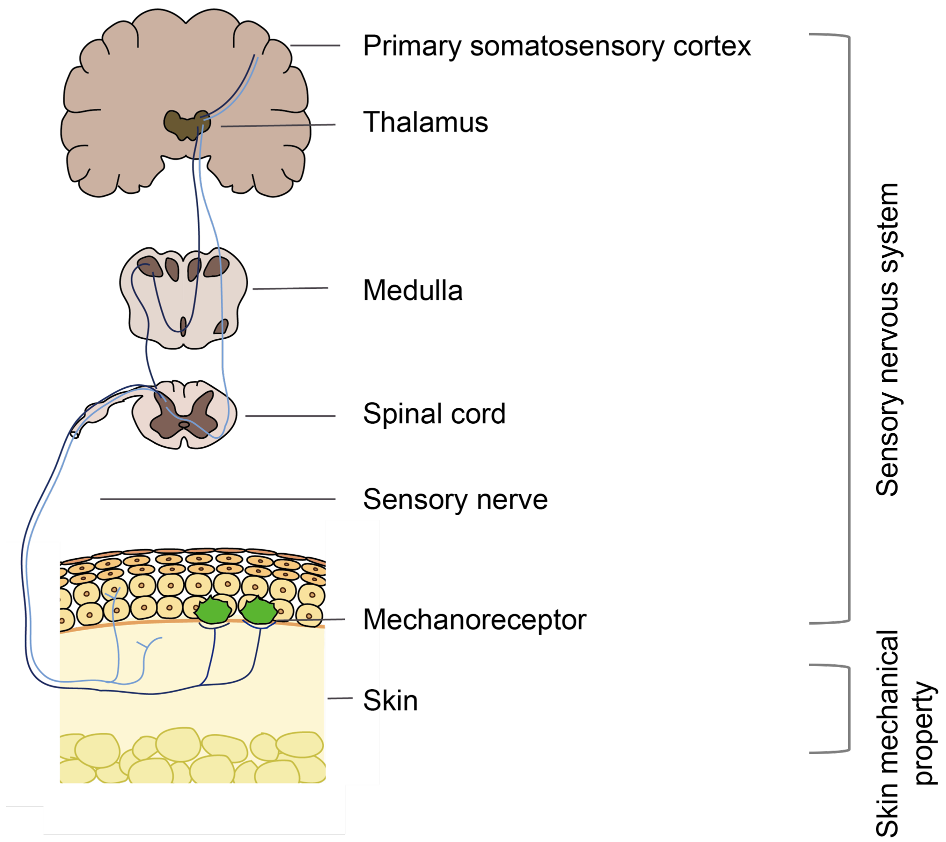


FIGURE 1.2: Perceptual pathways of tactile stimulus transmission.

The perceptual pathway through which humans process mechanical stimuli given to the skin as tactile sensations is composed of multiple elements. Regarding the perceptual pathway, it can be divided into three phases. Firstly, in the detection phase, mechanoreceptors and sensory nerves in the skin detect stimuli from the environment. Secondly, in transduction phase, the electrochemical signal transmitted from the mechanoreceptors triggers nerve firing in the connected sensory nerves, which are then conveyed as electrical impulses through the dorsal root ganglia to the spinal cord. Finally, in the integration phase, the electrical signals transmitted along sensory nerves are processed and integrated.

1.3.1 Skin mechanical property and sensory nervous system

First, we describe how the skin changes in response to daily environmental factors and throughout a person's lifetime, with a particular focus on the physical states and mechanical responsiveness that are likely to directly contribute to tactile detection. The mechanical response characteristics of the skin have been extensively studied, and it is well-documented that elasticity is lost with aging (Kim, Kim, and Lee, 2018; Luebberding, Krueger, and Kerscher, 2014; Takema et al., 1994; Bader and Bowker, 1983), particularly in terms of elastic recovery (Krueger et al., 2011; Escoffier et al., 1989). Dermatohistologically, degradation of elastic fibers is observed with aging (Daly and Odland, 1979; Braverman and Fonferko, 1982; Ritz-Timme, Laumeier, and Collins, 2003). Skin thickness increases until maturity and decreases for women over 50-60 years old and Young's modulus increases linearly with age (Diridollou et al., 2001). The regular exposure to ultraviolet radiation also has an impact on the skin, causing a decrease in collagen fibers and abnormal elastin morphology (El-Domyati et al., 2002) (Figure 1.3), leading to a decrease in elastic mechanical response properties. The compliance of the stratum corneum, the outermost layer of skin, can vary daily depending on the ambient humidity (Egawa et al., 2002; Egawa and Tagami, 2008). In winter, the skin becomes thinner compared to summer, with lower epidermal hydration and decreased elasticity (Uchegbulam et al., 2022). Psychological factors also have an impact on the surface properties of the skin, as skin hydration increases due to autonomic arousal in response to stress (Jacobs et al., 1994). People who are more prone to experiencing short-term stress tend to have higher levels of facial sebum and a greater population of propionibacterium acnes (Tanida, Katsuyama, and Sakatani, 2007). Remarkably, being directly exposed to the external environment, the mechanical characteristics of the skin are influenced by various factors in both the long-term and short-term.

Next, we describe how the sensory nervous system changes in response to daily environmental factors and throughout a person's lifetime. Age-related changes in the nervous system have been observed in the peripheral and central regions, respectively (Decorps et al., 2014; McIntyre et al., 2021). With aging, there is an overall decrease in the number of nerve fibers in the dermis, epidermis, and spinal cord roots, a decrease in the conduction velocity and amplitude of the compound action potential of sensory neurons, and degeneration of both myelinated and unmyelinated fibers in the peripheral nerves is also well known. Decreased density (Bolton, Winkelmann, and Dyck, 1966; García-Piqueras et al., 2019), and reduced function (Michel et al., 2020; Wu et al., 2011) of mechanoreceptors in nerve endings are also known. In the central nervous system, there is a loss of myelin and neurons with associated brain weight loss, and changes in cerebral blood flow and metabolism have also been observed with aging.

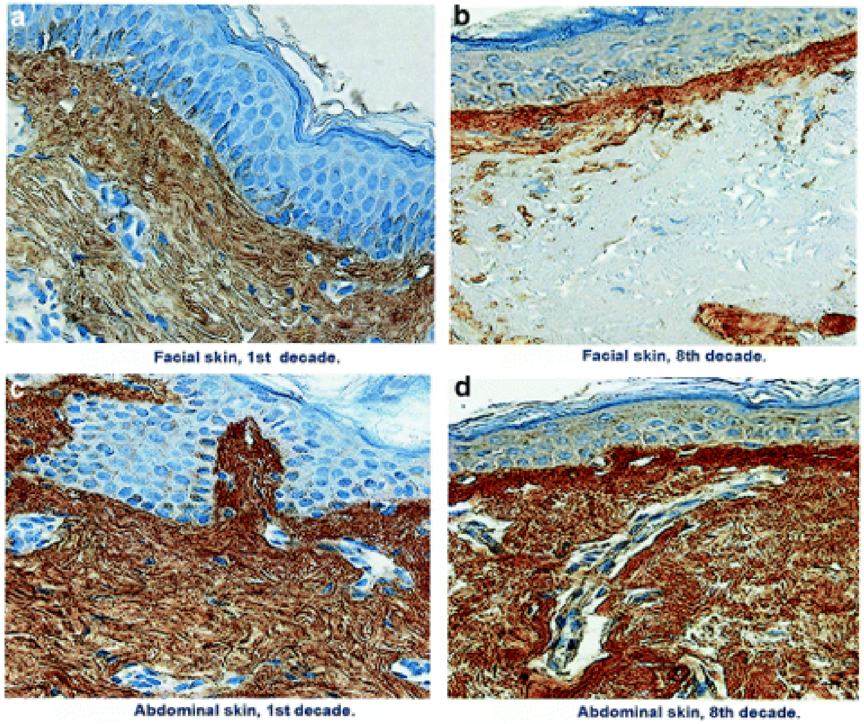


FIGURE 1.3: Human skin shows dramatic structural and compositional changes over lifetimes.

Immunohistochemical visualization of type III collagen in facial vs. abdominal skin in biopsies obtained from a 6-year-old female (1st decade) and a 77-year-old male (8th decade). Biopsies taken from the face revealed noticeable decrease in epidermis thickness and amount of collagen with age. (Original magnifications, ×400). Image adapted from (El-Domyati et al., 2002).

1.3.2 Tactile sensation

We here explain how tactile sensation itself changes in response to daily environmental factors and throughout a person's lifetime.

Tactile sensation is not a uniform feature, but varies widely among individuals and even within individuals. As mentioned earlier, it is becoming increasingly evident how crucial and intimately involved touch is in our lives. However, the benefits of touch may vary depending on the sensitivity of the tactile system at a given moment. In this section, we discuss research related to the variability of tactile sensation. The so-called discriminative touch, which asks whether touch is perceived or not, is a lower-order sense that is not easily affected by the context of the stimulus, and is therefore easy to quantify. There have been many efforts to quantify tactile sensation for a long time. Studies on tactile performance are often conducted using aging as an indicator, showing well known declines in the ability to detect light touch and vibration, and to discriminate roughness, distance between spatial features, and direction of movement (McIntyre et al., 2021).

The direct relationship between the changes in tactile sensation and the states and functional changes of the constituent elements of the sensory pathway, as mentioned earlier, is mainly discussed from the perspective of the sensory nervous system. There have been several reports on the relationship between nervous system alterations and tactile sensation in terms of nerve response (Schmidt, Wahren, and Hagbarth, 1990), nerve density (Van Boven and Johnson, 1994; Besné, Descombes, and Breton, 2002), mechanoreceptor density (Kennedy et al., 2011b; Skedung et al., 2018; Gescheider and Wright, 2021), nerve conduction velocity (Palve and Palve, 2018; Fukumoto et al., 2023), and somatosensory cortical areas (Pascual-Leone and Torres, 1993; Elbert et al., 1995). However, the clear mechanism that physiological and perceptual changes remains elusive, with contrasting results (Bruce and Sinclair, 1980; Bruce, 1980; Kalisch et al., 2009).

The influence of skin mechanical properties on changes in tactile sensation is beginning to be phenomenologically confirmed. It has been shown that the ease of deformation of the skin on the fingers is related to the perception of object hardness (Li and Gerling, 2021) and can partially explain the perception of spatial gaps in objects (Vega-Bermudez and Johnson, 2004). The influence of skin biomechanical properties on tactile perception has primarily been investigated through hydration interventions on the skin. For example, it has been demonstrated that increased skin hydration improves two-point discrimination ability (Lévêque et al., 2000) and enhances surface texture discrimination through an increase in the coefficient of friction between the finger and the texture surface (Skedung et al., 2018). Furthermore, studies have investigated long-term changes in the mechanical properties of the skin due to the use of skincare products and their impact on surface texture discrimination abilities (Aimonetti et al., 2019). On the other hand, on study found that skin hydration did not affect vibrotactile detection thresholds but did affect the perception of textured surfaces (Verrillo et al., 1998). There is also an example of non-woven fabrics that improve the ease of Braille tactile reading by reducing friction (Doi et al., 2004). These examples suggest that the mechanism of skin biomechanical influence on tactile sensation may vary depending on the physical scene. In recent years, it has become clear that neural firing responses are influenced not only by the current load applied to the skin but also by preceding load changes (Saal, Birznieks, and Johansson, 2023). There is a growing focus on the contribution of the skin in understanding the mechanisms of influence on tactile sensation.

1.4 Motivations

This section highlights the motivation behind our focus on skin mechanical properties for maximizing the value of touch by improving or maintaining tactile sensitivity.

In our lifelong experience, the sense of touch holds paramount importance and is a sensation that we strive to maintain in an optimal state. As discussed in Chapter 1.1, tactile sensitivity has a notable impact on motor function, even more so than age-related decline in muscle strength among older adults. Additionally, social contact contributes to the alleviation of psychological fear and pain, as well as to the mitigation of depression. Furthermore, the effects mediated through touch extend beyond the self and have been found to influence social aspects such as the establishment of interpersonal relationships, serving as a catalyst for fostering positive and harmonious communication with others.

However, as mentioned in Chapter 1.3, touch is a sensation that undergoes significant changes throughout a lifetime, and even individuals with a delicate tactile sensitivity may not necessarily retain it due to aging, lifestyle, and environmental factors. Although it is essential to investigate the direct factors contributing to sensory changes, it should be noted that not all factors are fully understood by focusing solely on the steps involving the conversion of mechanical stimuli into electrical signals, the transmission of signals, and the integration of signals within the sensory nervous system.

The skin in the pre-stage of the sensory nervous system is an aspect that deserves further investigation and holds potential effects on sensation (Figure 1.2). Tactile stimuli come into contact with the skin, leading to its deformation, and the mechanical quantities generated by this deformation are transmitted to mechanoreceptors. Naturally, the mechanical properties of the skin would influence this process, although the complexity of these interactions has not been clearly elucidated. In the case of vision, plenoptic functions used to create computer models of visual environments are typically described by a finite set of seven dimensions (Adelson and Bergen, 2020). However, in the context of touch, the mechanical properties of the skin give rise to plenhaptic functions with an infinite number of dimensions (Hayward, 2011). For vision, the retina, which is limited in size, and does not typically deform, is the interface between the environment and the sensory system. For touch, the interface is the skin, which, in contrast, is distributed over the entire body, and physically deforms in response to stimulation (Maallo et al., 2022). It becomes challenging to simplify the interaction between objects and the skin into a finite number of dimensions without oversimplifying the complexity of this interaction. Additionally, a simulation of the response of all afferent nerves innervating the glabrous skin of the hand has been developed (Saal et al., 2017), but it is based on deformations of a homogenized skin model.

We focus on the mechanical properties of the skin as a crucial component of tactile sensation, recognizing the challenges involved while highlighting its significance (Figure 1.4). It has been indicated and emphasized in academic literature that the skin holds potential for sensory perception, including how the skin tissue propagates and filters mechanical forces (Wickremaratchi and Llewelyn, 2006; Decorps et al., 2014; Handler and Ginty, 2021; McIntyre et al., 2021). Indeed, individual differences in tactile sensation are suggested to be more influenced by the state of peripheral function rather than central function (Schmidt, Wahren, and Hagbarth, 1990; Schmidt and Wahren, 1990; Gescheider et al., 1996). In other words, it is suggested that the quality of the process leading from the skin surface to the firing of peripheral nerves can significantly affect tactile sensation. This topic has become the focus of several recent studies (Li and Gerling, 2021; Saal, Birznieks, and Johansson, 2023). From a dermatological perspective, the mechanical properties of the skin exhibit disparate characteristics not only between individuals but also within individuals, showing marked changes over short and long periods of time, as mentioned in Chapter 1.3.1. In comparison to the intricacies of the sensory nervous system, the skin's mechanical properties offer a promising research target with potential solutions and interventions.

If we can clearly establish the contribution of skin mechanical properties to tactile sensation and advance applied research in this area, it holds the potential for significant contributions across multiple industries. In the cosmetics industry, it is possible to approach tactile sensation by altering the mechanical properties of the skin through skincare and massage. Application of moisturizers or surfactants changes the dynamic elastic modulus of the stratum corneum (Takahashi et al., 1984). The loss of elasticity associated with aging can be restored by facial massage (Iida and Noro, 1995). Four weeks of retinol treatments increased epidermal thickness, and protein expression of procollagen I and procollagen III (Kong et al., 2016). The ability to directly target the skin is a strong advantage when it comes to excessively dry or aging skin. This approach not only contributes to improving the appearance of issues like dark spots but also opens doors for developing products aimed at providing a new sensory experience through targeted care. In the ingestible industry, similar potential can be expected to capture new markets. A collagen supplement improves skin hydration, elasticity, roughness, and density (Bolke et al., 2019). Furthermore, it may contribute to medical diagnostics. Skin sensation, which reflects the characteristics of peripheral nerves, is known as a simple tactile diagnosis of neurological diseases and other conditions (Yang et al., 2010; Yang et al., 2015; Frade et al., 2022), but its accuracy could potentially be enhanced. Moreover, demonstrating the importance of the sensory aspect of the skin can also contribute to advancements in the field of engineering. Tactile feedback technologies, aimed at VR experiences, seek to convey more detailed information by utilizing an approach that goes beyond the previously focused sense of force and includes the sensory aspect of the skin (Minamizawa et al., 2007; Porquis et al., 2014; Leonardis et al., 2015; Fani et al., 2018). Taking into account the individual characteristics of different skin conditions, providing sensory stimulation to the skin can further enhance the sense of realism.

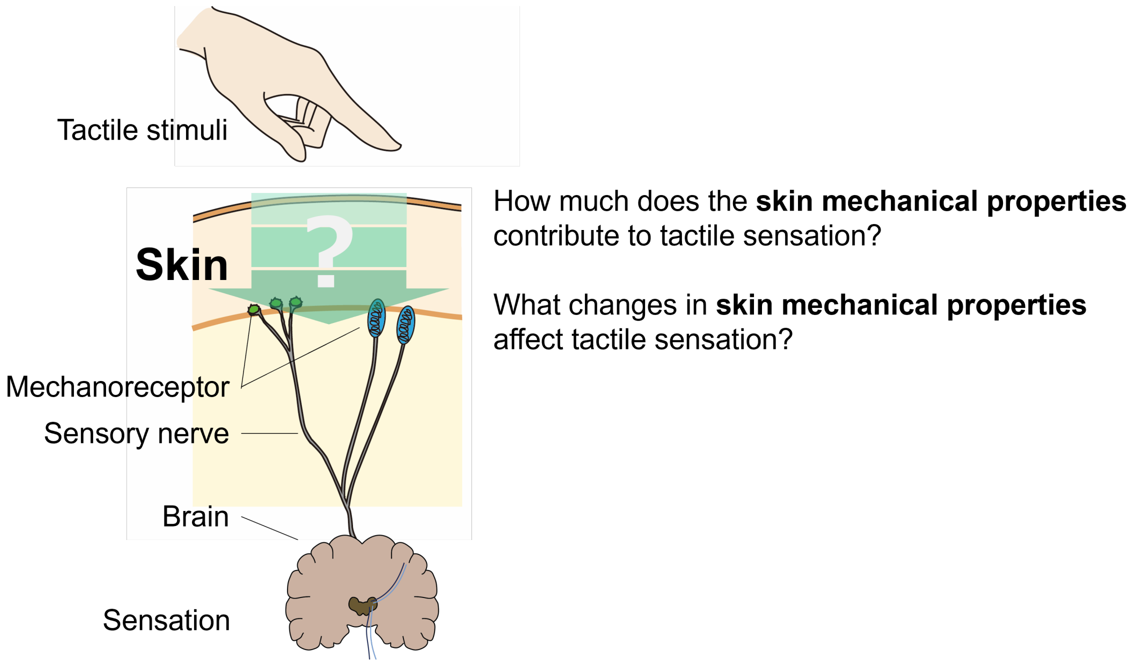


FIGURE 1.4: The focal point in this thesis.

This thesis emphasizes the crucial significance of incorporating the mechanical properties of the skin to uphold tactile sensitivity and maximize the value of tactile sensation. While changes in tactile sensation throughout an individual's lifespan have been acknowledged, the mechanisms have predominantly centered on the sensory nervous system. Yet, the role of skin mechanical properties in shaping tactile sensation has been largely overlooked, despite substantial inter-individual variability. By focusing on the understudied the skin condition, a better understanding of individual differences in touch can be achieved, leading to the improvement of diminished tactile sensitivity through interventions targeting skin mechanical properties.

1.5 Objectives

This study aims to investigate the contribution of skin mechanical properties to human tactile sensitivity towards building foundational knowledge for maximizing the value of touch. The structure of this thesis is shown in (Figure 1.5).

In chapter 2, we confirm the relationship between skin surface deformation and tactile sensitivity. While there have been several studies that qualitatively demonstrated the relationship between skin and tactile sensation from the perspective of mechanical response, it remains unclear how tactile sensation is affected by the different physical properties of the skin. This is because the physical phenomena occurring in the skin during contact with the object have not been observed. In order to understand the mechanisms of the skin's contribution to tactile sensation, it is necessary to elucidate the direct relationship between skin deformation and tactile sensitivity. We have developed a device that can measure the amount of skin surface deformation while tactile sensation occurs. Furthermore, we have ensured that the device can capture the influence of superficial skin rather than deep tissues such as muscles and tendons by suction. Targeting participants of diverse ages with varying skin characteristics, we aim to correlate skin mechanical properties with tactile sensitivity.

In chapter 3, we investigate the contribution of stratum corneum compliance to tactile sensitivity. Building upon the findings of relationship between skin condition and tactile sensation in Chapter 2, this chapter examines the specific contributions of the skin mechanical properties to tactile sensitivity through intervention trials on human. Previous research has shown that the mechanical properties of the skin and tactile sensation change depending on the type of water applied to the skin, but the specific mechanical properties of the skin have not been identified. Particularly, the mechanical properties related to the moisture content and roughness of the stratum corneum vary due to skincare and environmental factors. Therefore, it is crucial for us to utilize precise dermatological measurement techniques and study the quantifiable effects of the mechanical properties of the stratum corneum in order to develop appropriate interventions.

In chapter 4, we simulate mechanical propagation of vibratory stimuli between skin layers to assess the effect of skin stiffness and viscoelasticity. Chapter 2 and 3 confirmed the phenomenon that the skin mechanical properties affect tactile sensitivity, however, the mechanisms within the sensory pathway are still unknown. To reveal this, a skin finite element model based on the actual mechanical response of human skin, and the propagation of tactile stimuli from the skin surface to mechanoreceptors through the physical filter of the skin is examined. This approach advances previous simulation studies, which mainly treated the skin as linear elastic in static analysis, by focusing on the skin viscoelasticity, which represents individual differences. Along with the human tests (Chapter 2 and 3), the implications of this simulation finding for the contribution of skin viscoelasticity to tactile sensation are discussed.

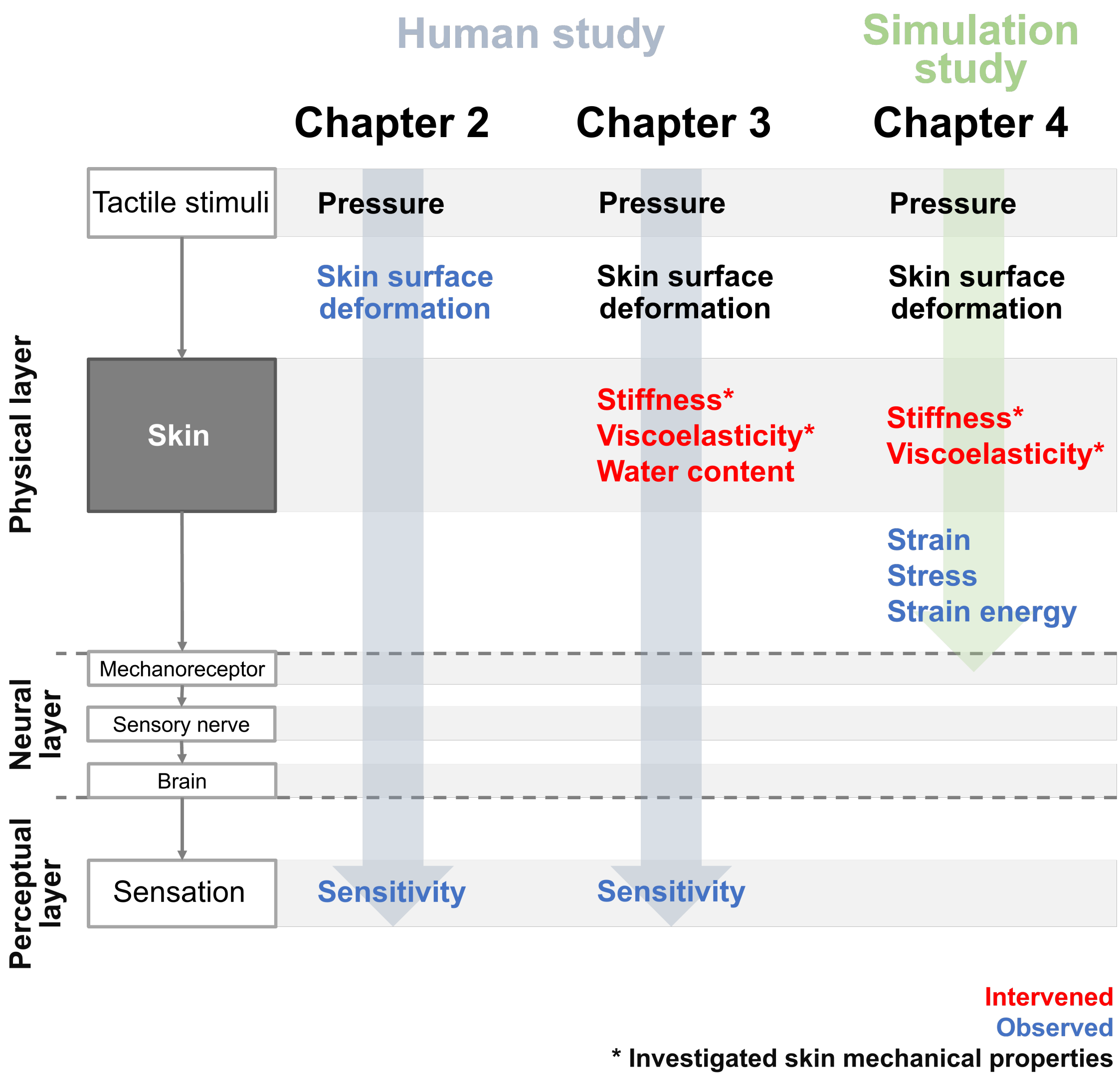


FIGURE 1.5: The structure of this thesis.

