Engineering Cosmetics to Combat Skin Stress and Promote Skin Comfort

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Abstract

Background: The formulation of performant cleansers and moisturizers should include their effects on the consumers sensorial perception of skin comfort. The biomechanical response of the stratum corneum (SC) to cleansers and moisturizers in the form of changes in SC stress is central to combatting skin stress and downregulating neural activity for improved skin comfort. Exploiting the link between skin stress and activation of neural activity provides a powerful tool to engineer improved cosmetic formulations that combat skin stress and enhance consumer skin comfort for extended durations after application.

Methods: Selected cleansers and moisturizers were evaluated using multiple consumer evaluation studies and clinical skin measurement techniques. The same cosmetic treatments were tested in laboratory *ex vivo* SC models to measure the evolution of skin stress over a period of 10-15 hours after application of the treatment, and the measurements informed finite element models of skin sections with realistic topographies.

Results: Strong linear trends between the reported skin comfort scores and measured SC drying stresses and between modeled neural activity and skin comfort scores were observed. The soothing mechanism of the best moisturizer after the barrier aggression with a harsh cleanser was also validated.

Conclusion: The results from consumer evaluation studies of the perception of skin comfort, *ex vivo* laboratory measurements and numerical simulations were found to provide a consistent and robust description of the performance of cosmetic treatments. Results from this study provide a more quantitative process for engineering cosmetic products to include wellness factors such as skin comfort.

Keywords: neuroscience; perception; skin stress; skin comfort; well-being; tightness

Introduction: The formulation of performant cleansers and moisturizers should include their effects on the consumers sensorial perception of skin comfort [1]. However, the connection between such subjective "feel-good" factors and the effect of the skin care formulation on salient neural activity including the activation of mechanoreceptors beneath the skin surface are only recently being revealed. In particular, the important role of skin stress on activating such neural activity provides a critical quantitative link between the formulation of skin care products and the perception of skin comfort. Exploiting this link provides a powerful tool to engineer improved cosmetic formulations that combat skin stress and enhance consumer skin comfort for extended durations after application (Fig. 1).

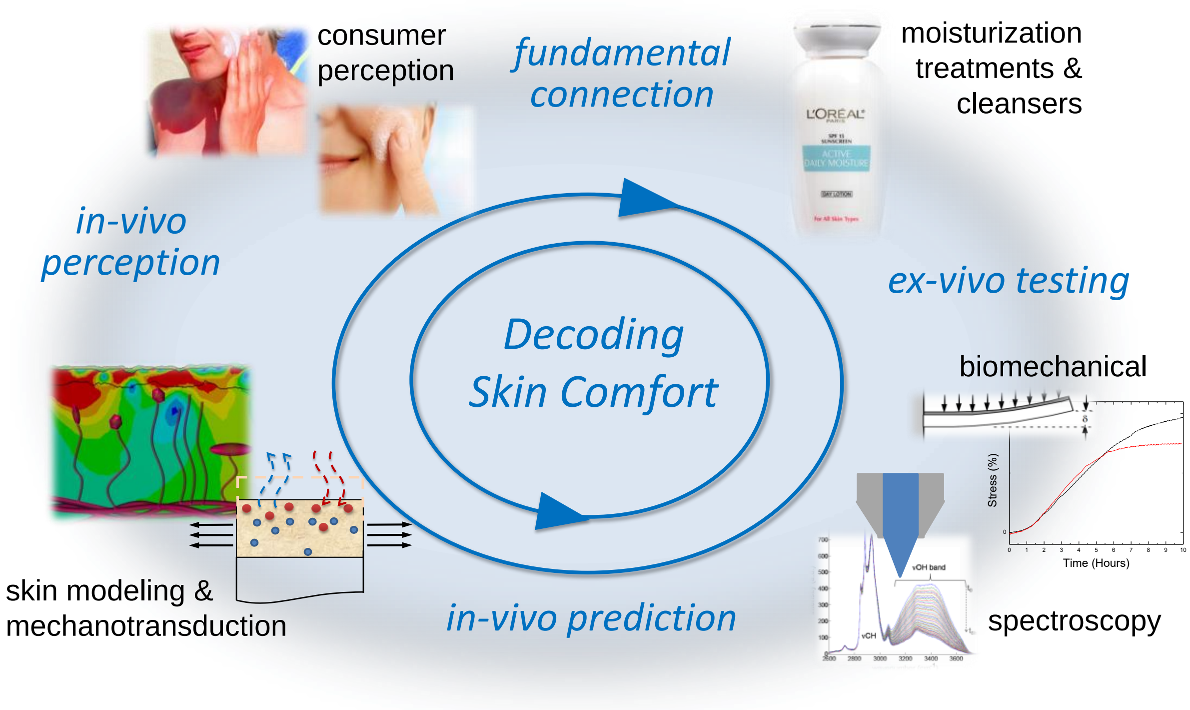

Figure 1: Engineering cosmetic products that are effective at combating skin stress and promoting skin comfort entails characterizing the skin and the perception of biomechanical changes in skin by several methods. *In vivo* evaluations are performed via clinical surveys that obtain feedback related to consumer perception of a cosmetic treatment. *Ex vivo* measurements are made to measure biomechanical changes in isolated human skin samples in response to the application of a cosmetic treatment. Numerical models are used to gain insight