This thesis is structured into three chapters, and this diagram illustrates the position of each chapter within the sensory pathway from the transmission of tactile stimuli through the skin to the sensation. Each chapter indicates the measured elements in the tactile sensory pathway. Chapters 2 and 3 involve studies conducted on humans, while Chapter 4 utilizes a simulation model based on the measured human skin deformation behavior. In Chapter 2, the relationship between the magnitude of skin deformation in response to tactile stimuli and the resulting tactile sensation was observed. Chapter 3 focused on observing the changes in tactile sensation through hydration-induced interventions in skin stiffness and viscoelasticity. In Chapter 4, simulations were conducted to observe the strain, stress, and strain energy density received by mechanoreceptors by intervening in skin stiffness and viscoelasticity.

Chapter 2

Confirming the Relationship between Skin Surface Deformation and Tactile Sensitivity in Response to Vibratory Stimuli

2.1 Introduction

The objective of this chapter is to investigated the relationship between skin surface deformation and tactile sensitivity, as an initial step towards investigating the contribution of skin mechanical properties to touch. Previous research has primarily focused on lower-order sensory perception, such as stimulus thresholds and discrimination thresholds, where perceptual responses become stronger and more pronounced in relation to the intensity of stimuli applied to the skin (Knibestöl and Vallbo, 1980; Srinivasan and Dandekar, 1996; Hao et al., 2015; Johnson, 2001; Sripati, Bensmaia, and Johnson, 2006; Vallbo and Johansson, 1976; Connor et al., 1990), and individual differences in sensory perception are often assessed using such measures (Stevens and Patterson, 1995; Stevens and Choo, 1996; Mildren et al., 2017). In this section, we describe why the relationship between tactile sensitivity and skin mechanical properties is still unclear in terms of the complexity of skin structures and present specific research questions.

We present relevant research articles that have explored the intra- and interindividual variations of tactile sensation from the perspective of skin mechanical properties. Li and Gerling, 2021 have shown that individuals with harder fingers tend to exhibit lower ability in discriminating the hardness of objects compared to those with softer fingers. It has been demonstrated that the ability to discriminate object hardness is more closely associated with changes in contact area and finger eccentricity, rather than finger curvature and penetration depth. Vega-Bermudez and Johnson, 2004 demonstrated that in young participants (19-36 years old), skin conformance accounted for 50% of the variance in tactile spatial acuity. However, in older adults (61-69 years old), the spatial acuity could not be explained by skin conformance, suggesting that age-related changes in spatial acuity may be attributed to neurological factors. Nevertheless, skin that has lost collagen and elastin and no longer conforms to stimuli may still exhibit considerable conformance, possibly due to the presence of fairly soft subcutaneous tissue. The logical connection between apparent surface deformation of the skin, including deformation into the subcutaneous layers, and spatial acuity needs further investigation. Abdouni et al., 2018 showed that measurements of actual contact area have revealed that mechanical properties of the finger, more than its size, should be considered in order to understand the effects of age and gender on static and active finger pressing sensation. Based on the mechanical properties of the skin, they argue that horizontal finger touch gestures produce a more active tactile perception than vertical ones. In various scenarios, particularly in the context of active touch, it has been discovered that people utilize characteristics such as changes in contact area and conformity to object shape as cues to discriminate object hardness and spatial characteristics, although these features do not explain the entirety of the relationship.

It is important to summarize the changes in skin mechanical properties that occur throughout our lifespan, not just limited to the fingers. The Cutometer, a widely used skin measurement device, is valuable because it allows for the evaluation of skin mechanical properties by applying suction, minimizing the influence of underlying muscles and bones. By using the Cutometer, there are significant changes in the skin elasticity with age, rather than its extensibility (Takema et al., 1994; Krueger et al., 2011; Luebberding, Krueger, and Kerscher, 2014; Kim, Kim, and Lee, 2018). These changes are more pronounced in areas such as the cheeks and neck, rather than the hands or cleavage. Regions of the body that are more exposed, such as the face, are more susceptible to the effects of ultraviolet (UV) radiation, leading to a decrease in elasticity (Zhang and Duan, 2018).

The direct relationship between skin mechanical properties and tactile sensitivity is still not well understood, making it challenging to consider the contribution of those to touch. In experiments involving pressing stimuli, the effects observed encompass the properties and structures of underlying tissues, including muscles and bones. Moreover, human skin itself exhibits markedly anisotropic and heterogeneous responses (Fung, 1993), possessing highly complex properties and structures. As a result, the skin's mechanical properties that contribute to tactile sensation may vary depending on how the stimulus is applied. One specific challenge in this regard is the difficulty in measuring net skin deformation in response to mechanical stimuli.

In this study, we focused on how the skin deforms in response to externally applied mechanical stimuli and investigated the relationship between skin surface deformation and tactile sensitivity. One unique feature of this study was the use of suction stimulation as the mechanical stimulus. By using the suction device developed in a previous report (Saito et al., 2019a; Saito et al., 2019b), the skin deformation in response to mechanical stimuli was measured while assessing tactile sensitivity. Since the skin is not pushed in by using suction stimulation, the mechanical properties of the superficial skin layer can be observed rather than the properties of the muscles and bones in the deeper layers (Pierard, Nikkels-Tassoudji, and Pierard-Franchimont, 1995; Barbarino, Jabareen, and Mazza, 2011). The results reflect various skin surface features that vary due to the effects of aging, exposure history, and daily skin care. Furthermore, by clearly defining the boundary conditions of the stimulated area with suction, specifically the region where the skin undergoes deformation, we can directly associate the mechanical properties of the skin in the stimulated area with sensory perception, without being confounded by the effects of complex skin properties.

The cheek was employed as the experimental site.The cheeks, being exposed to ultraviolet light and serving as a target area for skincare and massage, are subjected to the influences of an individual's lifestyle. However, there is a lack of research on the effects of individual differences in cheek skin properties on tactile sensation, despite the potential to observe substantial effects in touch. Furthermore, the cheek is a particularly sensitive area among hairy areas (Weinstein, 1968) and therefore has an important perceptual role in mechanical skin behavior, such as facial expressions. Hence, it is valuable to investigate the contribution of skin physical characteristics to the perception of fine mechanical stimuli on facial skin.

In brief, we measured the stimulus thresholds and the amount of skin deformation at the time of stimulation for participants aged 20 to 77 years with have various physical skin characteristics. First, the stimulus threshold results showed intra- and interindividual variations. Next, we compared the amount of skin deformation in response to stimuli of the same intensity during the stimulus threshold measurements and observed individual differences in skin deformation. Then, we considered the experimental skin deformation and stimulus threshold results and proposed that the magnitude of skin deformation affects the perceived pressure induced by suction stimulation. The finding that the behavior of the skin in response to mechanical stimuli differs among participants and is related to tactile sensation was demonstrated by using simultaneous sensory and skin behavior measurements. This finding indicates that skin physical properties contribute to tactile sensation, which has not previously been considered important.

2.2 Methods

2.2.1 Participants

Forty-one healthy female participants took part in the experiments (median ± median absolute deviation: 44.8 ± 16.7 years, seven participants from each age group, ranging from 20 to 77 years old, in 10-year age groups). The participants were required to meet the inclusion criteria shown in Table 2.1. Individuals were informed about the purpose of this study and gave their written informed consent to participate. The participants were informed that they could quit the experiment at any time if they so wished. The Ethics Committee of Shiseido Research Center approved this study, and all methods were carried out in accordance with the approved guidelines.

TABLE 2.1: Criteria for inclusion of participants in psychophysical experiments.

20–79 years old
Japanese female
Right-handed
No limb disabilities
No acne, atopy, or skin disease on the face
No excessive sunburn or other noticeable skin damage on the face
No piercings other than ears
No psychiatric disorders
No pregnancy or lactation

2.2.2 Apparatus

We used a previously developed device that presents quantitative suction stimulation to the skin and simultaneously measures skin deformation (Saito et al., 2019a; Saito et al., 2019b). A voice-coil linear actuator (H2W Technologies, VMS30-090-LB-1) compresses and expands the air in an air cylinder (SMC, MQQLL30-100DM). The generated oscillations are transmitted to the contactor through an air tube, and the skin is stimulated by suction pressure through the suction hole of the contactor. The contactor has a 2 mm diameter suction hole in the center. During the measurements, a spring-loaded contact force adjustment mechanism maintains a constant pressing force on the skin. By applying laser light with a 2D laser displacement sensor (Keyence LJ-V7080) attached inside the contactor, the skin deformation caused by suction stimulation was measured. The deformed shape of the skin on the irradiation line of the laser at the suction hole was observed (Figure 1). A pressure sensor (PISCO, VUS11-AR) was attached to the air tube to quantify the pressure applied to the cheek.

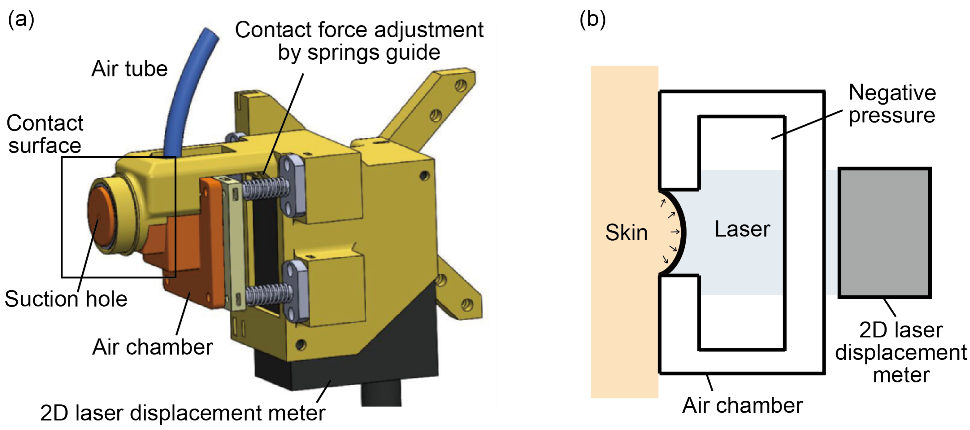


FIGURE 2.1: Configuration of a contactor of the developed suction device.

(a) Contactor of the suction device in contact with the skin and suction stimulation applied to the skin through the suction hole. The contact force of the contactor against the skin can be kept constant by a spring guide. The air chamber is sealed when the 2 mm diameter suction hole contacts the skin. The suction stimulus generated by the compression and expansion of the air in the cylinder by the actuator is transmitted to the air chamber through the air tube. The back side of the air chamber is made of glass, enabling a laser displacement meter installed on the back side to acquire the amount of skin deformation at the suction hole. (b) Schematic diagram of the contact surface with the skin. The skin deformation ridges at the suction hole caused by suction stimulation were acquired by a 2D laser displacement meter. The skin displacement at the center of the suction hole was the optimization target.

2.2.3 Measurement of stimulus thresholds

We quantitatively evaluated the tactile sensation of negative pressure applied to the participant's cheeks according to psychophysical methods. The study was performed in a room with a constant temperature of 22.0°C and a relative humidity of 45.0%. After a 15-minute acclimation period after each participant washed their face for the only time in this experiment with facial cleansing foam, we used a pen to mark the point where the stimulator contacted the skin on the left cheek to indicate the stimulation point. First, the participant was asked to place their face on a chin rest so that their cheek, which was the stimulus point, remained constant (Figure 2.2). To eliminate the influence of vibration stimulus sound on tactile sensation, participants wore earphones that played white noise during the experiment. Additionally, to determine the presence or absence of the stimulus, an LED light in front of them would illuminate during the period when the stimulus was presented. The participant was asked to raise their hands when the stimulus was perceived. The stimulus threshold was determined by the PEST method (Taylor and Creelman, 1967), a psychophysical method which has been used to evaluate stimulus thresholds. This method increases the accuracy of the stimulus threshold measurements while minimizing the number of measurements by adaptively changing the step of the presented stimulus based on the participant's responses. The method of determining the change in the stimulus was based on the following four rules: 1) When the direction of change in the stimulus step was reversed, the change step width was halved. 2) When the direction of change in the stimulus step remained constant, the change step width was held constant. 3) When the direction of change in the stimulus step remained constant three times in a row, the step width was doubled. 4) When the direction of change in the stimulus step remained constant twice in a row, the step width of the third change was kept the same or doubled, depending on the previous reversal of the stimulus direction. If the reversal of the stimulus step direction that occurred immediately before the current stimulus step was caused by doubling the stimulus step width, the third step width measurement was held constant and not doubled. However, if the reversal immediately preceding the current stimulus step was not caused by doubling the stimulus step change, the third change step width was doubled.

We used 10 Hz oscillation stimuli, which are known to be more easily perceived as mechanical stimuli by the skin than steady-state stimuli (Gescheider, Bolanowski, and Hardick, 2001). The use of dynamic vibrating stimuli that are easier to perceive than static stimuli allowed us to evaluate a wide range of tactile sensory characteristics in patients from 20 to 77 years of age using the same index without causing participant pain. The stimulus duration was 3.5 s, and within that time frame, 10 Hz stimulation was given for 2.0 s (Figure 2.3). The range of stimulus intensity was set to -0.05 to -13.5 kPa. The measurement started at the largest stimulus intensity of -13.5 kPa. The stimulus intensity was decreased if the participant perceived the stimulus and increased if the participant did not perceive the stimulus. The measurement ended when the step fluctuation was less than 0.1 kPa or when the upper or lower of stimulus intensity limit was presented three consecutive times. If the step fluctuation range did not converge after a maximum of 30 trials, the final presented stimulus was used as the stimulus threshold. The measurements were performed three times for each participant. Considering the influence of skin fatigue due to repeated stimulation on the mechanical properties of skin, the three trials were conducted by shifting the stimulus presentation point by 5 mm on the cheek, and the interval time between trials was at least 5 minutes. Practice trials were conducted before starting the test, and the measurements were acquired when the participants fully understood the stimulation procedure.

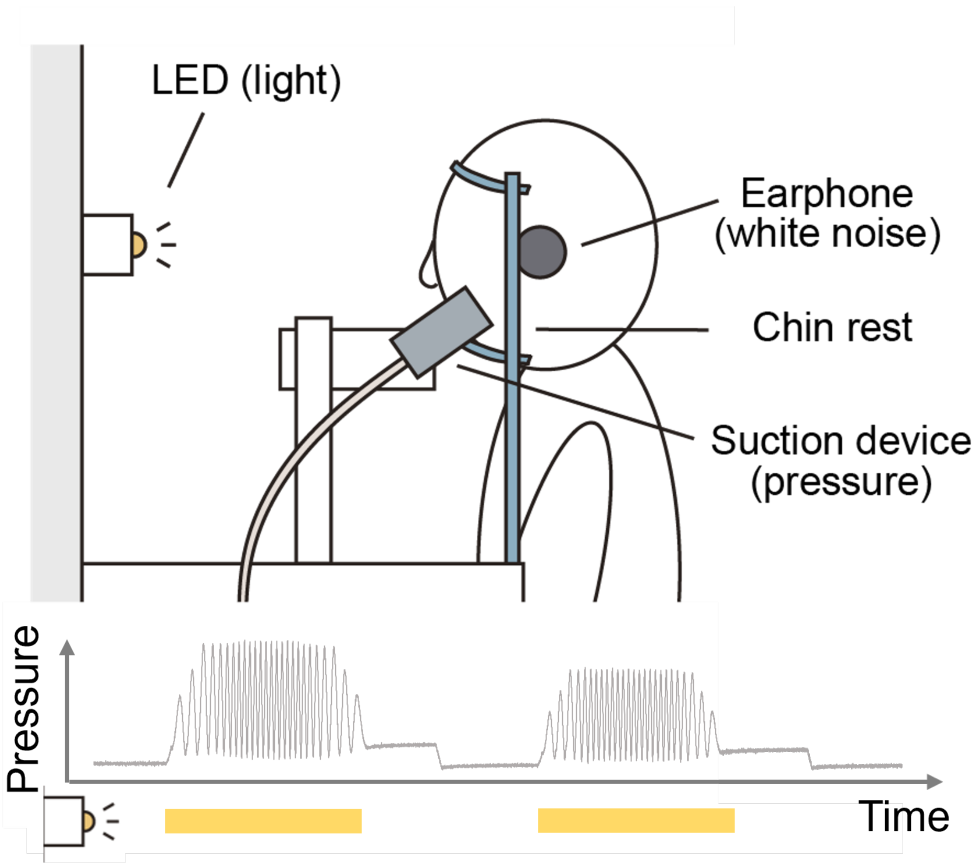


FIGURE 2.2: Conditions for stimulus presentation.

The participant was instructed to position their face on a chin rest in order to keep their cheek, which served as the stimulus point, consistent. To minimize the impact of auditory stimuli vibrations on tactile sensation, participants wore earphones that played white noise throughout the experiment. Moreover, to indicate the presence or absence of the stimulus, an LED light in front of them would illuminate when the stimulus was being presented.

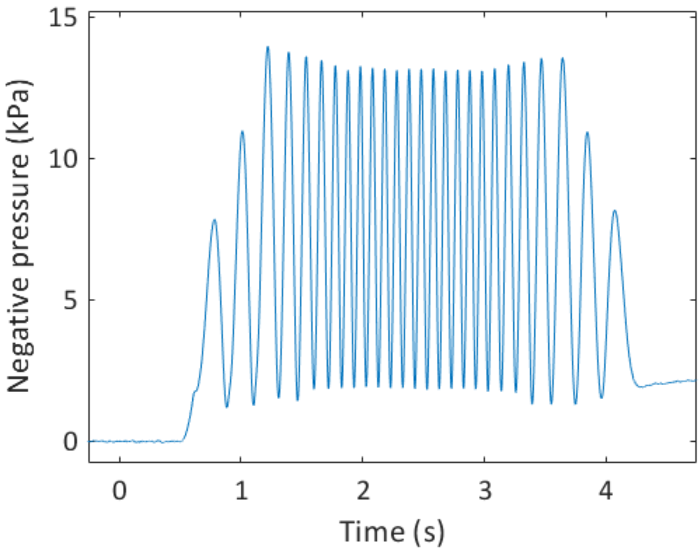


FIGURE 2.3: An example of a negative pressure stimulus presented during stimulus threshold measurement.

Negative pressure intensity (kPa) versus time (s). The stimulus duration was 3.5 s, and within that time frame, 10 Hz stimulation was given for 2.0 s.

2.2.4 Measurement of skin deformation

A two-dimensional laser displacement meter (Keyence LJ-V7080) mounted inside the contactor was used to measure skin deformation caused by suction stimulation at all times during the stimulus threshold measurements. In this study, we used the skin deformation data at the center of the suction hole in the shape of the skin deformation on the line of the laser irradiation of the suction hole (Figure 2.4). These data were calculated using the skin deformation measured immediately before the start of suction as the zero reference. The average of the five local maxima of skin deformation (peak skin deformation) at the center of the section where 10 Hz suction oscillation stimulation was applied was used as a skin deformation index. The peak skin deformation was calculated from the data at the time of the first stimulus presentation, when the same amount of negative pressure was presented in each threshold measurement. In the PEST method, the stimulus amount and the number of presentations changed with each threshold measurement. Therefore, by comparing the peak skin deformation at the first stimulus presentation, we could compare skin characteristics across trials without the influence of the stimulus intensity or skin fatigue caused by repeated stimulus presentation.

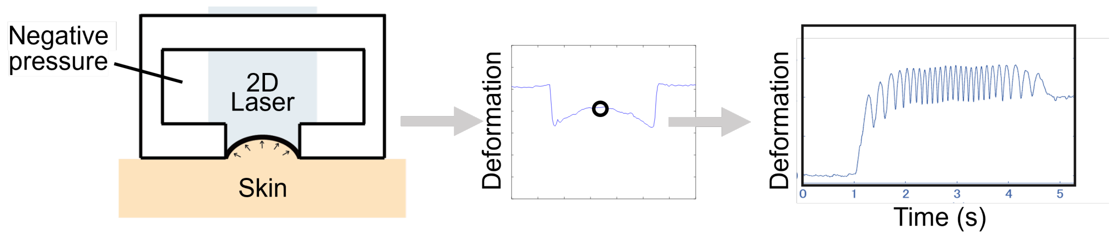


FIGURE 2.4: The method for obtaining skin deformation.

The skin deformation data was obtained at the center of the suction hole in the form of the skin deformation along the line of laser irradiation of the suction hole. These data were calculated with the skin deformation measured immediately before the start of suction as the reference zero.

2.2.5 Analysis

The measured skin deformation and negative pressure data were processed by MATLAB software (MathWorks, R2021b). The correspondence between skin deformation and tactile sensation was examined for each trial, as the skin response to the stimulus may differ for each trial. When the intrarater reliability was confirmed for repeated measurements, a linear mixed analysis approach was used. Intrarater reliabilities for the stimulus threshold and peak skin deformation were estimated using intraclass correlation coefficients (ICCs). To calculate the ICC scores, a two-way random model was used to examine the extent to which the scores were consistent across three occasions for the same participant. Values were considered to indicate intraparticipant reliability when the χ^2 value of the residual analysis of the null model with no explanatory variables was significant and the ICC was greater than 0.50 (considered moderate reliability (Koo and Li, 2016)). In such cases, a linear mixed model using the maximum likelihood method was used. Participants were added to the model as random effects, and age or peak skin deformation was added as a fixed effect. Likelihood ratio tests with the null model were conducted to examine the effects of the explanatory variables on the stimulus threshold or peak skin deformation. Different models were employed to study the effects of age and skin deformation. The significance probability was set at 5%. The statistical software R (version 4.1.3) was used for processing.

2.3 Results

2.3.1 Stimulus thresholds show characteristic intra- and interindividual variability among participants

To investigate the effect of skin deformation on tactile sensation, we first quantified tactile sensitivity to 10 Hz negative pressure stimuli for participants of various ages. To determine the individuals' tactile stimulus perception, we first determined each participant's optimal stimulus threshold by the PEST method. The stimulus thresholds for all participants are shown in Figure 2.5. The points connected by lines indicate the same participant. In all trials, the stimulus threshold values varied from 0.77 to 13.5. The agreement of the stimulus thresholds of the participants across the three trials was high (ICC = 0.74, p = 0.001), indicating that the three stimulus thresholds were nested in the participants. A linear mixed model showed no statistically significant relationship between age and stimulus threshold (χ^2 = 0.70, df = 1, p = 0.40). Similar stimulus thresholds were found for a wide range of ages, ranging from 20 s to 70 s. However, participants in their 20s were characterized by thresholds that were smaller than the median values of all trials for all participants. In contrast to participants in their 20s, 10 participants in their 30s and older (ages 39-70) had thresholds of 13.5 kPa, which was the upper limit of the stimulus intensity. Eleven older participants (46-77 years) had intraindividual threshold variabilities greater than the standard deviation for all trials (4.59). In summary, we observed no linear relationship between age and the stimulus threshold; however, we noted large intra- and interindividual variations in tactile perceptibility among some participants, particularly elderly participants.

2.3.2 Skin deformation in response to mechanical stimuli varies among individuals

To investigate the effect of skin deformation on tactile sensation, the actual dynamic skin behavior during threshold measurements was examined. Peak skin deformations were measured with a laser displacement meter and compared when negative pressure stimuli with the same intensity were applied. An example of the measured skin deformation and measured negative pressure data is shown in Figure 2.6. The skin began to stretch at the start of suction, and the skin repeatedly stretched and contracted in response to the 10 Hz negative pressure stimulation. For the trial shown in Figure 2.6, the peak skin deformation calculated from the local maxima of skin deformation during 10 Hz stimulation was 0.56 mm. The values of the peak skin deformation for 70 trials of 26 participants, for whom data were obtained from the first trial for both peak skin deformation and pressure among all trials, were analyzed. Figure 2.7 shows the peak skin deformation values. The points connected by lines indicate the same participant. In the trials, the mean value was 0.32 mm, and the values varied from 0.14 to 0.69 mm despite the pressure values being presented at the same intensity. The agreement of the peak skin deformation of the participants across the three trials was high (ICC = 0.93, p = 0.001). This estimate suggested that the differences in peak skin deformation among participants were larger than the differences of each participant among the three trials. A linear mixed model showed no statistically significant relationship between age and peak skin deformation (χ^2 = 2.62, df = 1, p = 0.11). In summary, although the peak skin deformation at the same

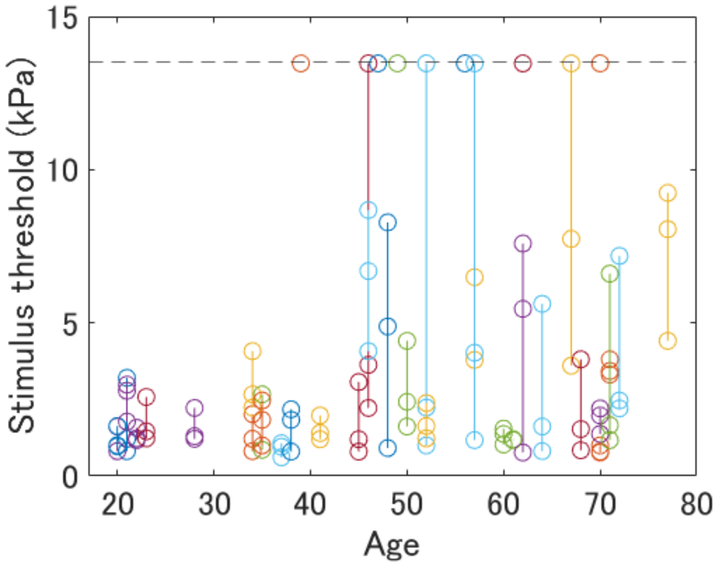


FIGURE 2.5: Stimulus thresholds have participant characteristic intra- and interindividual variability.

Relationship between subject age and Stimulus threshold (kPa). A single point indicates the threshold for a single trial. The points connected by a line represent the same subject. The dotted line at 13.5 kPa represents the upper stimulus limit presented. Data from 123 trials (n = 41). Intraclass correlation coefficients were obtained for the stimulus thresholds (ICC = 0.74, $p = 0.001$). A linear mixed model regression by maximum likelihood was performed for stimulus thresholds with participants as random effects and age as a fixed effect. To examine the effects of age on stimulus threshold, likelihood ratio tests compared to a null model were conducted at a 5% probability of significance. A linear mixed model showed no statistically significant relationship between age and stimulus threshold ($\chi^2 = 0.70$, $df = 1$, $p = 0.40$).

negative pressure differed among for each participant, this value did not change with age.

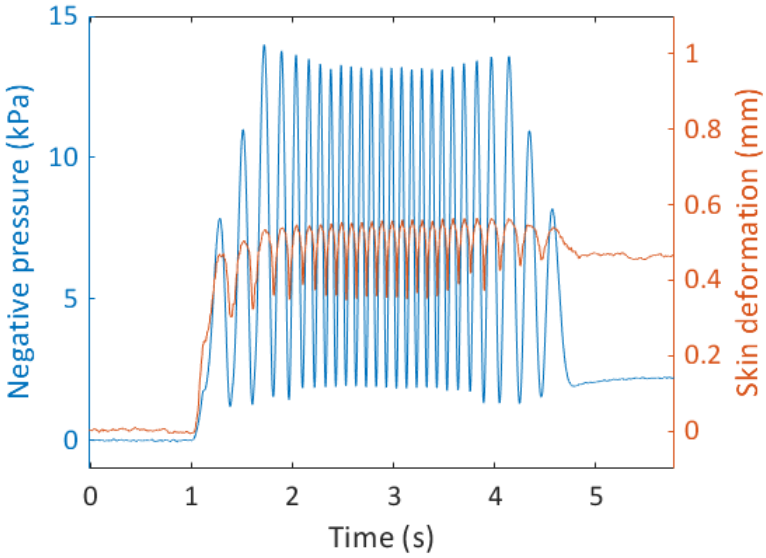


FIGURE 2.6: Skin stretches and contracts following 10 Hz suction stimulus.

Time-varying data of presented negative pressure (kPa) and skin deformation (mm). The left vertical axis shows the negative pressure intensity presented, and the right vertical axis shows the amount of deformation of the skin lifted by suction. The figure shows a representative single stimulus presentation in single trial (n = 1). The peak skin deformation (mm) calculated from the local maxima of skin deformation during 10 Hz stimulation was 0.56.

2.3.3 Large skin deformations lead to small stimulus thresholds

The stimulus thresholds for negative pressure were successfully quantified, and individuals showed high thresholds, low thresholds, and variable thresholds. In addition, the amount of skin deformation in response to mechanical stimuli during the threshold measurements reflected the characteristics of each individual. We then investigated whether these individual skin deformation characteristics were related to the unique tactile sensitivity of each individual. Figure 2.8 shows the relationship between the peak skin deformation and stimulus threshold. Data were acquired over 70 trials (n = 26) with successful skin deformation measurements. The points

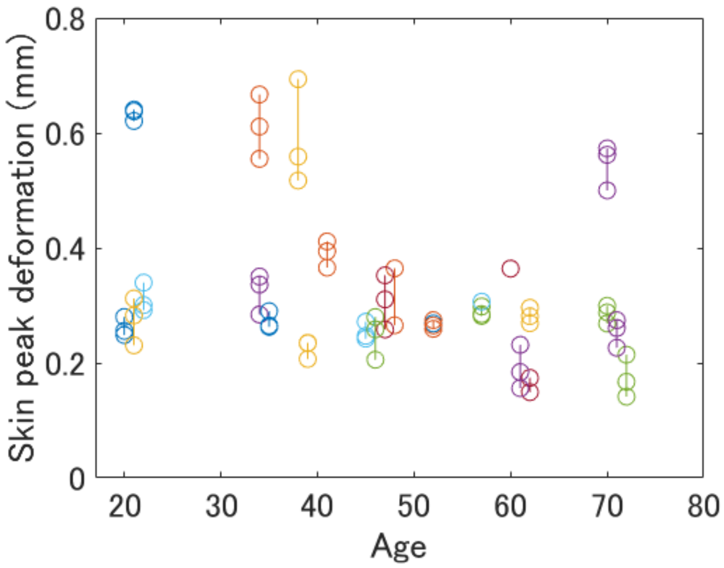


FIGURE 2.7: Skin deformation in response to mechanical stimuli varies among individuals.

Relationship between subject age and peak skin deformation (mm). The points connected by a line represent the same subject. Data from 70 trials (n = 26) with skin displacement measurements completed. Intraclass correlation coefficients were obtained for stimulus thresholds (ICC = 0.93, $p = 0.001$). A linear mixed model regression by maximum likelihood was performed for the peak skin deformation, with participants as random effects and age as a fixed effect. To examine the effects of age on peak skin deformation, likelihood ratio tests compared to a null model were conducted at a 5% probability of significance. A linear mixed model showed no statistically significant relationship between age and peak skin deformation ($\chi^2 = 2.62$, $df = 1$, $p = 0.11$).

connected by lines indicate the same participant. Participants with an upper limit stimulus threshold (13.5 kPa) showed the same stimulus threshold on all trials. The agreement of the stimulus thresholds of the participants across the three trials was high (ICC = 0.85, $p = 0.001$), indicating that the tactile sensation ability was consistent within individuals. A linear mixed model showed that the peak skin deformation appears to be a negative and significant predictor ($\chi^2 = 6.10$, $df = 1$, $p = 0.014$) of the stimulus threshold. When the peak skin deformations were smaller than 0.36 (mm), the stimulus thresholds varied greatly. Within this skin deformation range, the thresholds varied among individuals from 1.0 to 13.5 (kPa), and five participants showed intraindividual variabilities greater than the overall variability (4.14). In summary, the greater the peak skin deformation in response to mechanical stimuli, the more likely participants were to perceive small stimuli, and when the peak skin deformation was small, both interindividual and intraindividual variations in tactile sensitivity were observed.

2.4 Discussion

In this study, we focused on how the skin deforms in response to externally applied mechanical stimuli and investigated the relationship between skin surface deformation and tactile sensitivity. Although tactile sensation occurs through the skin, the direct relationship between skin mechanical properties and sensory perception is still not well understood. This study used the suction device to measure skin deformation in response to mechanical stimuli while evaluating tactile sensitivity. This allowed us to observe the mechanical properties of the superficial skin layer, which would change with aging, UV exposure history, and daily skin care, rather than the properties of deeper layers of muscle and fat, because suction stimulation does not push the skin into the skin. Furthermore, by clearly defining the boundary conditions of the suction-stimulated area, particularly the area of skin deformation, we were able to directly relate the sensation to the mechanical properties of the skin in the stimulated area without being distracted by the effects of complex skin properties. As a result, we confirmed the characteristic intraindividual and interindividual variability of the stimulus threshold, and skin deformation during tactile sensation was also found to vary among individuals. Moreover, the amount of skin deformation affects the stimulus threshold. Thus, we proposed that the behavior of skin in response to mechanical stimuli is related to tactile sensation. People perceive tactile stimuli differently, which may be due in part to the physical properties of their skin.

We also discuss the relationship between skin deformation and tactile sensation. Although studies focusing on the relationship between skin physical properties and

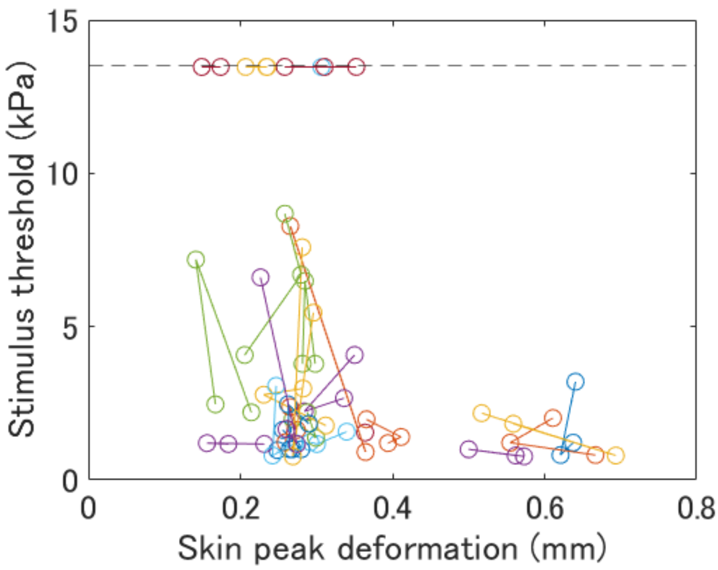


FIGURE 2.8: Large skin deformations lead to small stimulus thresholds.

Relationship between peak skin deformation (mm) and stimulus threshold (kPa). The points connected by a line represent the same subject. The dotted line at 13.5 kPa represents the upper stimulus limit presented. Data from 70 trials (n = 26) with skin deformation measurements completed. Intraclass correlation coefficients were obtained for stimulus thresholds (ICC = 0.85, p = 0.001). A linear mixed model regression by maximum likelihood was performed for stimulus thresholds, with participants as random effects and skin deformation as fixed effects. To examine the effect of peak skin deformation on stimulus threshold, a likelihood ratio test compared to a null model was performed with a 5% probability of significance. A linear mixed model showed that peak skin deformation appears to be a negative and significant predictor (χ^2 = 6.10, df = 1, p = 0.014) of stimulus threshold.

tactile sensation have shown that short-term skin hydration improves sensitivity to spatial details of objects within participants (Lévêque et al., 2000), it is not known why skin physical properties change the sensation of mechanical stimuli. In this study, we show that greater skin deformation in response to the same stimulus intensity may lead to more acute tactile sensation. Therefore, if hydration increases the amount of skin deformation in response to mechanical stimuli, this effect may cause the tactile sensation changes. The reason why tactile sensation changes with increasing skin deformation remains unknown and should be investigated in the future. Skin mechanical properties (e.g., stiffness ratio or viscoelasticity of each layer) that increase the amount of skin deformation in response to mechanical stimuli may change the tactile stimuli received by the mechanoreceptors (Hamasaki, Yamaguchi, and Iwamoto, 2018; Wang et al., 2016; Hendrickx-Rodriguez et al., 2022).

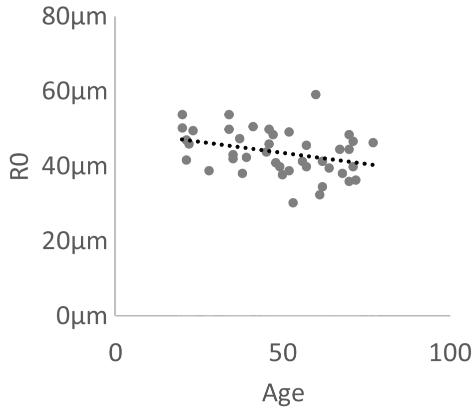
Small skin deformations during tactile sensation may reflect individual differences in the sensory nervous system, leading to interindividual variations in threshold values. The previous section indicated that the magnitude of skin deformation may be related to the subtlety of tactile sensation; however, we observed interindividual variations in the stimulus threshold when the peak skin deformations were smaller than 0.36 (mm). The reasons for this interindividual variation are discussed in terms of the mechanoreceptors. Even though participants had similar peak skin deformation characteristics in response to a given pressure stimulus, the observed stimulus thresholds varied from less than 1.0 to an upper limit of 13.5 kPa. This result is thought to be due to the influence of mechanoreceptors. A previous study showed that participants with fewer mechanoreceptors exhibited lower tactile abilities24. Thus, differences in mechanoreceptor densities may alter tactile sensation, even if the participants receive similar tactile stimuli that induce similar skin deformations. Participants with the upper stimulus threshold (13.5 kPa) may have fewer mechanoreceptors than the other participants. When the skin deformation was large, the thresholds were small, with little variation among individuals, suggesting that the participants may have had acute tactile sensation based on the large amount of mechanical information provided, reducing the impact of the mechanoreceptor density. Although tactile sensation can be understood using mechanical information, this understanding should be discussed by estimating the mechanical information transmitted by different skin deformations and observing the mechanoreceptor density.

Skin deformations during tactile sensation may largely reflect only the state of the sensory nervous system immediately below the stimulation site, leading to threshold variations due to shifts in the stimulation site. Although we focused on interindividual differences in stimulus thresholds, large intraindividual variations were also observed in a few participants with small skin deformations. Since the intraparticipant peak skin deformations were similar (ICC = 0.93), the large intraparticipant variation in the stimulus threshold was not solely due to the effects of the peak skin deformation. This intraparticipant variability in stimulus threshold may be due to the position of the stimulus presentation on the cheek. The positional relationship between the stimulus point and the mechanoreceptors changed because the stimulus presentation point was moved by 5 mm in each trial. Since mechanoreceptors are not evenly distributed45,46 and the stimulus point was moved by a distance equivalent to the distance of the two-point discrimination threshold on the cheek8, which is considered to be the receptive field connected to the nerve, the movement of the stimulus presentation point between trials may have produced these perceptual variations. Notably, this phenomenon is common with small skin deformations, and how skin deformations lead to the firing of mechanoreceptors should be investigated.

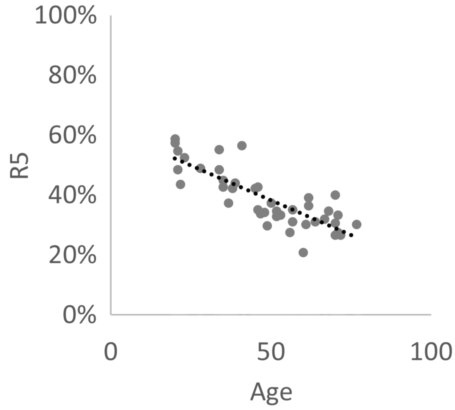
The effects of aging can be inferred from the variation in the stimulus threshold among elderly participants. Since the present study included participants with a wide range of ages, we focused on age and discussed the relationship between the peak skin deformation and stimulus threshold. First, participants in their 20s showed stimulus threshold values ranging from 0.81-3.20, which were smaller than the overall mean, and a wide range of peak skin deformations ranging from 0.23-0.64 mm (Figures 2.5 and 2.7). These participants showed relatively high tactile sensitivity regardless of the peak skin deformation. This may be because young participants in their 20s, who are considered to have relatively high nerve density, have sufficient nerve density to perceive the mechanical information transmitted by the peak skin deformation. Next, participants in their thirties and older were found to have varying stimulus thresholds (Figure 2.5). The probability of receiving mechanical information from mechanical stimuli may be reduced in older participants due to age-related decreases in the density of mechanoreceptors and sensory nerves. This decreased probability may have resulted in some trials with good stimulus thresholds and others with poor stimulus thresholds. While previous studies on tactile sensation associated with deformations caused by skin indentation have shown sensation decrease with age (Stevens and Choo, 1996; Stevens and Patterson, 1995; Woodward, 1993), this was not observed in the present study. Instead, we noted an increase in threshold variability in some elderly participants. There were several trials in which elderly subjects, who likely have lower mechanoreceptor densities, exhibited stimulus thresholds as low as those of younger participants. This may be because suction stimulation induces force propagation in the skin surface layer close to the mechanoreceptors (Makino and Shinoda, 2006); thus, the probability that the mechanoreceptors experienced the tactile stimuli was higher than that of the indentation stimuli. Tactile sensitivity can also be increased even in older subjects by extending the stimulation range (Stevens and Choo, 1996; Schmidt et al., 2020). These findings suggest that skin deformations that stimulate more mechanoreceptors in the surface area, rather than those induced by increasing the stimulus intensity, may improve somatosensory sensation.

Judgments of tactile sensation are considered to play important roles in how the skin mechanically deforms in response to mechanical stimuli. In the previous sections, we discussed various factors that may affect the intra- and interindividual threshold variability; however, the factor that was strongly related to sensitivity was the amount of skin deformation during the tactile sensation experiments. How the skin deforms during the tactile sensation trial is an important constitutive factor. Since, the peak skin deformation in response to the 10 Hz oscillation measured during the tactile stimulation experiments did not directly correspond with age (Figure 2.5), the peak skin deformation value likely reflects the characteristic viscoelasticity of the skin surface layer according to a short time constant that is not monotonically related to age. In general, skin distensibility and elasticity (Krueger et al., 2011; Luebberding, Krueger, and Kerscher, 2014; Takema et al., 1994) decrease with age. The Cutometer measurements in the present study also showed monotonous decreases in R0, which represents skin distensibility, R5, which represents net elasticity, and R7, which represents the ratio of elastic recovery to distensibility (see parameter definitions (Krueger et al., 2011)), with age, confirming that the participants show general skin change characteristics with age (Figure 2.9). The 10 Hz suction oscillation stimuli seem to reflect characteristic skin properties that cannot be determined through general skin measurements, and the use of these stimuli in the tactile threshold measurements reveals the impact of concurrent skin deformations on tactile sensation.

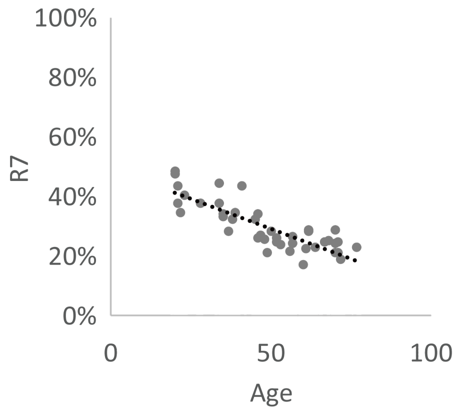
Using suction stimuli allows for a constructivist understanding of tactile sensation, limiting the mechanical and physical contribution to tactile sensation to the surface skin layer. Touch stimuli that push into the skin represent the sensations people typically experience when receiving touch gestures. However, the effects on the deeper layers of the skin may be reflected by the muscles and tendons, and the skin deforms more widely in accordance with pushing forces; thus, the geometric shape of the skin, such as microreliefs and wrinkles, may also be affected. On the other hand, by applying negative pressure through a 2 mm suction hole, these effects can be limited to a specific range of physical properties in the superficial layer of the skin. This allows us to discuss the magnitude of skin deformation and tactile sensation in terms of the amount and distribution of localized mechanical information transmitted to the sensory nervous system through the skin. While tactile sensation involves a complex interplay of many factors, focusing on the physical properties of the skin surface layer enables prediction and control of tactile sensation, leading to the realization of delicate tactile stimulus presentation via suction and a better understanding of the sensations produced during everyday touch.



(a) R0



(b) R5



(c) R7

FIGURE 2.9: Skin elastic recovery to distensibility and skin extensibility decreased with aging.

Relationship between skin physical property and age measured by the Cutometer. The dots show mean value of five measurements on the cheek, the target area. Linear regression analysis revealed negative and significance relationship between age and parameters R0, R5 and R7, which means skin extensibility and the elastic recovery to distensibility (R0: $r = -.34$, $p < 0.05$, R5: $r = -.82$, $p < 0.01$, R7: $r = -.83$, $p < 0.01$). Data from 41 participants.

The limitations of this study and future research directions can be summarized as follows. The skin deformation ranged from 0.14 to 0.69 mm in the present study, and more participants with particularly large skin deformity characteristics should be recruited to obtain a more comprehensive relationship between the peak skin deformation and tactile sensation. In addition, the amount and distribution of mechanical information transmitted to the sensory nervous system through the skin should be investigated to infer why skin deformation affects tactile sensation and the relationship between skin composition and tactile sensation. Furthermore, the mechanoreceptor density of each participant should be measured along with the amount of skin deformation, as this property may impact tactile sensation. It is very interesting to see how the mechanoreceptors that receive information generated by skin deformation contribute to tactile sensation.

2.5 Summary

In this study, we focused on how the skin deforms in response to externally applied mechanical stimuli and investigated the relationship between skin surface deformation and tactile sensitivity.

What has become evident here is that, firstly, even when the same amount of pressure stimulation is applied, the degree of skin deformation varies among individuals. Secondly, there was also intra- and interindividual variability of tactile sensitivity. Finally, the amount of skin deformation while tactile stimulation can partially explain the variability in tactile sensitivity both intra- and interindividuals. A characteristic relationship was observed in which intra- and interindividual differences in tactile sensitivity are greater when the peak of skin deformation is relatively small. Thus, we proposed that the behavior of skin in response to mechanical stimuli is related to tactile sensation. People perceive tactile stimuli differently, which may be due in part to the physical properties of their skin.

These findings have promising implications for future advancements. We have successfully established a direct correlation between the complex interplay of tactile sensations and observable physical phenomena occurring in the skin. This highlights the validity of focusing on the contribution of skin mechanical properties to touch. Particularly, the insight that there is a greater variability in tactile sensitivity when the peak skin deformation is relatively small offers the potential for a constructivist understanding of the tactile sensory mechanism in the periphery, including mechanoreceptors and neural fibers states, through collaboration with subsequent studies in dermatology and neuroscience. Furthermore, we have identified the skin's stretchability as a particularly useful mechanical characteristic that could serve as an indicator for subsequent research. By altering this characteristic through interventions on the skin, it is suggested that tactile sensation could be adjusted.

Chapter 3

Contribution of Stratum Corneum Compliance to Tactile Sensitivity in Response to Vibratory Stimuli

3.1 Introduction

The objective of this chapter is to investigated the contribution of the stratum corneum compliance to tactile sensitivity. It has been investigated that hydrating the skin alters tactile sensitivity, and that it also alters skin condition. However, it has not been investigated which mechanical properties of skin affect tactile sensitivity. In this section, we summarize the tactile sensitivity studies with hydrated skin and describe the stratum corneum properties that we focused on for specific intervention and measurement.

The effect of skin condition on tactile sensation has primarily been investigated through intervention experiments, primarily focusing on skin hydration. The stimulation threshold for passive touch during vibrotactile indentation with a displacement of approximately 0.5 mm remained unchanged before and after hydration on the finger. However, the ability to accurately perceive the fine roughness of sandpaper during active touch, which essentially involves the generation of friction, was compromised by the hydration (Verrillo et al., 1998). Furthermore, an increase in the friction coefficient, calculated from the tangential and vertical forces across the finger-texture contact surface, is associated with an improved texture discrimination ability that transcends the effects of aging (Skedung et al., 2018). These results highlight the influence of hydration on the frictional state, or surface lubrication, and its impact on tactile sensation.

On the other hand, the tactile sensation changes demonstrated in the studies discussed below appear to be attributed not solely to hydration itself, but rather to the mechanical properties of the skin as a material, its stretchability and ability to return to its original shape. Hydration of the forearm and cheek resulted in a reduction of the two-point discrimination threshold, indicating enhancing spatial resolution

(Lévêque et al., 2000). In that paper, it is hypothesized that the increased conformance of the skin in response to gap-shaped stimuli contributed to these improvements. In addition to short-term interventions, long-term use of skin care products, specifically the application of a cosmetic foam with an active ingredient twice daily for one month, enhanced tactile discrimination ability (Aimonetti et al., 2019). These changes are thought to be due to changes in the mechanical responsiveness of the skin caused by hydration, as greater skin deformation in response to tactile stimuli leads to heightened tactile sensation (Vega-Bermudez and Johnson, 2004; Sakaguchi et al., 2023b). Indeed, the application of different types of water (distilled or surfactant) to human skin can alter the dynamic elastic modulus of skin (Takahashi et al., 1984) as well as the tactile sensation in different way (Verrillo et al., 1998). Thus, skin deformability, i.e., compliance, as determined by the water content of the skin, is an important factor in tactile sensation.

While the causal relationship between the mechanical properties of the skin and tactile sensation has been established, it is still necessary to further examine which specific layers of the skin contribute to this relationship. The skin is a layered structure with different structures and compositions that determine its mechanical characteristics. From the perspective of developing appropriate intervention strategies, it is still unclear which specific intervention methods on the skin contribute to changes in tactile sensation during contact with various objects. To address this, it is necessary to utilize precise measurement techniques from the field of dermatology to clarify the specific skin layer effect on tactile sensation. The compliance of the stratum corneum, the outermost layer of the skin, can vary daily due to skincare and environmental factors (Egawa and Tagami, 2008; Egawa et al., 2002). However, few studies have quantified the effect of stratum corneum compliance on tactile sensation. It is crucial to examine the specific changes in stratum corneum compliance resulting from hydration interventions to gain deeper insights into tactile sensation.

In this study, we investigated the contribution of the stratum corneum compliance to tactile sensitivity resulting from skin hydration. We performed hydration interventions on the stratum corneum with a cosmetic treatment. The hydrating effect on this skin layer was evaluated by measuring the water content at different skin depths using two instruments (Clarys et al., 2012), while compliance was evaluated by isolating the stratum corneum and measuring its dynamic elastic modulus (Takahashi et al., 1984). By employing suction as a tactile stimulus, we were able to determine the contribution of the stratum corneum to tactile sensation without the influence of deep muscle or fat (Pierard, Nikkels-Tassoudji, and Pierard-Franchimont, 1995; Barbarino, Jabareen, and Mazza, 2011).

In this investigation, we accounted for the presence of factors other than compliance that can influence tactile sensation. The effect of hydration on tactile sensation depends on the participant's age and sex (Bowden and McNulty, 2013), and even within an individual, the tactile sensation itself varies according to the stimulated site due to the complexity of skin tissue that exhibits markedly anisotropic and heterogeneous responses (Fung, 1993). Therefore, we used a device that can measure skin deformation while simultaneously presenting tactile stimuli at the same site on the skin by suction (Sakaguchi et al., 2023b; Saito et al., 2019a; Saito et al., 2019b). This approach went beyond observing the compliance of the stratum corneum, allowing us to explore how it influenced the tactile sensation. Measuring the skin displacement caused by stimulation in correspondence with the tactile response is a pioneering approach in the field of tactile research and also a well-established technique for quantifying skin properties (Weickenmeier, Jabareen, and Mazza, 2015).

3.2 Methods

3.2.1 Participants

Thirty-nine female participants (mean age 45.3 ± 6.0 years) took part in the psychophysical experiments. The participants were required to meet the inclusion criteria shown in Table 3.1. Individuals were informed about the purpose of this study and gave their written informed consent to participate. The participants were informed that they could quit the experiment at any time if they so wished. The Ethics Committee of Shiseido Research Center approved this study, and all methods were carried out in accordance with the approved guidelines.

TABLE 3.1: Criteria for inclusion of participants in psychophysical experiments.

35–54 years old
Japanese female
Right-handed
No limb disabilities
No acne, atopy, or skin disease on the face
No excessive sunburn or other noticeable skin damage on the face
No piercings other than ears
No psychiatric disorders
No pregnancy or lactation

3.2.2 Apparatus

We used a previously developed device that applies quantitative suction stimulation to the skin while simultaneously measuring skin deformation (Saito et al., 2019a;

Saito et al., 2019b). A voice-coil linear actuator (H2W Technologies, VMS30-090-LB-1) compressed and expanded the air in an air cylinder (SMC, MQQLL30-100DM). The generated oscillations were transmitted to the contactor through an air tube, and the skin was stimulated by negative pressure through the suction hole of the contactor. The contactor had a 4 mm diameter suction hole in the center. During the measurements, a spring-loaded contact force adjustment mechanism was used to maintain a constant pressing force on the skin. By applying laser light with a 2D laser displacement sensor (Keyence LJ-V7080) attached to the inside of the contactor, the skin deformation caused by the suction stimulation could be measured. The deformed shape of the skin on the irradiation line of the laser at the suction hole was observed (Figure 3.1). A pressure sensor (PISCO, VUS11-AR) was attached to the air tube to quantify the pressure applied to the cheek.

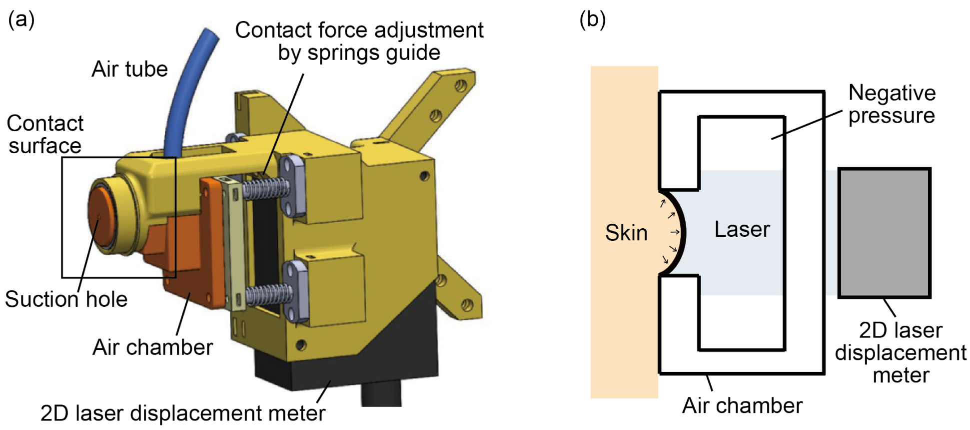


FIGURE 3.1: Configuration of a contactor of the developed suction device.

(a) Contactor of the suction device in contact with the skin and suction stimulation applied to the skin through the suction hole. The contact force of the contactor against the skin can be kept constant by a spring guide. The air chamber is sealed when the 4 mm diameter suction hole contacts the skin. The suction stimulus generated by the compression and expansion of the air in the cylinder by the actuator is transmitted to the air chamber through the air tube. The back side of the air chamber is made of glass, enabling a laser displacement meter installed on the back side to acquire the amount of skin deformation at the suction hole. (b) Schematic diagram of the contact surface with the skin. The skin deformation ridges at the suction hole caused by suction stimulation were acquired by a 2D laser displacement meter. The skin displacement at the center of the suction hole was the optimization target.

3.2.3 Experimental position and study design

The study was performed in a room with a constant temperature and humidity; the temperature was 22.0°C, and the relative humidity was 45.0%. A randomized controlled trial was conducted. The cheek was chosen as the experimental site because it provides a valuable opportunity to examine skin physical properties on a tactile sensitive area with hair (Weinstein, 1968) and considers the significant variations in skin physical properties caused by sun exposure and skin care and massage practices. The participants were randomly assigned to the intervention (n=20, 45.2 ± 6.0 y) or control (n=19, 45.5 ± 5.9 y) groups, which differed in terms of skin hydration conditions. The moisturizing effects of the applied products changed the mechanical properties of the skin (Takahashi et al., 1984; Parente, Gámbaro, and Solana, 2005; Tang et al., 2015; Egawa and Takahashi, 2006). A cream containing 0.2% polyethylene glycol/polypropylene glycol ethers (Fiume et al., 2016) with a skin conditioning agent and emollient function was selected as the common moisturizer for the intervention group, and Milli-Q water was chosen for the control group. The amount of product applied was 600 µl for the cream and 2 ml for the Milli-Q water based on the appropriate doses of cream and lotion for the whole face. Milli-Q water was used in the control group rather than no substance to eliminate changes in skin mechanical properties due to massage and any effects of the application.

The participant group assignment and application were performed by a third party in a separate room in a double-blind approach in which neither the experimenter nor the participant knew what substance was being applied to the cheeks. The participants first washed their faces, and after a 10-minute rest period, tactile and skin mechanical properties were measured and recorded as preapplication conditions. Cream or Milli-Q water was then applied to the cheeks; after a 10-minute waiting period, the skin was washed with lukewarm water to rinse the applied material off the skin surface. After another 10-minute break, the tactile sensitivity and skin mechanical properties were measured and recorded as postapplication conditions.

3.2.4 Measurement of tactile sensation in response to suction oscillation stimuli

Both groups of participants completed the psychophysical experiments. The difference threshold of the mechanical stimulus was used as an evaluation index of tactile sensitivity. To reduce evaluation bias, a method of constant stimulus (Guilford, 1954) was used as the experimental approach. In this method, the difference

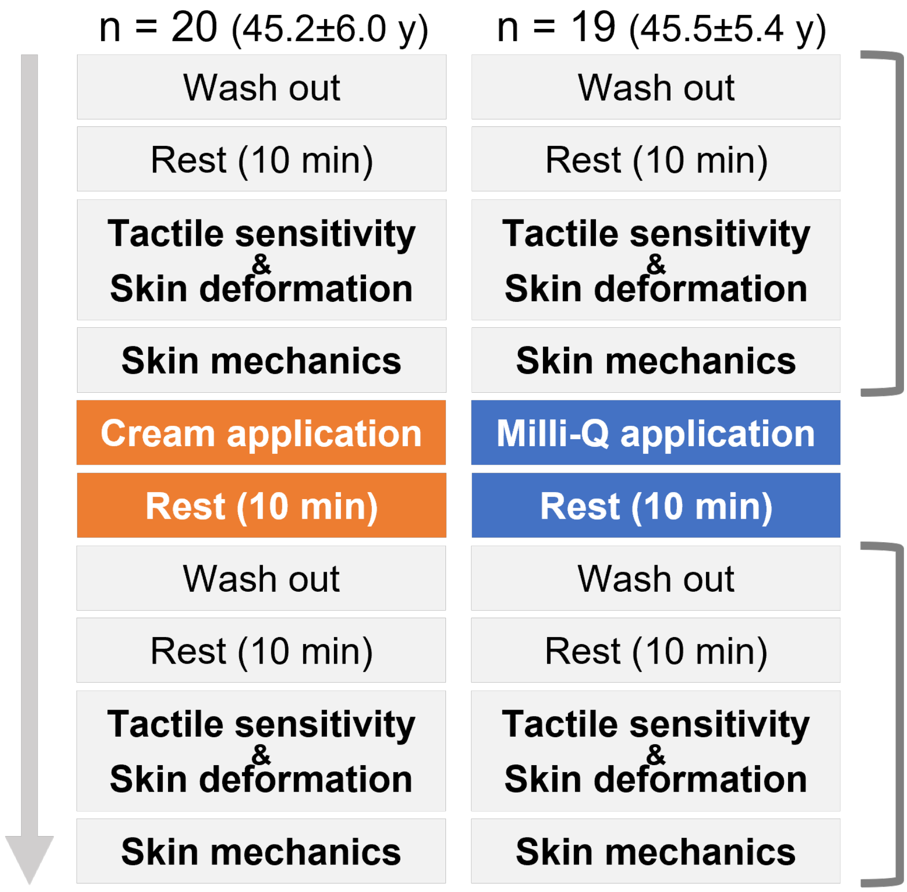


FIGURE 3.2: Experimental flow of randomized controlled trial.

The participants were randomly assigned to the intervention (n=20, 45.2 ± 6.0 y) or control (n=19, 45.5 ± 5.9 y) groups, which differed in terms of skin hydration conditions. The moisturizing effects of the applied products changed the mechanical properties of the skin. A cream containing 0.2% polyethylene glycol/polypropylene glycol ethers with a skin conditioning agent and emollient function was selected as the common moisturizer for the intervention group, and Milli-Q water was chosen for the control group. The amount of product applied was 600 µl for the cream and 2 ml for the Milli-Q water based on the appropriate doses of cream and lotion for the whole face. Milli-Q water was used in the control group rather than no substance to eliminate changes in skin mechanical properties due to massage and any effects of the application. The participant group assignment and application were performed by a third party in a separate room in a double-blind approach in which neither the experimenter nor the participant knew what substance was being applied to the cheeks. The participants first washed their faces, and after a 10-minute rest period, tactile and skin mechanical properties were measured and recorded as preapplication conditions. Cream or Milli-Q water was then applied to the cheeks; after a 10-minute waiting period, the skin was washed with lukewarm water to rinse the applied material off the skin surface. After another 10-minute break, the tactile sensitivity and skin mechanical properties were measured and recorded as postapplication conditions.

threshold is obtained by repeatedly comparing a standard stimulus with a comparison stimulus. Negative pressures were generated as the presented stimuli at five intensity conditions (3.5, 4.8, 6.7, 9.3, and 12.5 kPa) above the stimulus threshold. The comparison stimuli included these 5 conditions, and the standard stimulus was the third intensity stimulus. To better reflect changes in skin physical properties, we used 10 Hz oscillatory stimuli that produced repetitive skin deformations. The experimental condition is shown in Figure 3.3. We asked the participants to wear earphones through which white noise was played to eliminate auditory influence during the stimulus presentation. Moreover, to indicate the presence or absence of the stimulus, an LED light in front of them would illuminate when the stimulus was being presented. First, the participants were asked to place their faces on the chin rest so that the stimulus point remained constant. The stimulation point was the intersection point of a vertical line drawn from the outer corner of the left eye and a horizontal line drawn from the tip of the nose. In one trial, the standard and comparison stimuli were presented once each with a stimulus duration of 3.5 seconds, and the interval between the standard and comparison stimuli was one second. The participants were asked to choose the stimulus that they perceived as "stronger" after the presentation of stimuli (Figure 3.4). When the participants could not judge whether the stimulus strength or when they felt that the two stimuli had the same pressure, they were instructed to answer "the same". The order of the presentation of the standard and comparison stimuli was counterbalanced to eliminate order effects, and the five comparison stimuli were presented in a random order. The difference threshold was derived using least-squares fitting of the response rates for "stronger," "the same," and "weaker" (Guilford, 1954). The five comparison stimuli were applied with the standard stimuli 10 times each according to the method of constant stimuli. The procedure was repeated 5 times, with the cheek stimulation site changed by 5 mm each time, and thresholds were obtained from the data acquired during the 50 trials.

3.2.5 Measurement of skin deformation to suction oscillation stimuli

A two-dimensional laser displacement meter (Keyence LJ-V7080) mounted inside the contactor was used to measure the skin deformation caused by the suction oscillation stimuli. The skin displacement data at the center of the suction hole were obtained at the laser irradiation line (Figure 3.5). The displacement at the central

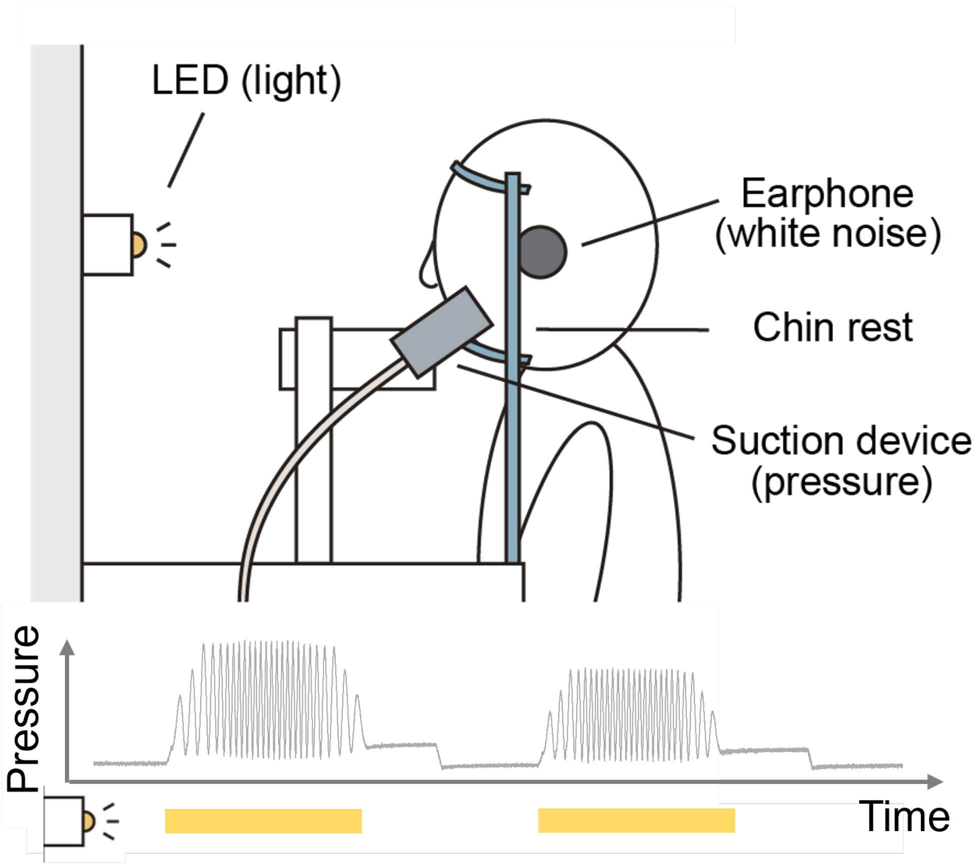


FIGURE 3.3: Conditions for stimulus presentation.

The participant was instructed to position their face on a chin rest in order to keep their cheek, which served as the stimulus point, consistent. To minimize the impact of auditory stimuli vibrations on tactile sensation, participants wore earphones that played white noise throughout the experiment. Moreover, to indicate the presence or absence of the stimulus, an LED light in front of them would illuminate when the stimulus was being presented.

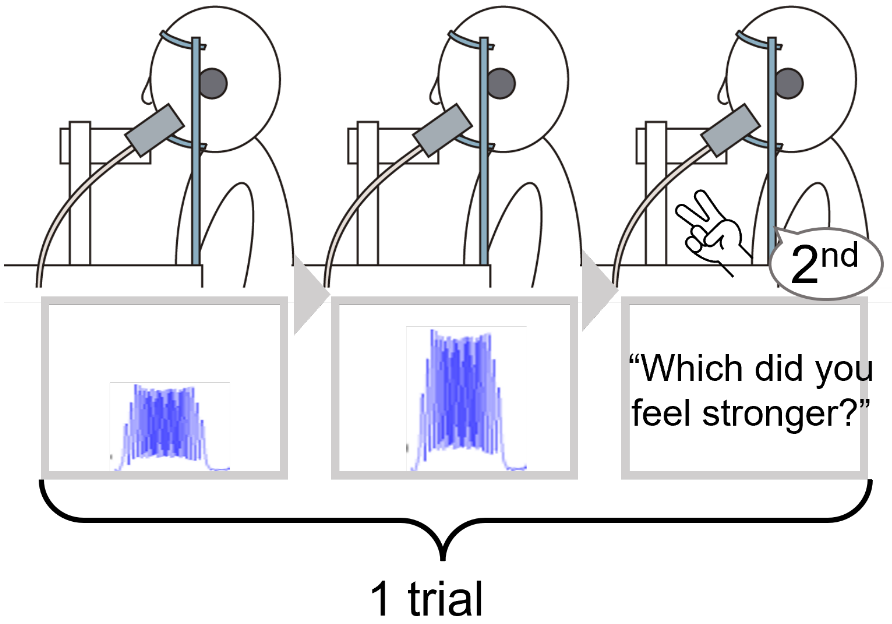


FIGURE 3.4: A method of responding to stimuli given to participants.

In one trial, the standard and comparison stimuli were presented once each with a stimulus duration of 3.5 seconds, and the interval between the standard and comparison stimuli was one second. The participants were asked to choose the stimulus that they perceived as "stronger" after the presentation of stimuli. When the participants could not judge whether the stimulus strength or when they felt that the two stimuli had the same pressure, they were instructed to answer "the same". The order of the presentation of the standard and comparison stimuli was counterbalanced to eliminate order effects, and the five comparison stimuli were presented in a random order based on the psychophysical method of constant stimuli.

point provides informative data for revealing the history-dependent mechanical response characteristics of the skin (Weickenmeier, Jabareen, and Mazza, 2015). The distance from the ground plane of the suction hole to the cheek was defined as the skin displacement. The average of the five local maxima of the skin displacement at the center of the section where the 10 Hz suction oscillation stimulation was applied was used as an index of the mechanical response of the skin.

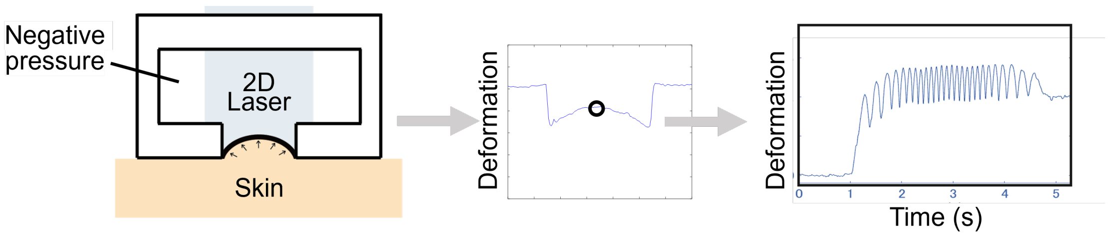


FIGURE 3.5: The method for obtaining skin deformation.

The skin deformation data was obtained at the center of the suction hole in the form of the skin deformation along the line of laser irradiation of the suction hole. These data were calculated with the skin deformation measured immediately before the start of suction as the reference zero.

3.2.6 Measurement of skin mechanical properties

Cheek water content was measured using a SKICON-200EX (IBS Corporation) and Corneometer CM825® (Courage+Khazaka). Each individual moisture value was an average of five repeated measurements on the left cheek. The mechanical properties of the cheek were determined with a Cutometer MPA 580 (Courage+Khazaka) by measuring the vertical displacement of the skin when pulled into a 2 mm diameter probe with an optical sensor. Each measurement consisted of two suction cycles of 2 s each using a constant, negative pressure of 400 mbar, followed by a 1 s period when the pressure was removed (the relaxation phase), allowing the skin to return to its original shape. Each individual parameter value was an average of five repeated measurements on the left cheek. A tape stripping test was performed to evaluate the transdermal absorption of the samples used in the psychological experiments. This test was performed in a room with a constant temperature of 22.0°C and a relative humidity of 45.0%. Four male participants (mean age 29.3 ± 4.0 years old) took part in the experiments. The cream used in the psychophysical experiments was applied (2.0 µl/cm^2) to demarcated areas on the left forearm. Ten minutes after application, the area to which the cream had applied and an area to which the cream had not been applied, serving as the experimental and control conditions, respectively, were washed to remove any residue, similar to the psychophysical experiments. D-Squame® tape with a diameter of 22 mm (CuDerm®, Texas, USA) was used (Figure 3.6). Tape discs were applied and removed by forceps. The first two discs were discarded, and discs three through seven were analyzed. The content of PEG/PPG-17/4 dimethyl ether in the tape strips was analyzed by liquid chromatography–mass spectrometry (LC–MS) after extraction procedures. The skin-softening effects of the two applications used in the psychophysical experiments were measured using the method reported by Takahashi et al. (Takahashi et al., 1984). The measurements were acquired with a specially constructed dynamic measuring instrument (DVA-200, IT keisokuSeigyo Corporation) at 32°C and 50% relative humidity. A human stratum corneum sample was obtained separately from the above experiments, following the methods of a previous study (Kligman and Christophers, 1963). The stratum corneum strip (20 x 3 mm) was prepared as previously described (Takahashi et al., 1984) and held horizontally by two clamps that were spaced 12 mm apart. The left clamp applied fixed-amplitude sinusoidal stress (strain 0.2%, 1 Hz) to the left end of the sample (Figure 3.7). The right clamp had a high-sensitivity sensor that detected the weak stress that was transmitted through the sample. The detected stress signal was calculated and transformed into digital data representing the dynamic elastic modulus (E′) by an operation circuit. Before each test sample measurement, the baseline values of the dynamic elastic modulus of each stratum corneum sample were acquired. A test solution (2 µl) was applied to the strip, and measurements were taken for 60 minutes. The data from 20 to 50 minutes after application, when the dynamic modulus (E′) had reached equilibrium, were analyzed. The skin-softening effect was evaluated according to the elastic modulus ratio before and after application.

3.2.7 Analysis

The measured skin displacement and negative pressure data were processed with MATLAB software (MathWorks, R2021b). A logistic regression model was used to examine the relationship between the applied pressure or skin displacement and tactile sensitivity. The statistical software R (version 4.1.3) was used for these analyses, with a 5% significance level. Wilcoxon signed-rank tests were performed to examine the effects of application for both groups. The χ^2 test was employed to examine the relationship between tactile assessments and skin displacement. The statistical analyses were performed using IBM SPSS Statistics V23, and the significance level was set at 5%.

FIGURE 3.6: Picture of the tape stripping experiment.

To investigate the effect of intervention on stratum corneum properties, tape-stripping experiments were conducted to quantify the amount of cream ingredients penetrating into the stratum corneum. The cream used in the psychophysical experiments was applied (2.0 µl/cm^2) to demarcated areas on the left forearm. Tape discs were applied and subsequently removed, then the content of PEG/PPG-17/4 dimethyl ether in the tape strips was analyzed by liquid chromatography–mass spectrometry (LC–MS).

3.3 Results

3.3.1 The magnitude of the skin displacement difference is directly related to the tactile strength assessment

To explore the relationship between tactile sensitivity and the compliance of the stratum corneum, our study initially focused on quantifying the skin's contribution to tactile sensitivity. This was achieved by simultaneously measuring the skin displacement elicited in response to a carefully selected range of stimuli. An example of the presented negative pressure and resulting skin displacement, measured continuously during mechanical stimulation, is shown in Figure 3.8. The skin began to stretch when the suction stimulus was applied and repeatedly stretched and contracted in response to the 10 Hz negative pressure stimulation. For the preapplication condition in both groups, the negative pressure difference and the measured skin displacement difference for the stimulus pairs presented during the psychophysical experiment were compared with the participant's intensity assessments in each trial, as shown in Figure 3.9. Compared to the stepwise presented negative pressure difference (Figure 3.9 a), the measured skin displacement difference varied (Figure 3.9 b), and the participants did not always show the same skin displacement difference when the same pressure stimulus difference was presented. Logistic regression models revealed that the participants' stronger or weaker responses to the intensity of the suction stimulus were related to the presented pressure difference and the amount of skin displacement difference (each, OR = 1.42, 95% CI: 1.32–1.52,

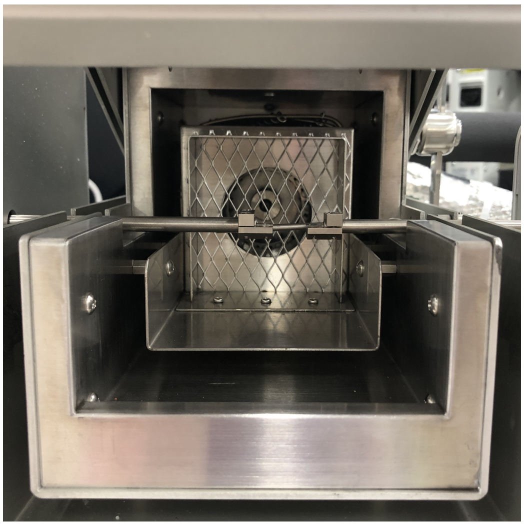


FIGURE 3.7: Photograph of the dynamic elastic modulus measuring apparatus.

The skin-softening effects of the two applications used in the psychophysical experiments were measured. The measurements were acquired with a specially constructed dynamic measuring instrument (shown in the photograph) at 32°C and 50% relative humidity. The stratum corneum strip (20 x 3 mm) was held horizontally by two clamps that were spaced 12 mm apart. The left clamp applied fixed-amplitude sinusoidal stress (strain 0.2%, 1 Hz) to the left end of the sample. The right clamp had a high-sensitivity sensor that detected the weak stress that was transmitted through the sample. The detected stress signal was calculated and transformed into digital data representing the dynamic elastic modulus (E′).

$p < 0.001$, OR = 7.08, 95% CI: 4.79–10.5, $p < 0.001$). Furthermore, the relatively small Akaike information criterion (AIC) and large log-likelihood values indicated that skin displacement differences fit the regression model better than the presented pressure differences and better explained the relationship with participant responses. In brief, simultaneous measurements showed that the actual amount of skin displacement induced by tactile stimuli and the corresponding tactile assessments of the participants were significantly related. This indicates that the employed stimulation method allows for the quantification of tactile sensitivity based on skin extensibility.

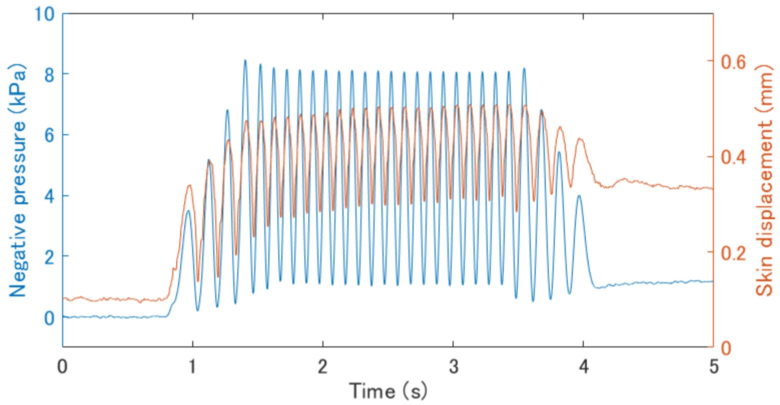
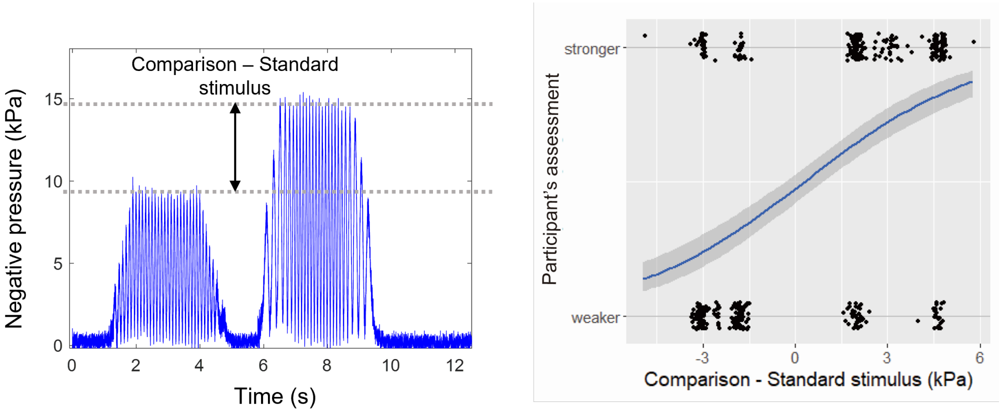


FIGURE 3.8: Skin response to periodic tactile suction stimuli that fluctuated at 10 Hz.

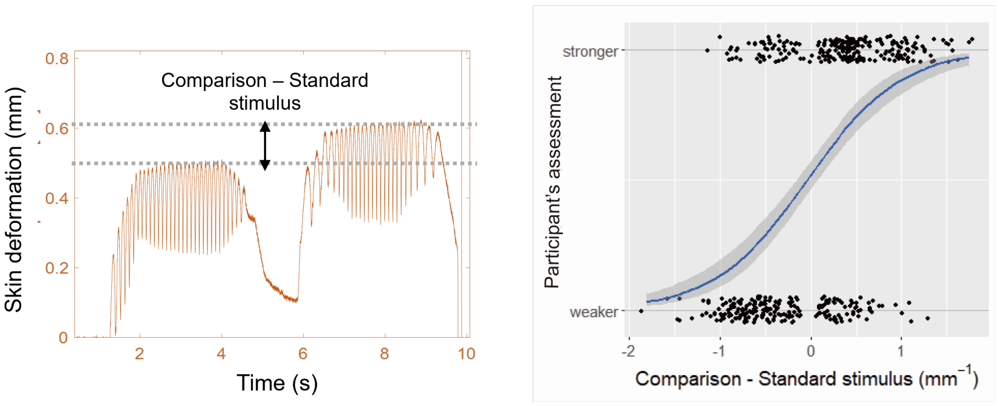
Time-varying data of the presented negative pressure (kPa) versus the skin deformation (mm). The left vertical axis shows the presented negative pressure, and the right vertical axis shows the amount of skin deformation in response to the suction. The graph shows a representative single stimulus presentation from a single trial (n = 1).

3.3.2 Hydration improved the discrimination of tactile stimulus intensity with an increase in skin displacement differences

Here, we examined the effect of the application intervention on tactile sensitivity. Additionally, we observed the corresponding actual skin displacement to investigate the underlying factors contributing to the changes in tactile sensitivity. First, we investigated whether tactile sensitivity was altered by the application interventions on the skin surface layer. We calculated the difference threshold from the participant's response to suction stimuli measured by the method of constant stimuli



(a) Negative pressure



(b) Skin displacement

FIGURE 3.9: Participants assessed stimulus intensity based on actual skin displacement differences.

The difference in intensity between the comparison stimulus and the standard stimulus is shown on the x-axis, and the participant's assessment of the intensity is shown on the y-axis. Each figure shows the 453 trials in which the participant responded "stronger" or "weaker" in both groups before the application, except for trials in which the comparison stimulus was equivalent to the standard stimulus. Logistic regression of participants' reactions and the presented pressure (a) or skin displacement (b). The presented negative pressure and skin displacement were associated with the participants' assessments of the stimulus intensity, with adjusted ORs of 1.42 for the presented negative pressure (95% CI: 1.32–1.52, $p < 0.001$, log likelihood = -259.7, AIC = 523.3) and 7.08 for the skin displacement (95% CI: 4.79–10.5, $p < 0.001$, log likelihood = -245.3, AIC = 494.6).

before and after applying cream or Milli-Q water to the cheek. Figure 3.10 shows the difference threshold before and after application. The vertical axis represents the difference threshold, which is the minimum amount of stimulus required to perceive the difference between two stimulus intensities. Therefore, a lower difference threshold indicates higher tactile sensitivity. Wilcoxon signed-rank tests revealed that the difference thresholds of the intervention group were significantly lower after application than before application ($Z = -2.80$, $p < 0.01$). A significant intervention effect was observed among the majority of participants, regardless of their difference thresholds. However, in the control group, the change in the difference threshold was not significant ($Z = 0.75$, $p = 0.46$). In brief, the participants perceived slight differences in the intensity of the mechanical stimulus after cream was applied to the skin, while the application of Milli-Q water did not significantly change the sensations felt. Second, we examined the relationship between the change in tactile sensitivity due to the application intervention and the corresponding skin displacement. We compared intraparticipant changes in the accuracy of participants' assessments of tactile intensity to the presented suction stimulus and the change in skin displacement difference (Figure 3.8 b) after the application intervention for both groups. As shown in Table 3.2, there was a significant relationship between improvement in the participant's assessment and increase in the skin displacement difference ($\chi^2 = 5.39$, $p < 0.05$). In short, the accuracy of tactile intensity assessments for each trial increased as the actual skin displacement difference during the tactile stimulation increased. The intervention group exhibited a greater number of trials with an "increased" skin displacement difference after the application, with a median increase of 1.9 µm. Conversely, the control group had more trials with a "decreased" skin displacement difference after application, resulting in a median decrease of 2.3 µm. Taken together, these results suggest that cream application increased tactile sensitivity to skin stretching in a limited area, and these perceptual changes corresponded directionally to the change in skin displacement during tactile stimulation.

3.3.3 Enhanced compliance and skin extensibility due to hydration in the stratum corneum

We have shown that cream application increased tactile sensitivity. Here, we identify the actual changes that occurred in the stratum corneum due to the application intervention in terms of skin mechanics and skin physiology. The amount of skin displacement before and after application was compared when the same stimulus

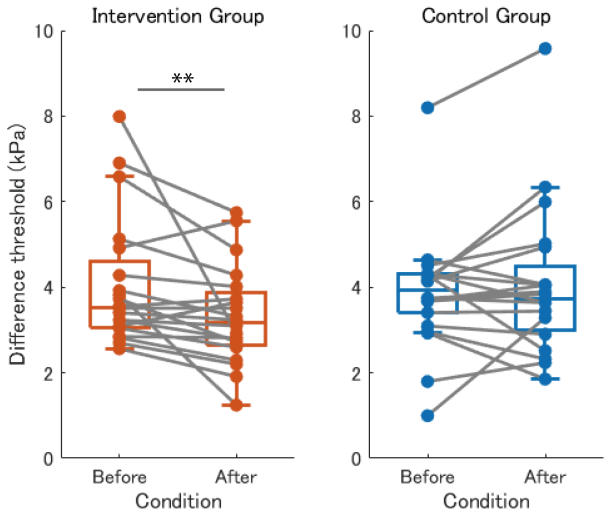


FIGURE 3.10: Applying skin cream increased tactile sensitivity.

Comparison of the tactile threshold before and after application between the two groups. The vertical axis represents the difference threshold, which is the minimum amount of stimulus required to perceive the difference between the two stimulus intensities. Therefore, the lower this value is, the higher the tactile sensitivity. Wilcoxon signed-rank tests revealed that the difference thresholds of the intervention group were significantly lower after application than before application (Z = -2.80, $p < 0.01$). On the other hand, in the control group, the change in the difference threshold was not significant (Z = 0.75, p = 0.46). **: $p < 0.01$

TABLE 3.2: Increased intraparticipant skin displacement differential change led to accurate stimulus intensity assessments.

		Skin displacement difference (Intervention/Control)	
		Increased	Decreased
Assessment (Intervention/Control)	Improvement	86 (50/36)	65 (34/31)
	Deterioration	71 (38/33)	91 (46/45)

The table shows how the change in skin displacement difference affects participants' intensity assessment accuracy. The trials with correct-to-incorrect assessment changes after application are labeled as "Deterioration", and those with incorrect-to-correct changes as "Improvement". The trials with larger postapplication displacement differences are labeled as "Increased", and those with smaller differences as "Decreased". To account for measurement errors, trials with skin displacement differences of 1 μm or less (n = 19) were excluded from analyses. The numbers in parentheses indicate the corresponding number of trials for the intervention and control groups, respectively. There was a significant relationship between the improvement in assessment accuracy and increase in the skin displacement (χ^2 = 5.39, p < 0.05).

intensity (in this case, a standard stimulus) was presented in a psychophysical experiment (Figure 3.11). Wilcoxon signed-rank tests showed that the intervention group exhibited significantly increased peak skin displacement during the presentation of the 10 Hz dynamic mechanical stimulus (Z = 3.17, p < 0.01). In contrast, no significant changes were observed in the control group (Z = -0.43, p = 0.67). Figure 3.12 shows the skin mechanical properties as measured by the Cutometer before and after the application of cream or Milli-Q water. As shown in Figure 3.12 a, only the intervention group showed significantly greater skin distensibility (R0; Z = -2.11, p < 0.05). For net elasticity (R5), gross elasticity (R2, data not shown), and the ratio of elastic recovery to distensibility (R7, data not shown), which indicates elasticity, no significant differences were observed between the groups (Figure 3.12 b). Thus, the application of cream resulted in increased skin extensibility, which was confirmed through the tactile stimulation experiment.

Figure 3.13 shows the skin water content before and after the application of cream or Milli-Q water. Regarding the conductance values measured by SKICON (Figure 3.13 a), only the values of the intervention group were significantly greater after application (Z = -3.12, p < 0.01). The capacitance values were not significantly changed by application in either group (Figure 3.13 b). The tape stripping experiment showed that PEG/PPG-17/4 dimethyl ether, a component of the cream that is expected to have a softening effect, penetrated into the superficial skin layer at the sites where the cream was applied. In the control condition, the amount was below the detection limit (Figure 3.14). According to the dynamic elastic modulus measurements, skin softening was observed in the cream-applied stratum corneum samples, while no skin softening was observed in the Milli-Q water-applied stratum corneum samples (Figure 3.15). To summarize the effects of the application interventions, the stratum corneum was characterized by higher water content and compliance after cream application, contributing to greater skin extensibility against mechanical stimuli. On the other hand, the application of Milli-Q water did not significantly change any of the evaluation indices.

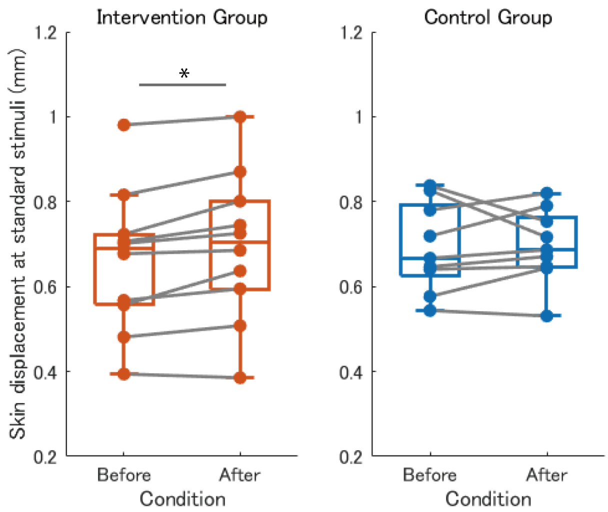


FIGURE 3.11: Applying skin cream modulated skin deformation in response to 10 Hz periodic tactile stimulus.

Comparison of skin displacement before and after application between the two groups. The vertical axis represents the skin deformation when standard stimuli were presented. The values correspond to trials with the same participant at the same stimulus position. Wilcoxon signed-rank tests showed that the intervention group had significantly increased peak skin deformation during the presentation of a 10 Hz dynamic mechanical stimulus ($Z = 3.17$, $p < 0.01$). In contrast, no significant changes were observed in the control group ($Z = -0.43$, $p = 0.67$). The data are from 19 subjects for whom skin displacement could be measured (intervention group: 10 subjects, control group: 9 subjects). *: $p < 0.05$

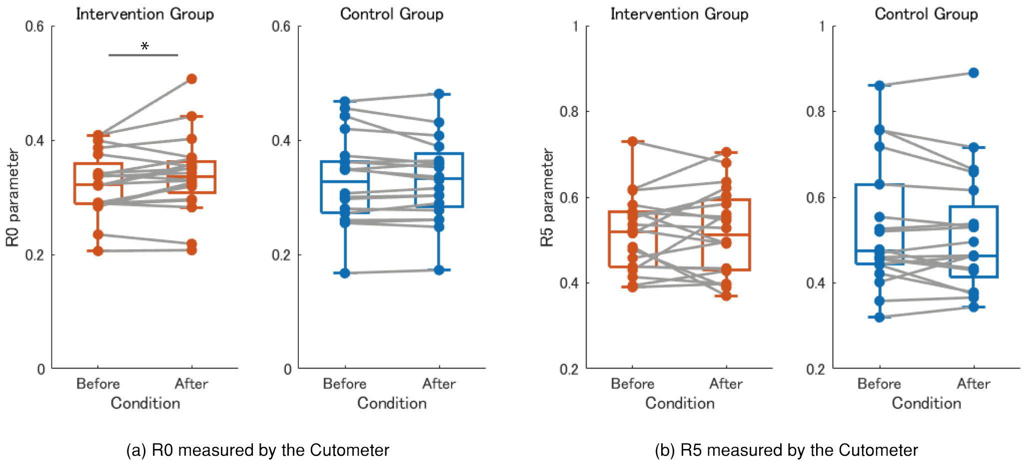
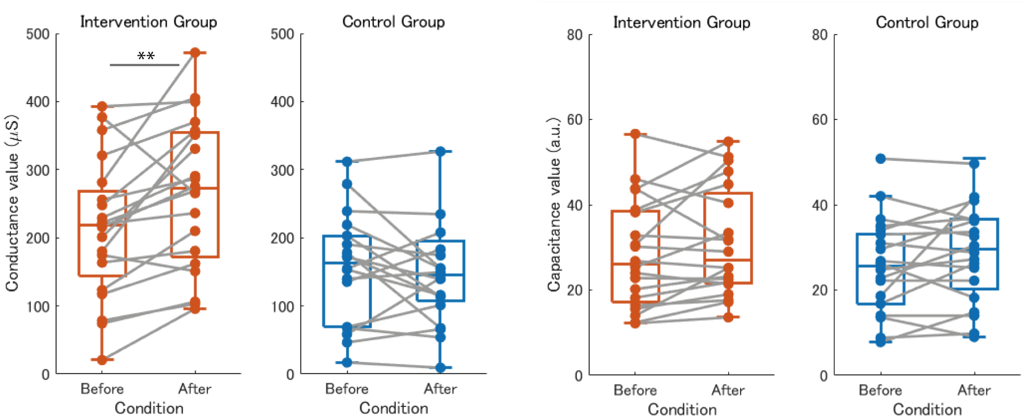


FIGURE 3.12: Applying skin cream increased skin extensibility but did not change elasticity.

Comparison of skin extensibility before and after application between the two groups. (a) R0 is an index of skin extensibility; a higher value indicates that the skin is easier to stretch. (b) R5 is an index of elasticity; a higher value indicates more elastic skin. The values correspond to trials with the same participant. (a) Wilcoxon signed-rank tests showed a significant increase in the R0 value before and after application in the intervention group (Z = -2.11, $p < 0.05$), while no significant difference was observed in the control group (Z = -0.74, $p = 0.46$). (b) R5 values were not significantly different before and after application in either group (Z = 0.11, $p = 0.91$, Z = 1.25, $p = 0.21$, respectively). *: $p < 0.05$



(a) SKICON measurement

(b) Corneometer measurement

FIGURE 3.13: Applying skin cream hydrated the superficial layer of the skin.

Comparison of skin water content before and after application between the two groups. The y-axis represents the conductance and capacitance values, with higher values indicating higher water content. The values correspond to trials with the same participant. (a) Wilcoxon signed-rank tests showed a significant increase in the conductance values measured by SKICON before and after application in the intervention group (Z = -3.12, $p < 0.01$), while no significant difference was observed in the control group (Z = 1.31, $p = 0.19$). (b) Capacitance values measured with the Corneometer, which reflect the water content in deeper layers than those detected by SKICON, were not significantly different in the two groups before and after application (Z = -1.55, $p = 0.12$, Z = -0.99, $p = 0.32$, respectively). Data for one participant in the control group with a conductance value of 1332 before and 288 after application are not shown in the graph. **: $p < 0.01$

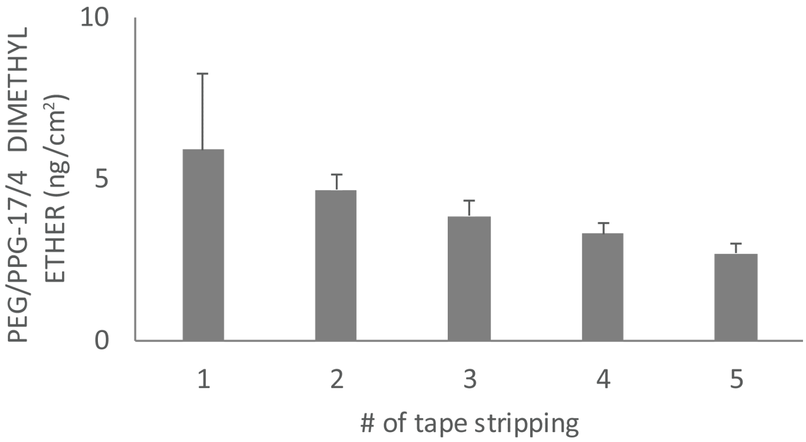


FIGURE 3.14: Hydrating ingredients penetrate the stratum corneum after ten minutes of application.

The vertical axis shows penetration profiles for human stratum corneum of PEG/PPG-17/4 dimethyl ether formulated in the cream used in the psychophysical experiments (mean ± SE; n = 4). The LOD value (2.6 ng) or lower is not shown. The bars represent the penetration profiles after cream application (experimental condition). PEG/PPG-17/4 dimethyl ether was not detected in the control condition.

3.4 Discussion

In this study, we investigated the contribution of the stratum corneum compliance to tactile sensitivity resulting from skin hydration. We performed hydration interventions on the stratum corneum with a cosmetic treatment. While the causal relationship between the mechanical properties of the skin and tactile sensation has been established, it is still necessary to further examine which specific layers of the skin contribute to this relationship. From the perspective of developing appropriate intervention strategies, it is still unclear which specific intervention methods on the skin contribute to changes in tactile sensation during contact with various objects. To address this, we focused the compliance of the stratum corneum which can vary daily due to skincare and environmental factors. First, we observed skin displacement behavior during tactile stimulation to quantify changes in tactile phenomena and psychophysically evaluated the impact of hydration on tactile sensation during skin stretching. Our findings revealed a clear association between tactile stimulus intensity perception and the extent of skin deformation. Second, experimental investigations into the contribution of the stratum corneum to tactile sensitivity, from the perspective of both skin mechanics and skin physiology, confirmed that the immediate mechanical response due to the compliance of the stratum corneum plays a notably important role in shaping the perception of tactile stimulus intensity associated with skin stretching. These phenomena were brought about by hydration interventions in the stratum corneum, a thin layer of the skin. This concrete evidence is highly promising for advancing our comprehension of the intricate relationship

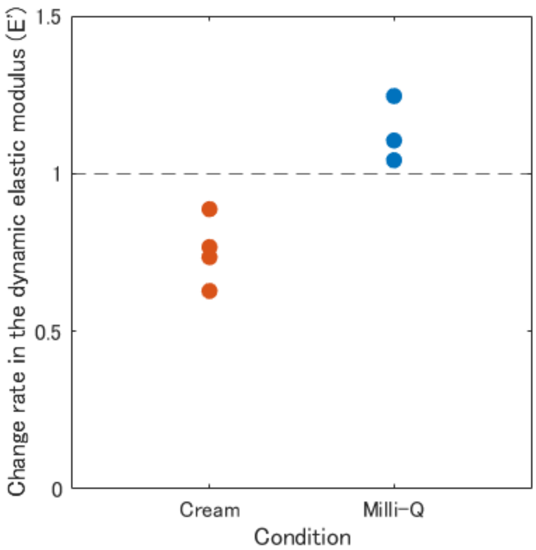


FIGURE 3.15: Cream application decreases the dynamic elastic modulus of the stratum corneum.

Smaller values indicate greater stratum corneum compliance. Each point represents the dynamic elastic modulus after application compared to the preapplication baseline value for each test sample. The dynamic elastic modulus of the cream-applied sample decreased, while that of the Milli-Q water applied sample increased compared to the preapplication condition.

between the stratum corneum and the tactile experience. These findings will be pivotal in guiding the development of interventions that can effectively modulate skin physical properties, thus facilitating the attainment of the desired tactile experience.

The tactile sensation is influenced by the skin's mechanical response characteristics, specifically observed as the phenomenon of skin displacement in response to stimulation. By observing the physical phenomena occurring during tactile sensation, we focused not on skin hydration per se but on how any skin mechanical response affects tactile sensitivity. There are precedents of reduced light pressure sensitivity induced by monofilaments with the addition of petrolatum (Weinstein, 1977) despite its presumed ability to hydrate the skin, which is thought to be due to reduced skin displacement in response to mechanical stimuli. Hence, it is crucial to measure the actual skin displacement to gain insights into the mechanism of tactile sensation. In our study, we employed simultaneous measurement of skin displacement during tactile stimulation, allowing us to directly observe the relationship between perceived tactile intensity and skin displacement magnitude. By measuring the skin displacement occurring at the time of each touch intensity assessment, as shown in Figure 3.8 b, we were able to show that the stimulus intensity can be discriminated approximately 50% of the time when skin displacement induced by the comparison stimulus differs by approximately 50 μm from the skin displacement induced by the standard stimulus (median value of approximately 700 μm) (Figure 3.11). Although a very small skin displacement of 5-10 μm has been used as the stimulus threshold for detecting a 10 Hz vibration amplitude in the human finger (Verrillo and Gescheider, 1979; Fukuda, Satow, and Miyaoka, 1982; Gescheider, Bolanowski, and Hardick, 2001), we were also able to infer a discriminable tactile skin displacement difference on the cheek. Moreover, our findings from the application intervention revealed that the accuracy of tactile intensity assessments was contingent upon the magnitude of the skin displacement difference. This indicates the importance of capturing the actual physical phenomenon of skin displacement occurring during tactile stimulation on the skin, rather than solely focusing on the applied intervention. This is crucial for advancing our understanding of tactile sensation and facilitating the development of effective interventions.

Hydration-induced alterations in skin structural mechanics are believed to influence mechanotransduction processes in the deeper layers of the skin, where the mechanoreceptors are situated. Previous simulation studies have evaluated the extent to which changes in skin stiffness (Hamasaki, Yamaguchi, and Iwamoto, 2018) and structure (Jobanputra et al., 2020) influence the tactile stimuli received by mechanoreceptors. The tactile stimuli received by mechanoreceptors were greater in conditions where the skin was softer or the structure was more easily deformed. Thus, mechanoreceptors were expected to receive richer mechanical information from tactile stimuli that propagate into the skin due to increased skin displacement. Specifically, the mechanoreceptors that predominantly respond to the applied 10 Hz stimulus are thought to be Merkel cells and Meissner corpuscles (Gescheider, Bolanowski, and Hardick, 2001). The received mechanical information is thought to be stresses and/or strain (Johnson, 2001; Sripati, Bensmaia, and Johnson, 2006; Pham et al., 2017; Gerling, 2010). According to the hydration experiments, larger displacement of the skin surface may have increased the skin tissue strain near these receptors, and the softening of the relatively stiff stratum corneum may have caused stress to be generated in the deeper areas where mechanoreceptors are located, rather than in the superficial layers. To understand the role of skin mechanical properties in the transmission of mechanical information within the skin, further investigation through simulation studies is warranted. These findings can then be interpreted in conjunction with actual tactile sensitivity data. These studies may discover the skin mechanical properties and stimulus presentation methods that facilitate the transmission of tactile stimuli to mechanoreceptors.

The stratum corneum with heightened compliance increased tactile sensitivity while increasing skin displacement to periodic stimulation. The application of skin care creams increased tactile sensitivity, and the associated changes in skin properties included an increase in skin water content, heightened compliance, and amplified skin displacement due to mechanical stimuli. Concerning skin water content, the conductance values measured by SKICON increased after cream application, while the capacitance values measured by a Corneometer did not change significantly. Since the cream remaining in the superficial layers of the stratum corneum was washed off before skin measurements, these results suggest a change in the amount of moisture inside the skin due to cream application. The penetration depth of the SKICON probe is very superficial (15 µm), while that of the Corneometer probe is 45 µm (Clarys et al., 2012). Our results suggest that while short-term moisturization may have changed the physical properties of the superficial skin layer, this moisturization did not significantly change the physical properties of the deeper skin layer. The results of the transdermal absorption tests of the stratum corneum samples and the dynamic elastic modulus ratio indicated that the skin-hydrating component penetrated into the stratum corneum by passive diffusion and softened. This finding is consistent with the fact that the top layer of the stratum corneum is known to experience hydration even after short periods (Egawa and Tagami, 2008)]. The R0 value measured with the Cutometer increased significantly after cream application. Similar to the Cutometer data, the skin displacement in response to 10 Hz periodic tactile stimuli during the tactile threshold measurements also increased, and the suction stimulation induced skin mechanical properties that were consistent with those typically measured using the Cutometer. Skin hydration results in greater strain in response to mechanical stimuli (Hendriks et al., 2004) and more elastic properties in the stratum corneum (Kennedy et al., 2011a). The modifications in the viscoelastic characteristics of the skin's outer layer likely contributed to a more rapid and pronounced response of the skin to oscillation stimuli, leading to significant skin displacements. By employing a controlled hydration intervention and applying suction stimulation to stretch the skin, we were able to isolate and assess the specific alterations in the properties of the outermost layer of the skin (stratum corneum) that influence tactile sensitivity.

In the present study, we were able to evaluate the effects on tactile sensitivity that were limited to the contribution of the stratum corneum. In fact, while the compliance of the skin surface layer changed after cream application, the elasticity parameters did not change significantly according to the Cutometer data. This may be because the cheek application process and short penetration time did not significantly affect the composition of elastin and collagen in the dermal layer, which contribute to skin viscoelastic properties (Silver, Freeman, and Devore, 2001). The influence of skin's physical properties on tactile sensitivity is not limited to the superficial layer of the skin. One of the most noticeable changes in skin physical properties between individuals, especially with aging, is decreased elasticity and extensibility (Kim, Kim, and Lee, 2018; Krueger et al., 2011; Luebberding, Krueger, and

Kerscher, 2014; Takema et al., 1994). Thus, considerable work should be conducted to determine what physical properties in skin layers other than the superficial layer influence tactile sensitivity.

The limitations of this study and future research directions can be summarized as follows. First, the present study focused on skin deformation at a single point inside a limited 4-mm stimulus area. However, we know that tactile sensation is a function of the population of many afferents over the entire body surface and their recruitment patterns. The contributing effects of the stratum corneum can be further clarified by examining the effects of the stimulation area (Schmidt et al., 2020) and the effects of skin anisotropy and heterogeneity (Fung, 1993) in detail. In addition, we used the peak skin displacement of 10 Hz stimulation as an index of skin mechanical responsiveness, but it could be useful to investigate the history-dependent response of the skin to periodic stimulation. It could also be valuable to focus on time-series changes in skin deformation behavior to clarify the contribution of viscoelastic properties, which change significantly with aging (Takema et al., 1994), to sensory perception. Moreover, although the present study measured tactile sensation of local skin deformations using suction stimulation to clarify the constraint conditions, the universality of the present findings in stimulation methods other than suction needs to be confirmed. Some previous papers have suggested that the ability of the skin to conform to the shape of the stimulus is important for the spatial perception of touch (Vega-Bermudez and Johnson, 2004), while others have indicated that thin or soft skin does not necessarily result in a lower vibration threshold (Holowka et al., 2019) or age is related to the two-point discrimination threshold, not for skin compliance in the case of glycerol applied uniformly to the skin surface (Woodward, 1993). To comprehensively understand these factors, it is important to consider not only externally observable physical phenomena (such as skin displacement) but also what external mechanical information is ultimately sensed by the mechanoreceptors inside the skin. Quantification of the tactile phenomena affected by stratum corneum compliance in this study is an important step for promoting research to visualize mechanotransduction within the skin.

3.5 Summary

In this study, we investigated the contribution of the stratum corneum compliance to tactile sensitivity resulting from skin hydration. We performed hydration interventions on the stratum corneum with a cosmetic treatment.

What has become evident here is that, firstly, by employing tactile stimulation using a suction device and conducting limited hydration interventions in the stratum corneum, we were able to evaluate sensory thresholds while observing skin deformation during tactile stimulation. Our findings revealed that hydrating the stratum corneum significantly enhances tactile sensitivity and is accompanied by changes in skin deformability.

These findings have promising implications for future advancements. We got valuable insights for advancing our ability to effectively modulate stratum corneum compliance and elicit appropriate tactile sensations. This thin layer is likely to have a significant impact on tactile experiences involving skin stretching, such as interpersonal touch gestures, gentle massage, and product application. Impaired mechanical responsiveness of the skin, such as extreme dryness of the stratum corneum, can have negative consequences on tactile comfort and the accurate interpretation of interpersonal tactile cues and intentions. Skin care formulations that selectively modulate skin mechanical responses by regulating moisture levels can enhance their effectiveness in achieving the desired tactile experience. In addition, tactile sensation varies depending on the skin condition even with the same stimulus. To eliminate individual differences in sensation and provide or estimate the desired tactile experience, it may be effective to control the skin deformation that occurs during tactile stimulation instead of the stimulus intensity or adjust the tactile stimuli according to the skin condition. These considerations could contribute to the advancement of tactile presentation techniques.

Chapter 4

Simulated Effect of Skin Stiffness and Viscoelasticity on Mechanical Propagation of Vibratory Stimuli between Skin Layers

4.1 Introduction

The objective of this chapter is to evaluate the effects and trends of changes in the stiffness and viscoelasticity of the skin on the propagation of mechanical quantities between skin layers where mechanoreceptors are present when subjected to periodic stimuli. Up to Chapter 3, tactile phenomena have been observed in human subjects, but there are some skin mechanical properties, such as deep skin layers, that are difficult to intervene in. Therefore, we used simulation studies to estimate the effects of parametric changes in the skin mechanical properties, especially stiffness and viscoelasticity, on tactile sensitivity. In this section, we summarize the simulation studies of tactile sensation, modeling studies of skin mechanics, and describe our motivation for focusing on changes in skin viscoelasticity.

Simulation studies are commonly conducted to investigate the contribution of skin mechanics to tactile sensation. When trying to quantify the influence of skin mechanics on tactile sensation, it is challenging to evaluate the isolated effects of skin mechanical properties in human experiments due to the complex interplay of various factors. However, efforts have been made to elucidate these effects through computer simulations that replicate skin mechanics and estimate the propagation of mechanical quantities occurring within the skin during deformation. This is because mechanical quantities, such as strain, stress, and strain energy density (SED), at the epidermal-dermal interface are known to correlate with the recorded slowly-adapting (SAI) or rapidly-adapting (RA) afferent firing, terminating in the mechanoreceptors Merkel cells and Meissner corpuscles, respectively (Phillips and Johnson, 1981; Srinivasan and Dandekar, 1996; Johnson, 2001; Ge and Khalsa, 2002; Gerling, 2010).

The effect of changes in skin stiffness and structure on the propagation of mechanical quantities within the skin has been the focus of simulation studies. It has been shown that the presence of dermal papillae leads to an increase in the Von Mises stress and SED at the mechanical receptor locations when the fingertip is in contact with a rigid body (Maeno, Kobayashi, and Yamazaki, 1998; Gerling, 2010; Pham et al., 2017). As the Young's modulus of the fingertip epidermis increases, the Von Mises stress distribution becomes less distinguishable through two-point discrimination (Hamasaki, Yamaguchi, and Iwamoto, 2018). In the assumed hairy skin, the contraction of the stratum corneum leads to a significant increase in strain fields including the epidermis region near the dermal papillae (Bennett-Kennett et al., 2023; Hendrickx-Rodriguez et al., 2022). Age-related changes in the fingertip, stiffness of each layer, and the structural shape of dermal papillae were quantitatively shown to affect the propagation of SED, strain, and Von Mises stress within the mechanoreceptor area at the epidermal-dermal interface (Jobanputra et al., 2020). The effects of skin layer structure and stiffness on the propagation of mechanical quantities within the skin resulting from skin deformation have been elucidated, but it should be noted that these models do not consider viscoelasticity.

Skin viscoelasticity is an important parameter for simulating mechanical propagation, as it represents individual characteristics. As a general phenomenon of aging, the elastic response rate to instantaneous loading decreases, and the elastic recovery after load relaxation also becomes slower, particularly in exposed areas like the cheeks, indicating that these viscoelastic properties serve as indicators of individual differences in skin, rather than skin stretchability and stiffness (Bader and Bowker, 1983; Escoffier et al., 1989; Kim, Kim, and Lee, 2018; Krueger et al., 2011; Luebberding, Krueger, and Kerscher, 2014; Pawlaczyk, Lelonkiewicz, and Wieczorowski, 2013; Takema et al., 1994). *In vitro* measurements have also shown that elastin significantly decreases with aging (Daly and Odland, 1979; Braverman and Fonferko, 1982; Ritz-Timme, Laumeier, and Collins, 2003) and contributes to the loss of elastic recovery in aged skin.

Skins viscoelastic behavior has been modeled based on the mechanical responses of the skin to various loadings (Mostafavi Yazdi and Baqersad, 2022; Sachs et al., 2021). The quasi-linear viscoelasticity (QLV) approach (Fung, 1993) is effective for modeling the viscoelastic behavior of various soft tissues including skin (Benítez and Montáns, 2017; Joodaki and Panzer, 2018), and has been widely used in many studies for material identification based on the time-dependent behavior observed in *in vivo* measurements of the skin. Skin viscoelasticity has been modeled based on the stable indentation load (Crichton et al., 2013), single-cycle compression with a strain rate of 35/s (Flynn and Mccormack, 2008), and periodic tension stimulation with an amplitude of 1.5 mm and a frequency of 0.1 Hz (Flynn, Taberner, and Nielsen, 2011; Flynn et al., 2013). Even with shorter stress relaxation time constants, these models were able to reproduce time-dependent deformations of the skin within the range of 0.3-1.6 s.

Skin viscoelasticity is gaining attention for its potential impact on the propagation of mechanical quantities within the skin. In a computer simulation study, it has been shown that the presence of viscoelasticity contributes to temporal changes in the propagation of static indentation-induced SED, and the viscoelastic tissue around mechanoreceptors plays a role in regulating the rate of adaptation of SAI mechanoreceptors (Kumar et al., 2015). Attention has also been focused on the effects of variations in viscoelastic properties. It was found that individual differences in the viscoelastic properties of rat skin, determined based on measurements of indentation displacement and reaction force, along with variations in skin thickness and stiffness, contribute to the variability in the neural response of SAI afferents (Wang et al., 2016). However, since the estimation involves the combined effects of geometric and material properties of the skin, the parametric influence of viscoelasticity of each skin layer on the propagation of mechanical quantities has not been investigated.

The motivation of this study lies in exploring the contribution of skin viscoelasticity to the propagation of mechanical quantities during periodic skin deformation. In the field of tactile sensation research, while it is known that skin stiffness and structure influence the propagation of mechanical quantities during skin deformation, the specific effects of changes in viscoelasticity within individuals are not well understood. Furthermore, time-dependent behavior and hysteresis during periodic loading (Troyer and Puttlitz, 2011), where viscoelastic effects are more pronounced, need to be better understood, as skin viscoelasticity models are often based on single-cycle or static loading. This study aims to enhance our understanding of tactile sensation and provide insights for various fields, such as optimizing mechanical therapies for pain relief (Liu et al., 2015), by examining how skin's mechanical properties influence the propagation of mechanical quantities during periodic deformation.

The objective of this study was to evaluate the effects and trends of changes in the stiffness and viscoelasticity of the skin on the propagation of mechanical quantities between skin layers where mechanoreceptors are present when subjected to periodic stimuli. First, a skin finite element model was created by optimizing material parameters to reproduce the actual skin response obtained by using a special device developed to evaluate the time-dependent response of skin. This device could simultaneously provide periodic stimulus and measure skin deformation (Saito et al., 2019a; Saito et al., 2019b; Sakaguchi et al., 2023b; Sakaguchi et al., 2023a). Here, suction stimulation was used to identify the skin material properties while eliminating the influence of the subcutaneous muscle and bone (Pierard, Nikkels-Tassoudji, and

Pierard-Franchimont, 1995; Barbarino, Jabareen, and Mazza, 2011). The stimulus frequency was set to 10 Hz, which has a high response sensitivity for sensory nerves terminating in Merkel cells and Meissner corpuscles (Gescheider, Bolanowski, and Hardick, 2001). It is a new challenge to target such relatively fast frequencies, which are not common in modeling skin history-dependent properties. Next, we calculated how parametric changes in the material parameters of the skin model affect the propagation of mechanical quantities between skin layers where Merkel cells and Meissner corpuscles are present. Furthermore, the implications of these simulation findings regarding the contribution of skin viscoelasticity to tactile sensation are discussed, since it was confirmed in human tests under the experimental conditions referred to in this study that larger skin deformation is associated with higher tactile sensitivity under periodic suction stimulation (Sakaguchi et al., 2023b).

4.2 Methods

To simulate how periodic mechanical stimuli are transmitted to skin mechanoreceptors, we first constructed a skin finite element model by optimizing material parameters to reproduce actual human cheek skin deformation. Then, the material parameters of the optimized model were parametrically varied to calculate the mechanical quantities propagated at the mechanoreceptor locations. The purpose of the investigation here was to establish the effects and trends of skin material parameter changes on the magnitude of mechanical quantities, rather than to obtain biologically accurate absolute values.

4.2.1 Skin deformation measurement

Deformation findings on female cheek skin in response to 10 Hz periodic suction stimuli, simultaneously measured with the tactile sensitivity by the suction device (Sakaguchi et al., 2023b), were used to construct the skin finite element model. The participants were 26 Japanese women, ranging in age from 20 to 72 years, who had no physical disability, skin disease, or significant skin damage such as excessive sunburn on the face. The measurement was performed in a room with a constant temperature of 22.0°C and a relative humidity of 45.0%. For the measurements, the participant was instructed to position their face on a chin rest to ensure that the stimulus point, which was the cheek, remained constant. Each participant underwent skin deformation measurements repeated three times. Figure 4.1 shows the configuration of the suction device. The contact force of the contactor against the cheek can be kept constant by a spring guide. Skin deformation in response to suction oscillation stimulus presented through a suction hole with a diameter of 2 mm was acquired with a two-dimensional laser displacement meter (Keyence LJ-V7080) mounted inside the contactor of a suction device. Time-series data of skin deformation by suction at the center of the suction hole was used for the material parameter optimization described below.

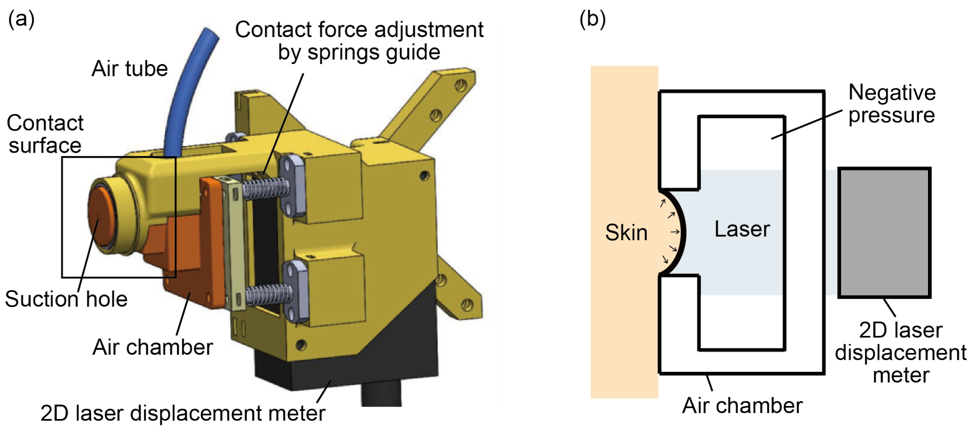


FIGURE 4.1: Configuration of a contactor of the developed suction device.

(a) Contactor of the suction device in contact with the skin and suction stimulation applied to the skin through the suction hole. The contact force of the contactor against the skin can be kept constant by a spring guide. The air chamber is sealed when the 2 mm diameter suction hole contacts the skin. The suction stimulus generated by the compression and expansion of the air in the cylinder by the actuator is transmitted to the air chamber through the air tube. The back side of the air chamber is made of glass, enabling a laser displacement meter installed on the back side to acquire the amount of skin deformation at the suction hole. (b) Schematic diagram of the contact surface with the skin. The skin deformation ridges at the suction hole caused by suction stimulation were acquired by a 2D laser displacement meter. The skin displacement at the center of the suction hole was the optimization target.

4.2.2 Contstruction of the finite element model

A two-dimensional, incompressible, isotropic, cheek skin model was constructed and run using a nonlinear finite element analysis solver (MSC. Marc/Mentat) with reference to previous skin suction modeling studies (Hendriks et al., 2003; Hendriks et al., 2004; Hendriks et al., 2006). The model was axi-symmetric and reproduced the conditions described in the previous section in which the contactor of the suction device is pressed against the skin to apply negative pressure (Figure 4.2). The boundary conditions were set as follows: the bottom layer was fixed in the X-direction, and the symmetry-axis side and outer side of the tissue structure were fixed in the Y-direction for displacements. The model consisted of four layers: the stratum corneum, epidermis, dermis and hypodermis. Table 4.1 presents the thickness of each layer in the model. The thickness of the stratum corneum was based on the averaged measured value (Hara et al., 2013), and the hypodermis tissue was set to a sufficient thickness so as not to affect the analysis. The thicknesses of the epidermis and dermis were based on ultrasound images of the participants' cheek skin from the previous study (Sakaguchi et al., 2023b) measured with DermaScan (Cortex Technology, DER-S)(Phillips, Reynolds, and Gordon, 2020). The total number of elements (quad4) constituting each layer was 3347 (187 in the stratum corneum, 720 in the epidermis, 1884 in the dermis, 556 in the hypodermis). For all models, the density was 1.1×10^3 kg/m^3 for the stratum corneum, epidermis, and dermis and 9.7×10^2 kg/m^3 for the hypodermis tissue (Maeno, Kobayashi, and Yamazaki, 1998; Hendriks et al., 2003). The indentation displacement of the contactor of the suction device to the skin was represented as a displacement constraint. The negative pressure in the suction hole was applied by edge loading. The contact condition between the probe and the skin was defined by a coefficient of friction of 0.6.

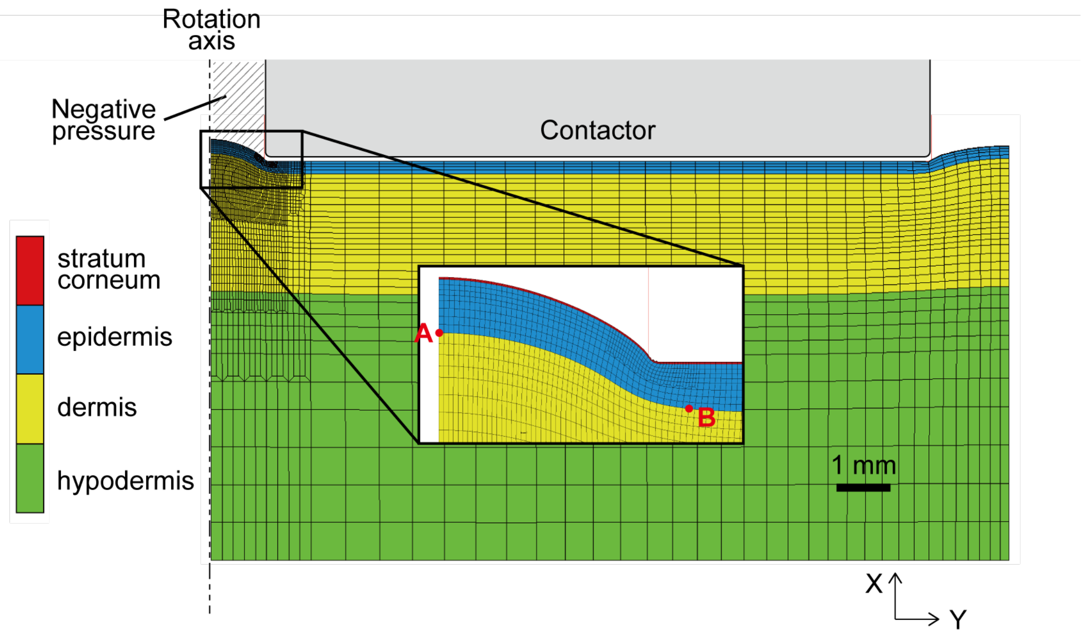


FIGURE 4.2: Illustration of the finite element (FE) model used in the analysis.

The model was axi-symmetric and reproduced the conditions in which the contactor of the suction device is pressed against the skin to apply negative pressure. The boundary conditions were set as follows: the bottom layer was fixed in the X-direction, and the symmetry-axis side and outer side of the tissue structure were fixed in the Y-direction for displacements. The model was composed of four layers with 3347 elements. The indentation displacement of the contactor of the suction device to the skin was represented as a displacement constraint. The negative pressure in the suction hole was applied by edge loading. The contact condition between the contactor and the skin was defined by a coefficient of friction of 0.6. The strain, stress and SED were recorded from the nodes at the epidermal-dermal interface from A to B on the mechanoreceptor locations.

Extended Mooney material behavior was modeled to account for the non-linear stress–strain relationship of the skin. The following strain energy function was used:

$$W = C_{10}(I_1 - 3) + C_{11}(I_1 - 3)(I_2 - 3) \tag{4.1}$$

This function is based on the strain energy function (MSC.MARC, 2003), where I_1 and I_2 are the first and second invariant of the strain tensor, while C_{10} and C_{11} are the hyperelastic parameters. As for the hyperelastic properties, we referred to Young's modulus E of the stratum corneum, epidermis, and dermis (Hara et al., 2013; Maeno, Kobayashi, and Yamazaki, 1998) and obtained C_{10} for each layer based on $E = 6C_{10}$ (Hendriks et al., 2003). The epidermal and dermal C_{11} were averaged from the dermal C_{11} of the forearm (Hendriks et al., 2003). The material parameters of hypodermis tissue were obtained by accurately simulating unconfined compression of human hypodermal tissue (Flynn and Mccormack, 2008; Flynn and McCormack, 2010).

The total stress in the specimen is assumed to be equal to an elastic stress, $\sigma_e[\lambda(t)] = \frac{\lambda \partial W}{\partial \lambda}$, due to the instantaneous tissue response decreased by a viscous component depending on the past history, where λ is the principal strain. The viscoelasticity was modeled using the QLV approach (Fung, 1993). The stress as time t is given by the model as:

$$\sigma(t) = \sigma_e[\lambda(t)] + \int_0^t \sigma_e[\lambda(t-\tau)] \frac{\partial G(\tau)}{\partial \tau} d\tau \tag{4.2}$$

$$G(t) = 1 - \sum_{i=1}^{2} G_i (1 - e^{\frac{-t}{\tau_i}}) \tag{4.3}$$

where G_i represents the modulus coefficients and τ_i represents the relaxation times. To reproduce skin deformation behavior at 10 Hz, τ_1 was optimized in the range of 0.001 to 0.1 and G_1 in the range of 0.1 to 0.9, and the second term of the Prony series was set to a relatively long time constant (τ_2 = 10 s, G_2 = 0.09).

4.2.3 Material parameter optimization based on human skin deformation behavior

Skin modeling studies conducted with periodic skin deformation are insufficient, while the skin material parameters are not uniquely determined. Therefore, following previous studies (Delalleau et al., 2008; Weickenmeier, Jabareen, and Mazza, 2015), we optimized the skin material parameters, targeting the measured human skin deformation (Sakaguchi et al., 2023b) induced by suction pressure.

We have extracted four skin displacements as optimization targets from the time-series data of skin deformation shown in Figure 4.5 b,d,f. These skin displacements were calculated using the skin deformation measured immediately before the start of suction as the zero reference. The optimization targets were the average peak displacement (*PK*), the average peak-to-peak displacement (*PPK*), the peak displacement trend (*TPK*) during the steady-state interval (3.1-3.6 s in Figure 4.5 b,d,f), and the peak-to-peak of the initial three stimulus cycles (*IPPK*). Here, peak refers to local maxima, and peak-to-peak refers to the difference between local maxima and local minima.

These optimization targets were derived from three selected participants. The *PK* values ranged from 0.14-0.69 mm for 26 participants exposed to a suction pressure of 13.5 kPa. Since a high intraclass correlation coefficient was confirmed for this *PK* value (Sakaguchi et al., 2023b), the median value of the skin deformation measurements repeated three times for each participant was adopted as the characteristic representing the participant's individuality. Specifically, these optimization target values were calculated from time-series data from three participants (47, 62, and 46 years old) representing the *PK* quartiles (0.35, 0.28, and 0.25 mm, respectively).

A schematic representation of the optimization scheme is shown in Figure 4.3. Five material parameters—the three hyperelastic parameters ($C_{10,cor}$, $C_{10,epi}$, $C_{10,der}$) and two viscoelastic parameters (G_1 and τ_1)—and the indentation displacement of the contactor of the suction device to the skin (D) were determined in parallel. As an initial exploratory study for modeling the deformation behavior at 10 Hz, the same viscoelastic parameter values were used from the stratum corneum to hypodermis, and the effects on skin displacement were examined in a simplified manner. The optimization scheme minimized the weighted cost function (f) between numerically predicted skin displacement and experimentally observed skin displacement using the fminsearch procedure in MATLAB (Weickenmeier, Jabareen, and Mazza, 2015). For the weighted cost function (f), the difference between the experimental (targets) and simulated (results) values of *PK* in Eq. (4), *PPK* in Eq. (5), *TPK* in Eq. (6), *IPPK* in Eq. (7) and the reaction force (*RF*) on the suction device contactor in Eq. (8) were processed by the norm function in MATLAB. Eq. (9) shows the weighted cost function. In this function, weights were represented by w_j, and err_1 was considered the error with the most weight since the *PK* was found to have a significant positive relationship with higher tactile sensitivity (Sakaguchi et al., 2023b). For the participant who exhibited *PK* of 0.28 mm, the weights were set as follows: w1 = 4, w2 = 3, w3 = 1, w4 = 1, w5 = 3. Three to four sets of 50 iterations were performed in the optimization process to reproduce a wide range of skin deformation behavior characteristics, adding to the robustness of the optimization scheme (Figure 4.4). The converged parameters were treated as constants in the next optimization set. The weights of all errors except err1 were fine-tuned in the final optimization set to align with the participant's deformation behavior. For example, participant 3, with smaller skin deformation, had similar weights for err_2 and err_4 as err_1 due to the ease of replicating *PK*.

$$err_1 = \frac{norm(PK_{target} - PK_{result})}{PK_{target}} \tag{4.4}$$

$$err_2 = \frac{norm(PPK_{target} - PPK_{result})}{PPK_{target}} \tag{4.5}$$

$$err_3 = \frac{norm(TPK_{target} - TPK_{result})}{abs(4TPK_{target})} \tag{4.6}$$

$$err_4 = \frac{1}{3}\sum_{i=1}^{3} \frac{norm(IPPK_{target_i} - IPPK_{result_i})}{IPPK_{target}} \tag{4.7}$$

$$err_5 = \frac{norm(RF_{target} - RF_{result})}{RF_{target}} \tag{4.8}$$

$$f = \frac{\sum_{j=1}^{5} w_j err_j}{\sum_{j=1}^{5} w_j} \tag{4.9}$$

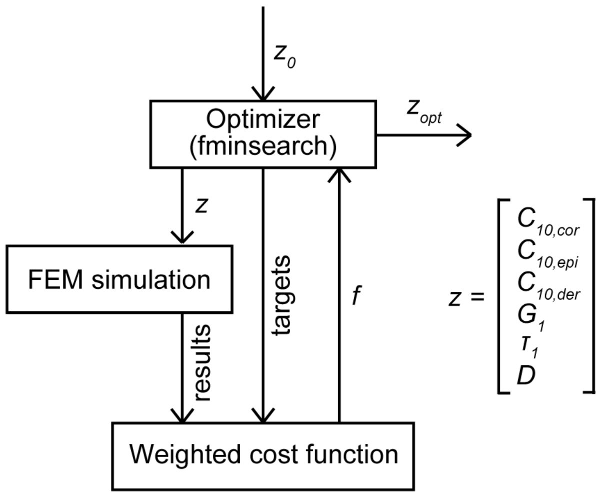


FIGURE 4.3: Schematic representation of the optimization scheme for the material parameter identification.

The optimizer (MATLAB function fminsearch) minimizes the weighted cost function of the difference between the numerically predicted and experimentally observed skin displacement. z_0 represents the vector of initial parameters, z is the vector of the iteratively adapted parameters, “result” contains the numerically predicted skin displacement of the periodic suction stimulation, “target” provides the experimentally observed skin displacement, f is a weighted cost function, and z_{opt} stores the final results of the optimization scheme.

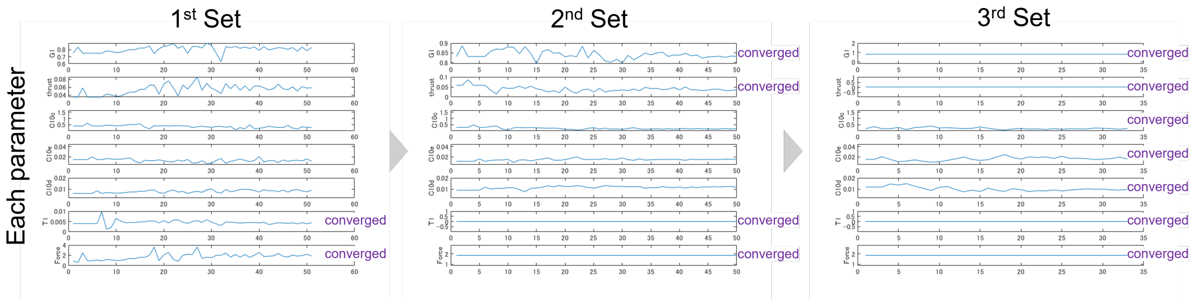


FIGURE 4.4: Example of optimization process.

Three to four sets of 50 iterations were performed in the optimization process to reproduce a wide range of skin deformation behavior characteristics, adding to the robustness of the optimization scheme. The converged parameters were treated as constants in the next optimization set.

4.2.4 Observation of the mechanical stimuli propagated at the mechanoreceptor location

The magnitude of mechanical stimuli propagated to mechanoreceptors was investigated by parametrically varying the material parameters of the optimized model. The G_1 and C_{10} parameters of the dermis, epidermis, and stratum corneum were adjusted parametrically to include the optimized G_1 and C_{10} values of three representative participants. Specifically, G_1 was varied in a range of 0.54 (65%) to the maximum setting of 0.91 (110%), $C_{10,cor}$ ranged from 50 (25%) to 480 kPa (225%), $C_{10,epi}$ ranged from 4 (25%) to 36 kPa (225%), and $C_{10,der}$ ranged from 2 (25%) to 22 kPa (225%), with 10 levels of variation for G_1 and 9 levels of variation for C_{10}. The independent effects of each material parameter in each skin layer were investigated. For example, when varying G_1 in the dermis, the C_{10} value of the dermis layer and the material parameters of other layers were kept constant at the same values.

At each time increment of the simulation, four quantities were extracted from the model output. In addition to the skin surface displacement value at the center of the suction hole, we extracted the major principal value of elastic strain, the equivalent Von Mises stress (σ_{VM}), and the total strain energy density (SED) with reference to a previous study (Jobanputra et al., 2020). The major principal value of elastic strain

TABLE 4.1: Skin mechanical properties of the 3 participants model used in the simulation.

	Hyperelastic parameters (kPa)								Viscoelastic parameters				Thickness (mm)			
Participant	$C_{10,cor}{}^*$	$C_{10,epi}{}^*$	$C_{10,der}{}^*$	$C_{10,hypo}$	$C_{11,cor}$	$C_{11,epi}$	$C_{11,der}$	$C_{11,hypo}$	$G_1{}^*$	$\tau_1{}^*$ (s)	G_2	τ_2 (s)	stratum corneum	epidermis	dermis	hypodermis
1 (0.35 mm)	305.5	22.7	4.8	1.6	0.0	82.0	82.0	0.0	0.893	0.0018	0.09	10	0.01	0.19	2.21	4.82
2 (0.28 mm)	212.2	16.1	9.6	1.6	0.0	82.0	82.0	0.0	0.832	0.0044	0.09	10	0.01	0.22	2.05	4.82
3 (0.25 mm)	332.2	22.2	3.5	1.6	0.0	82.0	82.0	0.0	0.804	0.0060	0.09	10	0.01	0.20	1.87	4.82

Numbers in the participant column indicate the measured peak skin displacement values. The asterisks (*) are the values estimated through the optimization process for each participant. Larger peak skin displacements are optimized with larger G_1 and smaller τ_1. Variable names and units are in the parentheses; if no unit is shown, the values are dimensionless.

refers to the larger absolute value between the maximum and minimum principal strains, while the equivalent Von Mises stress is expressed by the following equation:

$$\sigma_{VM} = \sqrt{\frac{1}{2}\{(\sigma_1 - \sigma_2)^2 + (\sigma_2 - \sigma_3)^2 + (\sigma_3 - \sigma_1)^2\}} \tag{4.10}$$

where σ_1, σ_2, and σ_3 represent the maximum, intermediate, and minimum principal stresses, respectively. SED is expressed as the integral of the stress–strain function:

$$SED = \int_0^{\lambda} \sigma_{ij} d\lambda_{ij} \tag{4.11}$$

where σ_{ij} and λ_{ij} represent the respective components of the stress tensor and strain tensor. Each quantity was obtained from nodes at the epidermal-dermal element interface, labeled A to B in Figure 4.2, where the Merkel cell-neuron complex and Meissner's corpuscle are located (Moll, Moll, and Franke, 1984; Vallbo and Johansson, 1984).

4.3 Results

4.3.1 Optimized model reproducing the deformation behavior of human skin

In all three representative cases, the optimization of the material parameters was completed (Table 4.1). It was found that G_1 required larger values approaching the upper limit (0.90), while τ_1 required smaller values approaching the lower limit (0.001). Figure 4.5 shows the comparison between experimental and simulated values of skin deformation in response to suction stimulation. For all three cases, the phase of the simulated values matched the experimental values. The error between the simulated and measured values of the average peak displacement (PK), with the largest optimization weight, was 1.5, 0.1, and 0.3 µm for each case, respectively, with an error rate below 1%. The viscoelastic parameters were optimized with larger G_1 values and smaller τ_1 values in order of magnitude of PK in the steady-state interval (3.1-3.6 s). Considering the skin viscoelasticity, the model successfully reproduced the skin's history-dependent response to a 10 Hz periodic mechanical stimulus.

4.3.2 Effect of the skin material parameters on mechanical stimuli propagation

The behavior of each mechanical stimulus shown hereafter was estimated when a suction stimulus with a peak pressure of 13 kPa at 10 Hz was applied to the skin

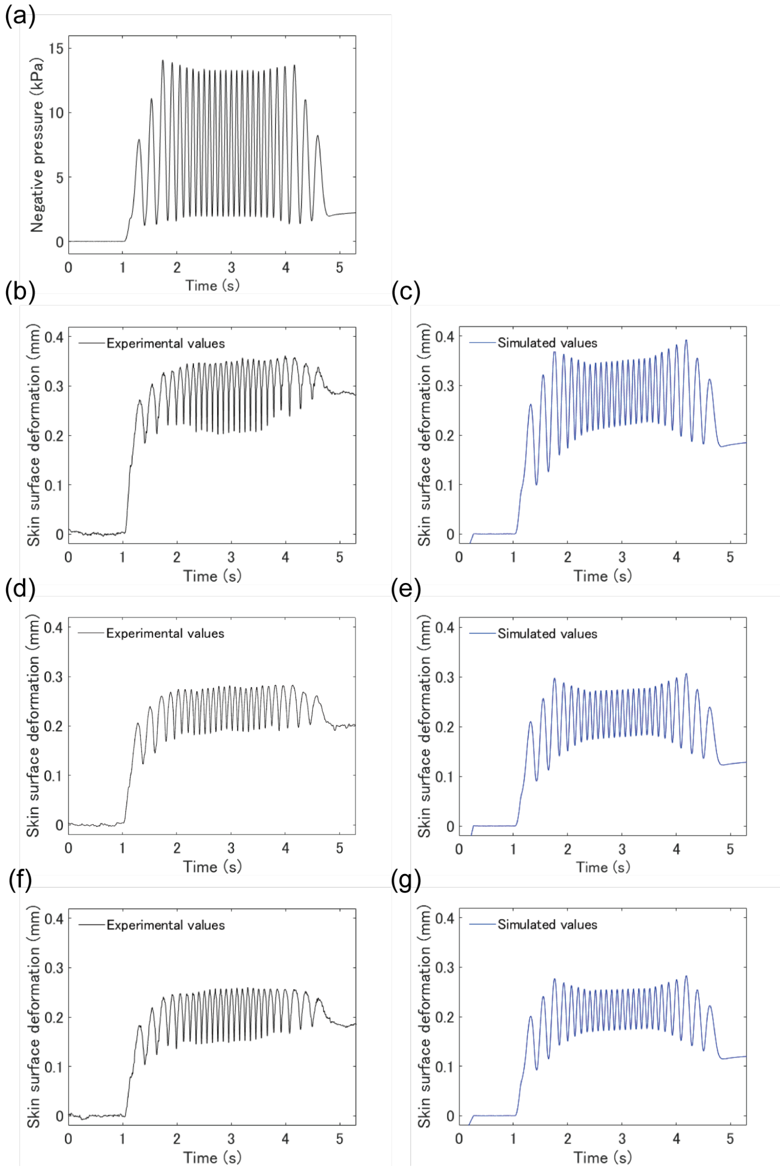


FIGURE 4.5: Comparison of the experimental data and numerical simulation based on the optimized material parameters.

(a) Measured values of negative pressure applied to human skin. This value was also used in the skin model in the simulation. (b,d,f) Experimental values for the skin deformations of representative participants. (c,e,g) Simulated skin deformation values for the skin model with the optimized material parameters. These figures depict a comparison between experimental and simulated values of three participants who exhibited distinct characteristics in terms of skin deformation. The average peak displacement values measured during the steady-state period (3.1-3.6 s) were recorded as 0.35 mm for participant 1 (b,c), 0.28 mm for participant 2 (d,e), and 0.25 mm for participant 3 (f,g). The error between the measured and simulated values for the average peak displacement was less than 1% for all three participants' data.

model, as shown in Figure 4.5 a. The G_1 and C_{10} parameters of the dermis, epidermis and stratum corneum were independently varied up and down relative to the optimized model. Figure 4.6 a,c,e shows the distribution of each mechanical stimulus in the 10 Hz steady-state interval. Figure 4.6 b,d,f shows the magnitude of each mechanical stimulus that propagates to the depth of the epidermal-dermal interface. Each mechanical stimulus showed propagation into the skin around the contact point between the suction hole edge and the skin and a locally large value just below the suction hole edge at the epidermal-dermal interface. The values of each mechanical stimulus significantly varied depending on the skin material parameters, and for SED, the influence of skin material parameters was particularly evident in the maxima near the suction hole nadir.

The skin surface displacement (Figure 4.7 a) and the temporal changes in each mechanical stimulus (Figure 4.7 c,e,g) at the depth of the epidermal-dermal interface at the peak position near the nadir of the suction hole are provided. As the skin material parameters changed, each value changed in magnitude while maintaining the phase of the 10 Hz suction pressure oscillation. In particular, the SED showed an accumulation of values with periodic stimulation, and the skin material parameters affected the magnitude of the slope. Figure 4.7 b,d,f,h shows the specific effects of the skin material parameters on the skin surface displacement and the amount of mechanical stimuli on the internal skin. As a major trend, the mechanical stimuli propagated at the epidermal-dermal interface were greater as G_1 was larger and C_{10} was smaller in the stratum corneum and dermis. This tendency differed for each layer, with relatively greater effects in the dermis layer. For Von Mises stress, the material parameters of the epidermis had a different effect than those of the other two layers.

4.3.3 History-dependent response induced by skin viscoelasticity

We investigated the effect of viscoelastic properties on the propagation of mechanical stimuli at the epidermal-dermal interface during periodic stimulation. We compared two models here: the optimized model (referred to as the Mooney & QLV) and a modified version of that model without the inclusion of the viscoelastic term (referred to as the Mooney), which is represented by Eq. (1). Figure 4.8 shows the values of mechanical quantity propagation simulated by the two models. The presence of the viscoelastic term significantly increased the strain inside skin, but had

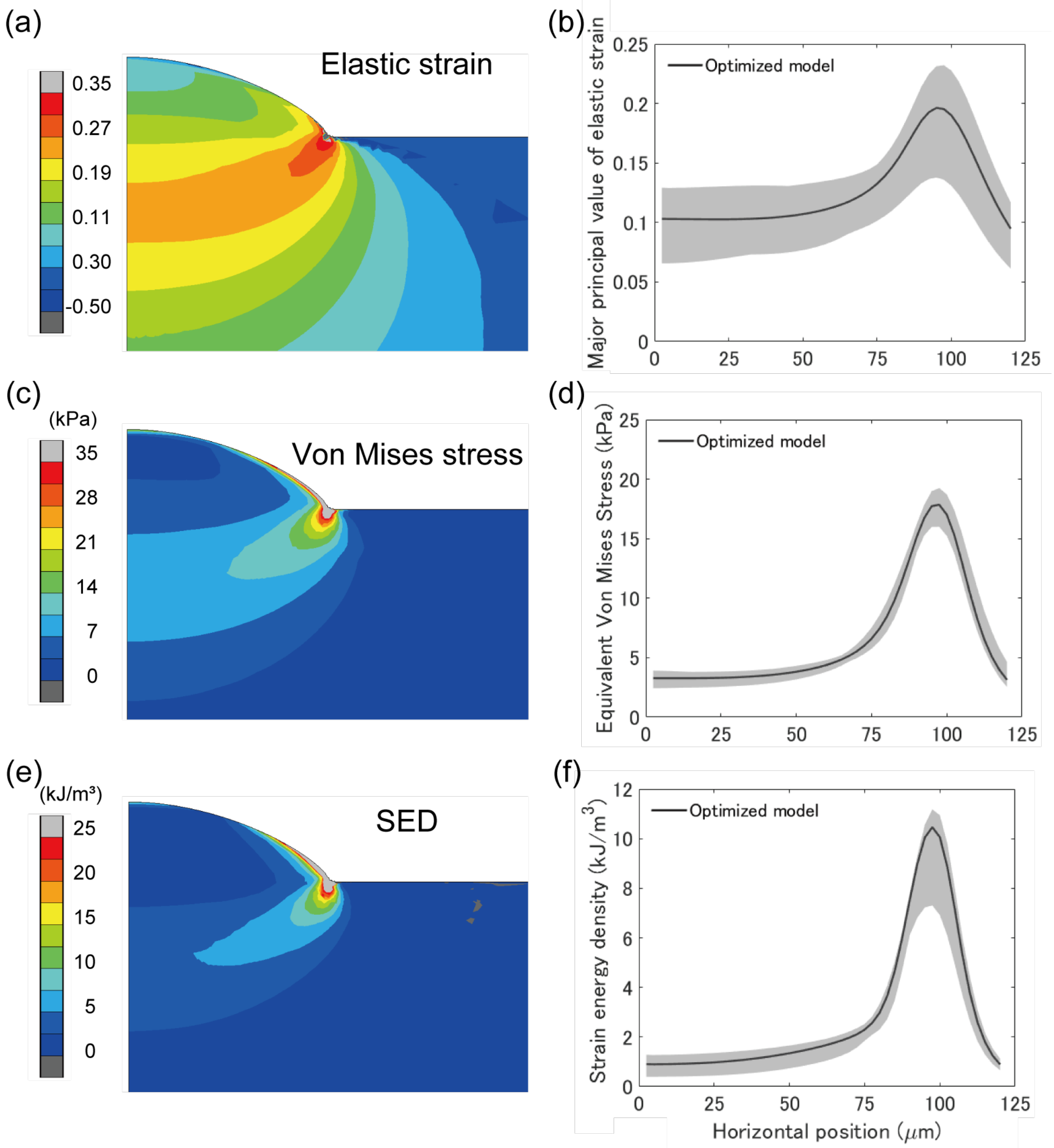


FIGURE 4.6: Simulated effect on how changes to skin material properties influence the interior mechanical quantities propagation.

Simulated values of (a,b) major principal value of elastic strain, (c,d) equivalent Von Mises stress, and (e,f) total strain energy density (SED) calculated optimized model at 3.3 s during stimulation shown in Figure 4.5. (a,c,e) represent contour plots, and (b,d,f) represent the respective indices at the epidermal-dermal element interface, the nodes between A and B shown in Figure 4.1. The solid black line denotes the propagated mechanical stimuli given by optimized skin material properties, whereas the gray shaded area denotes the range of variation due to skin material parameters varied with respect to the optimized model. Each mechanical stimulus shows a locally large value just below the suction hole edge at the epidermal-dermal interface. Those values varied depending on the skin material parameters.

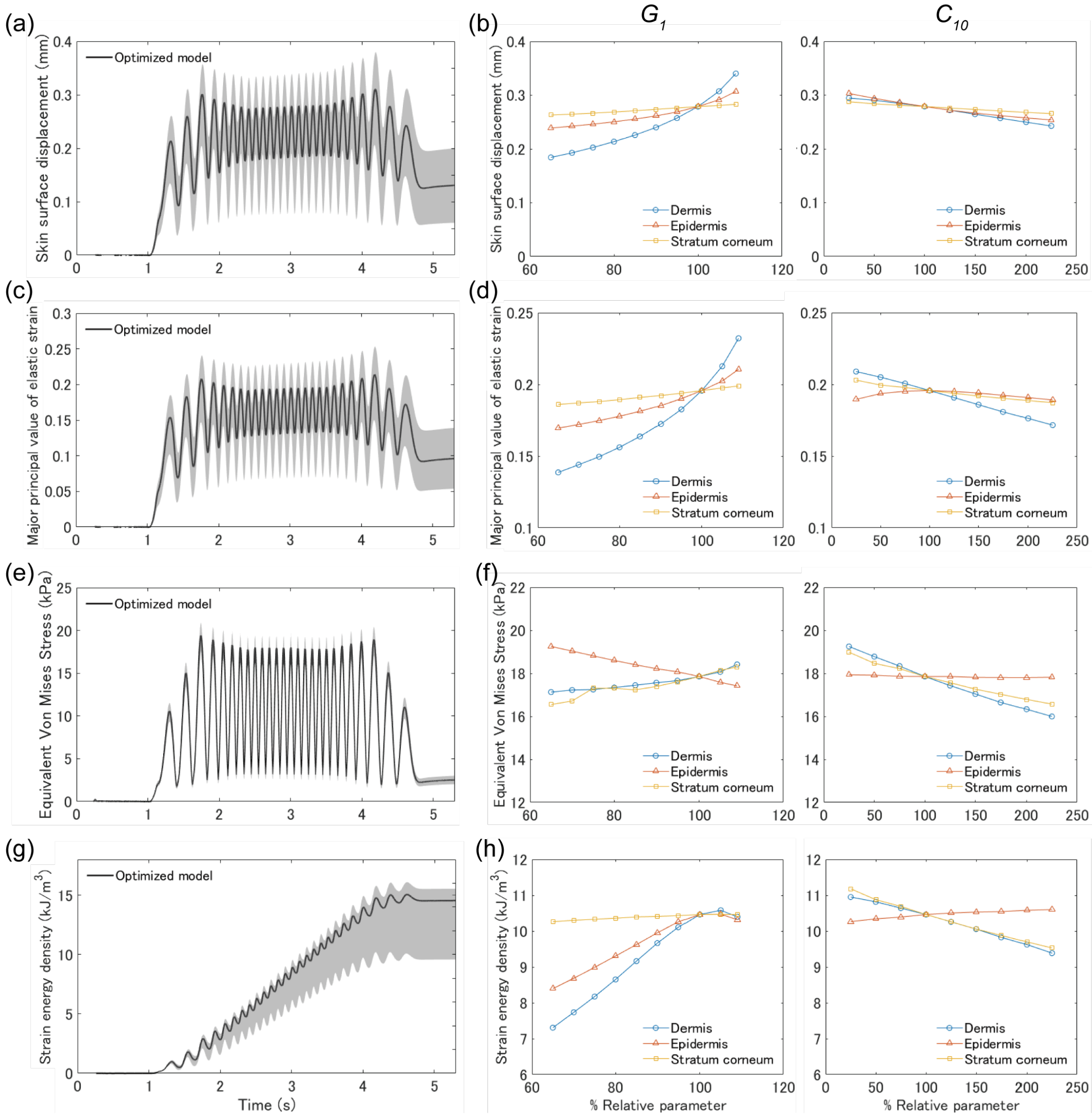


FIGURE 4.7: Simulated effect on how changes to skin material properties influence the interior mechanical quantities propagation.

Simulated values of (a,b) major principal value of elastic strain, (c,d) equivalent Von Mises stress, and (e,f) total strain energy density (SED) calculated optimized model at 3.3 s during stimulation shown in Figure 4.5. (a,c,e) represent contour plots, and (b,d,f) represent the respective indices at the epidermal-dermal element interface, the nodes between A and B shown in Figure 4.1. The solid black line denotes the propagated mechanical stimuli given by optimized skin material properties, whereas the gray shaded area denotes the range of variation due to skin material parameters varied with respect to the optimized model. Each mechanical stimulus shows a locally large value just below the suction hole edge at the epidermal-dermal interface. Those values varied depending on the skin material parameters.

relatively little effect on the stress. An accumulation of the SED with periodic stimulation was observed only in the Mooney & QLV model, resulting in a significant difference in the magnitude of the SED due to the viscoelastic effect. The stress–strain relationship is shown in Figure 4.8 d, where the Mooney model followed the same stress–strain history from the onset of suction. On the other hand, the Mooney & QLV model showed a different stress–strain history for each stimulation period with a larger strain. The sum of the integrals of the stress–strain histories for each tensor showed the same as the calculated SED.

4.4 Discussion

4.4.1 Validation of the developed viscoelastic model

The periodic human skin deformation data was accurately simulated using a finite element model incorporating the Moony strain energy function and quasilinear viscoelasticity (Figure 4.5). The viscoelastic parameters were observed to have a significant impact on the amount of skin peak displacement. Specifically, in the optimization process, we observed that the smaller value of τ_1 primarily increased the peak-to-peak displacement amplitude, while the larger value of G_1 contributed to greater peak displacement. These trends were consistent with the numerical data provided in Table 4.1. To replicate the history-dependent behavior at 10 Hz, short time constants, like 0.001-0.006 s, are likely necessary. These time constants were not identified in skin behavior modeling for static loads or slow 0.1 Hz periodic loads (Joodaki and Panzer, 2018; Mostafavi Yazdi and Baqersad, 2022). G_1 was estimated to be much larger than G_2, newly indicating that the short time constant played a very important role when focusing on skin deformation behavior as fast as 10 Hz.

The optimized C_{10} values decreased from the surface to deeper skin layers, as expected in previous research (Hara et al., 2013). Although the change from the initial to estimated values was observed, the contribution of stiffness was not significant in the optimization process. We observed that human skin exhibits such significant displacements that cannot be adequately represented solely by hyperelastic parameters. Since all material parameters were simultaneously estimated, the determined solution was likely a global minimum, and hyperelasticity was shown to have a smaller contribution to skin deformation than viscoelasticity in the optimization process.

By focusing on fast skin deformation behaviors, such as 10 Hz, which have not been extensively studied in skin modeling, we were able to confirm the universal contribution of viscoelastic parameters, even for three participants exhibiting such

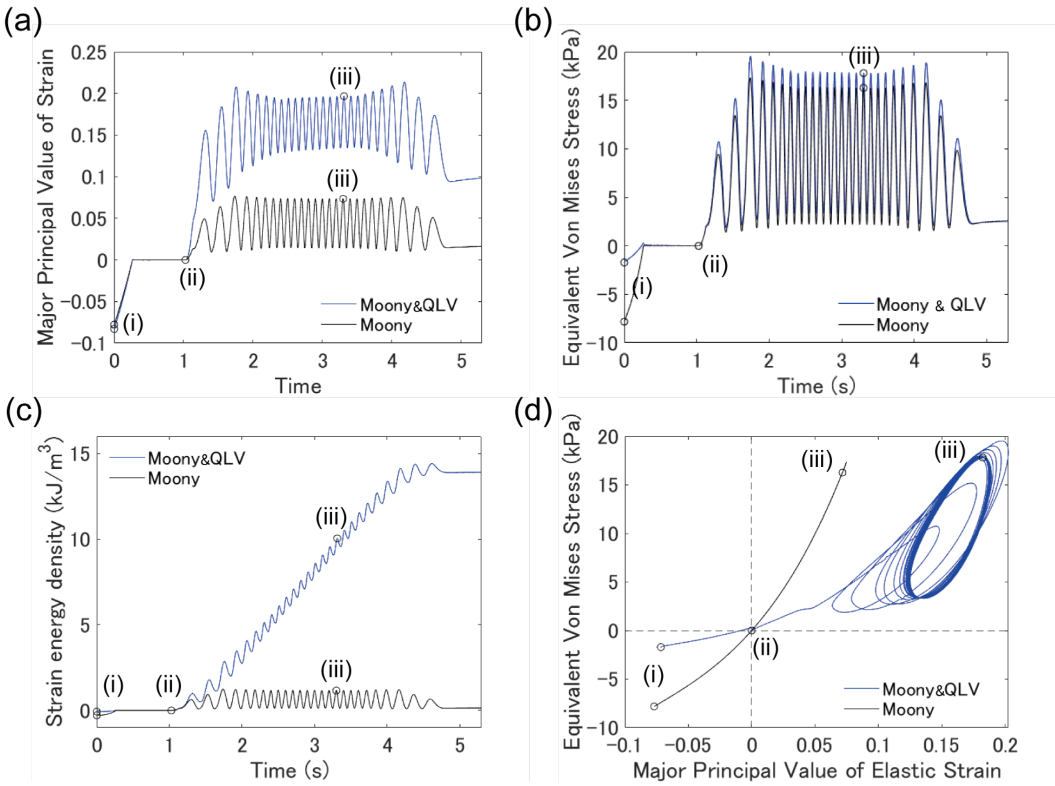


FIGURE 4.8: SED accumulation induced by periodic stimulation occurs due to viscoelastic effect.

Effects of viscoelasticity on (a) the major principal value of elastic strain, (b) the equivalent Von Mises stress, (c) the SED propagating at the epidermal-dermal interface, and (d) the stress–strain curve. Two models are compared here: the optimized model (referred to as the Mooney & QLV) and a modified version of that model without the inclusion of the viscoelastic term (referred to as the Mooney). The SED is expressed as the integral of the stress–strain function, and the sum of the integrals of the stress–strain histories for each tensor showed the same value as the SED (c). The captions in the figures indicate (i) the start of the suction device contactor pushing into the skin, (ii) the start of suction, and (iii) the peak skin displacement in the steady-state interval (3.3 s). For all cases, the value at (ii) the start of suction is plotted as a zero reference. For the Moony model shown in (d), a periodic history plot overlaps between (ii) and (iii). The presence of a viscoelastic term significantly increased the strain but had relatively little effect on the stress. The accumulation of SED due to periodic stimulation was attributed to viscoelasticity, showing different stress–strain histories within the stimulation cycle.

wide variations in skin deformation. We were then able to develop a skin viscoelastic model that represented the history-dependent mechanical response characteristics of each participant, specifically related to the magnitude of peak displacement.

4.4.2 Effect of viscoelasticity and stiffness on mechanical stimuli propagation

This work was primarily designed to comprehensively evaluate the differences in mechanical stimuli transfer. According to our model, which reproduced the history-dependent skin deformation behavior reasonably well, the mechanical stimuli generated by suction stimulation were significantly higher from the contact edge of the suction hole to the depth of the skin (Figure 4.6). The effects of skin material properties on mechanical stimuli propagation were discussed, focusing on the unimodal maxima at the epidermal-dermal interface, which were found to vary with the skin material properties.

The effects of viscoelasticity, stiffness, and their layer-specific effects on the major principal value of elastic strain of the skin in response to periodic stimuli are described. From Figure 4.8 a, the viscoelasticity had significantly elevated the strain, which was quite different from the estimation based on stiffness alone; this result indicated the large contribution of viscoelasticity to the skin deformation. Skin with a larger G_1, i.e., a more immediate response, tended to exhibit greater strain. Skin with smaller C_{10}, i.e., softer skin, showed a similar tendency for higher strain as in the previous study (Jobanputra et al., 2020). Among the three layers, the effect of these skin material parameters on strain was greatest in the dermis (Figure 4.7 d). As the dermis is a tissue that is prone to large strain (Soetens et al., 2018), its contribution to skin tissue strain was considered significant.

The effect of skin material changes on Von Mises stress during periodic stimulation was smaller than that of the major principal value of elastic strain and SED. The presence of viscoelasticity had relatively little effect on the stress (Figure 4.8 b), and the effect of changes in skin material parameters on the internal Von Mises stress (90-108%) was relatively low compared to that of other mechanical stimuli, strain (71-119%) and SED (70-107%) (Figure 4.7 e). Our result showed that stress was the most robust to changes in the skin material properties when compared to the amount of mechanical information related to strain, which was consistent with other studies simulating sustained pressing and sliding movements on skin with different material parameters (Jobanputra et al., 2020; Wang et al., 2016). This finding may be applicable to various other skin deformation behaviors.

The effect of the skin material properties on Von Mises stress was observed, although to a lesser extent than for the other indices, as mentioned above. The effect of G_1 and C_{10} of the epidermis on the stresses occurring at the layer interface appeared to be different from the other layers, which could be considered in the magnitude of the apparent stiffness ratio between adjacent layers (Figure 4.7 f). A smaller G_1 with a fairly short time constant (0.004 s) and a larger C_{10} could be interpreted as stiffer skin that was less deformable. When the stratum corneum, which is sufficiently stiffer than the epidermis, was apparently softened (larger G_1 smaller C_{10}), the stratum corneum-epidermis stiffness ratio was reduced, resulting in greater stress in other areas (epidermal-dermal interface). Similarly, softening of the dermis or stiffening of the epidermis increased the stiffness ratio of the epidermal-dermal interface, resulting in large stresses at that interface. The focus here was on the stiffness ratio to the adjacent layers and not on the absolute value of stiffness. Specifically, we can discuss the possibility of accounting for the composition of the stratum corneum and dermis adjacent to the epidermis, rather than forcibly adjusting the stiffness of epidermis, which is composed of living cells (Burns et al., 2010), when altering the mechanical quantities propagated inside skin.

Skin viscoelasticity and stiffness both affect the SED differently. The effect of C_{10} on the SED was similar to a previous study (Jobanputra et al., 2020), where the SED increased as the stiffness of the stratum corneum and dermis decreased, although the epidermis did not show a significant effect (Figure 4.7 h). Although the stratum corneum had a similar effect to the dermis for C_{10}, G_1 showed a greater effect with deeper layers. This result indicated that factors, such as layer thickness and location, could potentially modulate the effects of material parameters (stiffness, viscoelasticity) on the mechanical stimuli propagation in different ways. A common finding in G_1 and C_{10} was the large contribution of dermal layer material parameters to the SED.

4.4.3 Possible causes of SED accumulation

SED accumulation, which had not been observed in previous static analyses, was confirmed and caused by viscoelastic effects (Figure 4.8 c). The presence of the viscoelastic property showed realistic skin behavior that did not immediately return to its initial position after the suction stimulus was relaxed while maintaining the same phase. Under periodic stimulation, the different stress–strain history curves due to the viscoelastic effect led to SED accumulation, which was the integral value of stress with respect to strain (Zhang et al., 2018). By considering viscoelastic properties, the effect of the time lag in skin tissue strain in response to periodic stimulation on skin SED could be clarified.

4.4.4 Insights into the tactile perception phenomena

A decrease in the stiffness and an increase in the elastic response of the stratum corneum and dermis tend to increase the strain, stress, and SED at the mechanoreceptor location, which may provide more information for clear tactile sensation.

The present simulations provide one mechanical interpretation of the tactile phenomenon in which a decrease in the stiffness of the stratum corneum significantly increases tactile sensitivity to 10 Hz suction pressure (Sakaguchi et al., 2023a).

Our simulations further show that the dermal layer significantly contributes to the mechanical stimuli propagated to the mechanoreceptors. This implies that the dermis layer, which responds immediately to stimuli, efficiently propagates mechanical stimuli to the mechanoreceptor location, thereby increasing tactile sensitivity. Regardless of how much the stratum corneum is softened, the mechanical stimuli may not be sufficiently transmitted to the mechanoreceptors due to the low time response characteristics of the deeper layers. Thus, massage or medications that increases the elasticity of the dermal layer can be effective against age-related loss of tactile sensation. This study elucidated the differential transmission of periodic mechanical stimuli within the skin, indicating that it was important to consider the viscoelastic properties of the deeper layers as well as the superficial layers to obtain proper tactile sensation.

Exploring a mechanical interpretation between the history-dependent behavior of the skin and tactile sensation is an intriguing area of tactile research. It can be hypothesized that if the magnitude of SED propagated to the mechanoreceptors is greater, the perception will become clearer (Kumar et al., 2015). However, the phenomenon in which tactile perception becomes clearer through continuously presenting suction oscillations leading to SED accumulation has not yet been observed in our preliminary experiments. It is possible that what is associated with tactile sensation (which has been indirectly interpreted in terms of nerve firing frequency) is information other than the magnitude of the mechanical quantity. In order to comprehend the tactile sensation during complex skin contact, which goes beyond the conventional focus on static touch, we believe it is effective to exploratively describe the mechanical interpretations using the history-dependent changes in mechanical quantities propagating through the skin, as discovered in this analysis.

4.4.5 Limitations

It is important to recognize the effect of reproducing skin deformations based on material parameters alone. To achieve large deformations, G_1 had almost reached its upper limit (0.90, maximum 1.00 together with $G_2 = 0.09$). There are likely other geometric factors, such as microrelief and large wrinkles, that could increase the deformation. Our model relies too heavily on the effect of G_1 on reproducing skin deformation, potentially resulting in extreme conditions. Thus, the adoption of geometric factors during skin material property optimization is worth considering.

It should also be recognized that viscoelastic features between layers are not taken into account during skin material property optimization. In this study, to avoid excessive complexity from factors contributing to the mechanical response of the skin as an initial exploratory study for modeling the deformation behavior at 10 Hz, viscoelasticity was treated as the same value for four layers. However, there is a possibility that the values of G_1 in the stratum corneum and dermis are completely different. Exploring the variation of each viscoelastic parameter from a model in which each layer has different viscoelastic properties could potentially reproduce a more complex mechanical skin response.

In the present study, the time-dependent response was reproduced using a two-term Prony series, but the effect of the time constant on the mechanical behavior still needs to be investigated. The stimulus frequency was fixed at 10 Hz, and the time constant parameter was optimized because our focus was on the viscoelastic effect and not on the frequency response of the skin. The time constant was set to a very low value, which was unprecedented among previous studies, to reproduce fast skin deformation behavior. A point of insufficiency was that the optimized model exhibited larger deformations compared to the experimental results at the beginning and end of the suction stimulation, where the frequency was lower than 10 Hz. This discrepancy in displacement could potentially be attributed to a weighted optimization of the time response characteristics of the skin model (τ_1: 10^{-3} s and τ_2: 10 s) for the targeted oscillation frequency of 10 Hz. Thus, it might be necessary to add a time constant term to account for complex skin mechanical characteristics. Furthermore, stimulus frequency can cause differential propagation of the mechanical quantities to the skin (Wu, Welcome, and Dong, 2006; Wu et al., 2008). Therefore, it is valuable to reproduce the prevailing frequency response characteristics of the skin by adjusting multiple time constants.

4.5 Summary

In this study, we evaluated the effects and trends of changes in the stiffness and viscoelasticity of the skin on the propagation of mechanical quantities between skin layers where mechanoreceptors are present when subjected to periodic stimuli, using a finite element model.

What has become evident here is that, first, we found that it is effective to tune viscoelastic parameters with short time constants (0.001-0.006 seconds) to reproduce the individual variability in skin deformability to periodic stimuli observed in humans. Next, we found that changes in the viscoelasticity of each layer, as well as the stiffness, modulate the propagation of the mechanical stimulus at the mechanoreceptor location. In particular, the more immediate the skin response, the more elastic its behavior, the more strain and SED were found to propagate. The magnitude of the effect was also found to vary between layers. Finally, in the viscoelastic skin model, the effect of SED accumulation, which is not seen in steady-state stimulation, was revealed in periodic skin deformation, indicating the importance of considering the viscoelasticity of the skin in the history-dependent behavior of the skin.

These findings have promising implications for future advancements. Our findings contribute to providing basic knowledge of the viscoelastic contribution to tactile sensation, and provide important implications for skin intervention methods for age-related tactile degradation in cosmetic and biomedical applications. Furthermore, the skin feature of viscoelasticity itself may express the tactile sensation of each individual, and it may be useful to incorporate viscoelasticity evaluation into simple skin sensory measurement, which is currently used to evaluate peripheral sensory abnormalities in medical practice. In terms of understanding individual differences in tactile sensation, tactile feedback in wearable devices and the development of textures for cosmetics that match the viscoelastic characteristics of the skin are expected to advance in the future as a means of creating personalized experiences. Thus, it is expected that more attention would be paid to the evaluation criteria of not only skin stiffness but also temporal response characteristics in the fields of medicine, cosmetics, and entertainment.

Chapter 5

Conclusion

In our life, the sense of touch holds paramount importance and is a sensation that we strive to maintain in an optimal state. Tactile sensitivity has a notable impact on motor function, even more so than age-related decline in muscle strength among older adults. Additionally, social contact contributes to the alleviation of psychological fear and pain, as well as to the mitigation of depression. Furthermore, the effects mediated through touch extend beyond the self and have been found to influence social aspects such as the establishment of interpersonal relationships, serving as a catalyst for fostering positive and harmonious communication with others.

Touch is a sensation that undergoes significant changes throughout a lifetime, and even individuals with a delicate tactile sensitivity may not necessarily retain it due to aging, lifestyle, and environmental factors. We focus on the mechanical properties of the skin as a crucial component of tactile sensation. From a dermatological perspective, the mechanical properties of the skin exhibit disparate characteristics not only between individuals but also within individuals, showing marked changes over short and long periods of time. In comparison to the intricacies of the sensory nervous system, the skin's mechanical properties offer a promising research target with potential solutions and interventions.

This study aims to investigate the contribution of skin mechanical properties to human tactile sensitivity towards building foundational knowledge for maximizing the value of touch.

This study has revealed the phenomenological and mechanical mechanisms through which the skin mechanical properties, such as stiffness and viscoelasticity within the range of variability in properties observed in healthy individuals, as well as the changes in properties induced by the application of skincare products, can alter the deformation of skin tissue and thus affect tactile sensation during deformative tactile stimulation. The significance of this study lies in the element-by-element elucidation of the complex mechanisms underlying human tactile sensation, with a focus on the skin condition of the recipient of external stimuli involving skin deformation.

The overall contribution of this paper is twofold. Firstly, it clarified the significance and validity of focusing on the skin as a constituent of tactile sensation that is dependent on our individual lifestyles, which has traditionally been predominantly focused on the sensory nervous system. Secondly, it provided concrete phenomenological and mechanical evidence of the intervention effects on skin mechanical properties, laying the foundation for future development of solutions to enhance or maintain tactile sensitivity. The findings of this study are expected to contribute to a more individualized understanding of tactile sensation and provide a richer tactile experience.

5.1 Contributions of the Individual Chapters

5.1.1 Chapter 2: Confirming the Relationship between Skin Surface Deformation and Tactile Sensitivity in Response to Vibratory Stimuli

The main contribution in this chapter is the clarification of the relationship between the mechanical response characteristics of the superficial skin layer and tactile sensitivity. Our results revealed several key findings. Firstly, even when the same amount of pressure stimulation is applied, the degree of skin deformation varies among individuals. Secondly, there was also intra- and interindividual variability of tactile sensitivity, although age alone was not sufficient to explain this variability. Finally, the amount of skin deformation can explain the variability in tactile sensitivity both intra- and interindividuals. In addition, a characteristic relationship was observed in which intra- and interindividual differences in tactile sensitivity were greater when the skin deformation was relatively small.

5.1.2 Chapter 3: Contribution of Stratum Corneum Compliance to Tactile Sensitivity in Response to Vibratory Stimuli

The main contribution in this chapter is the clarification of the contribution of the stratum corneum compliance to tactile sensitivity, laying the groundwork for targeting interventions on skin mechanical properties. While the causal relationship between the mechanical properties of the skin and tactile sensation has been established, it is still necessary to further examine which specific layers of the skin contribute to this relationship. Our results showed that after 10 minutes of hydration, the dynamic modulus of the stratum corneum decreased, leading to an increase in skin compliance during suction stimulation. Furthermore, tactile sensitivity significantly improved only in group that applied the cream. By applying suction stimulation and conducting limited hydration interventions in the stratum corneum, it was revealed that the decreased stiffness of the stratum corneum resulted in an improvement in tactile sensitivity through increasing skin compliance.

5.1.3 Chapter 4: Simulated Effect of Skin Stiffness and Viscoelasticity on Mechanical Propagation of Vibratory Stimuli between Skin Layers

The main contribution in this chapter is the clarification of the contribution of viscoelasticity changes to skin mechanical propagation, while minimizing the effects of factors other than material parameters. While simulation studies are commonly conducted to investigate the contribution of skin mechanics to tactile sensation, the effects of changes in skin stiffness and viscoelasticity when a history-dependent stimulus is applied were not yet known. In this Chapter, firstly, based on experimentally obtained human skin deformation during high-frequency vibrations of 10 Hz, we developed finite element models that replicated the measured human skin deformation. Secondly, we showed that not only stiffness but also viscoelasticity markedly affected mechanical stimuli propagation in the skin, and that the effect differed depending on the layer. Particularly, greater immediate responsiveness of the dermis contributed to greater propagation of mechanical stimulus. Furthermore, we observed the phenomenon of the accumulation of strain energy within the skin in response to vibrational stimuli. These observational results represent mechanically explainable phenomena based on the relative changes in time-dependent mechanical properties within specific skin layers and the relative changes in mechanical properties occurring between layers, providing a universal mechanical understanding of skin mechanical properties and tactile sensation.

5.2 Practical implications

Our findings hold the potential for significant contributions across multiple industries. In the cosmetics industry, it is possible to approach tactile sensation by altering the mechanical properties of the skin through skincare and massage. Application of moisturizers or surfactants changes the dynamic elastic modulus of the stratum corneum (Takahashi et al., 1984). The loss of elasticity associated with aging can be restored by facial massage (Iida and Noro, 1995). The ability to directly target the skin is a strong advantage when it comes to excessively dry or aging skin. This approach not only contributes to improving the appearance of issues like dark spots but also opens doors for developing products aimed at providing a new sensory experience through targeted care. In the ingestible industry, similar potential can be expected to capture new markets. A collagen supplement improves skin hydration, elasticity, roughness, and density (Bolke et al., 2019). Furthermore, it may contribute to medical diagnostics. Skin sensation, which reflects the characteristics of peripheral nerves, is known as a simple tactile diagnosis of neurological diseases and other conditions (Yang et al., 2010; Yang et al., 2015; Frade et al., 2022), but its accuracy could potentially be enhanced. Moreover, demonstrating the importance of the sensory aspect of the skin can also contribute to advancements in the field of engineering. Tactile feedback technologies, aimed at VR experiences, seek to convey more detailed information by utilizing an approach that goes beyond the previously focused sense of force and includes the sensory aspect of the skin (Minamizawa et al., 2007; Porquis et al., 2014; Leonardis et al., 2015; Fani et al., 2018). Taking into account the individual characteristics of different skin conditions, providing sensory stimulation to the skin can further enhance the sense of realism.

5.2.1 Chapter 2: Confirming the Relationship between Skin Surface Deformation and Tactile Sensitivity in Response to Vibratory Stimuli

We have successfully established a direct correlation between the complex interplay of tactile sensations and observable physical phenomena occurring in the skin. This highlights the validity of focusing on the contribution of skin mechanical properties to touch. Particularly, the insight that there is a greater variability in tactile sensitivity when the peak skin deformation is relatively small offers the potential for a constructivist understanding of the tactile sensory mechanism in the periphery, including mechanoreceptors and neural fibers states, through collaboration with subsequent studies in dermatology and neuroscience. Furthermore, we have identified the skin's stretchability as a particularly useful mechanical characteristic that could serve as an indicator for subsequent research. By altering this characteristic through interventions on the skin, it is suggested that tactile sensation could be adjusted.

5.2.2 Chapter 3: Contribution of Stratum Corneum Compliance to Tactile Sensitivity in Response to Vibratory Stimuli

We got valuable insights for advancing our ability to effectively modulate stratum corneum compliance and elicit appropriate tactile sensations. This thin layer is likely to have a significant impact on tactile experiences involving skin stretching, such as interpersonal touch gestures, gentle massage, and product application. Impaired mechanical responsiveness of the skin, such as extreme dryness of the stratum corneum, can have negative consequences on tactile comfort and the accurate interpretation of interpersonal tactile cues and intentions. Skin-care formulations that selectively modulate skin mechanical responses by regulating moisture levels can enhance their effectiveness in achieving the desired tactile experience. In addition, tactile sensation varies depending on the skin condition even with the same stimulus. To eliminate individual differences in sensation and provide or estimate the desired tactile experience, it may be effective to control the skin deformation that occurs during tactile stimulation instead of the stimulus intensity or adjust the tactile stimuli according to the skin condition. These considerations could contribute to the advancement of tactile presentation techniques.

5.2.3 Chapter 4: Simulated Effect of Skin Stiffness and Viscoelasticity on Mechanical Propagation of Vibratory Stimuli between Skin Layers

The modeling of history-dependent skin behavior, which has received relatively little attention in the past, holds potential for application in various research fields. The elucidation of the importance of short time constants representing stress relaxation will likely accelerate research on skin modeling based on various skin deformation behaviors. Moreover, while previous studies have focused on the stratum corneum due to the ease of intervention, our research has provided new insights into the contributions of the hardness and viscoelasticity of deeper layers like the dermis and demonstrated the potential of approaches which enhancing dermal elasticity such as massage and oral intake of nutrients in addition to percutaneous interventions. Furthermore, SED accumulation, which was not evident in previous studies that simulated static loading conditions, highlighting the value of considering the involvement of skin viscoelasticity in the mechanical interpretation of touch. This finding holds potential for realizing clear tactile sensation and optimizing mechanical therapies for pain relief.

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Research Achievements

Peer-reviewed Publications

1. Saito Sakaguchi, Kaoru Saito, Naomi Arakawa, Masashi Konyo, The dynamic behavior of skin in response to vibrating touch stimuli affects tactile perception, *Skin Research and Technology*, 29;e13295, pp.1-9, 2023

2. Saito Sakaguchi, Kaoru Saito, Naomi Arakawa, Masashi Konyo, Stratum corneum compliance enhances tactile sensitivity through increasing skin deformation: A study protocol for a randomized controlled trial, *Journal of Cosmetic Dermatology*, 2023;00, pp.1-12, 2023

3. Saito Sakaguchi, Masashi Konyo, Skin viscoelasticity effects on the periodic mechanical stimuli propagation between skin layers, *Journal of the Mechanical Behavior of Biomedical Materials*, 152;106416, pp.1-12, 2024

4. Saito Sakaguchi, Moe Tsutsumi, Shinsuke Akita, Masashi Konyo, Kentaro Kajiya, Do human epidermal Merkel cells solely detect light-pressure? Linking the animal model to humans, *Journal of Investigative Dermatology*, (under review)

International Conference

1. Saito Sakaguchi, Moe Tsutsumi, Naomi Arakawa, Kentaro Kajiya, Masashi Konyo, Live-cell imaging of the response of human Merkel cells to skin deformation induced by a microscope-mounted mechanical stimulation device. *Neuroscience 2022 51th annual meeting*, 2022

2. Saito Sakaguchi, Moe Tsutsumi, Kazuki Takagaki, Naomi Arakawa, Kentaro Kajiya, Masashi Konyo, Age-related changes of Merkel cell distribution in the human cheek and visualization of touch force propagation to activate Merkel cells. *Neuroscience 2021 50th annual meeting*, 2021

3. Kaoru Saito, Masashi Konyo, Hikaru Nagano, Saito Sakaguchi, Naomi Arakawa: Simultaneous Measurement of Skin Deformation and Perceptual Sensitivity Using Suction Pressure. *IEEE World Haptics Conference*, 265-270, 2019 (peer-reviewed)

Domestic Conference

1. Saito Sakaguchi, Moe Tsutsumi, Naomi Arakawa, Kentaro Kajiya, Masashi Konyo, Live-cell imaging of the response of human Merkel cells to skin deformation induced by a microscope-mounted mechanical stimulation device. *NEURO2022*, 2022

2. Saito Sakaguchi, Naomi Arakawa, Kaoru Saito, Hikaru Naofumigano, Masashi Konyo, Effect of cream application on skin tactile perception to suction pressure stimulation, *The 21st Annual Meeting of Japan Society of Kansei Engineering*, 13P-19, 2019

3. 斉藤薫，昆陽雅司，永野光，坂口歳斗，荒川尚美，吸引圧を用いた皮膚変形と皮膚知覚感度の同時測定装置 Simultaneous Measurement Device of Skin Deformation and Perceptual Sensitivity with Suction Pressure，*ロボティクス・メカトロニクス講演会 2019*, 1P1-T10, 2019

4. 斉藤薫，昆陽雅司，坂口歳斗，荒川尚美，吸引圧に対する皮膚知覚感度の増強 -吸引孔配置が刺激閾に及ぼす影響- Hole Number Effect on Perceptual Sensitivity: Cutaneous Stimulation Using Static Suction Pressure，*第 24 回日本バーチャルリアリティ学会大会論文集*，2019

Patent

1. 北村尚美，坂口歳斗，昆陽雅司，斉藤薫，永野光，肌の感度測定方法，感度測定装置及び肌吸引デバイス，特願 2019-154087 (2019.08.26)，特開 2020-182818 (2020.11.12)

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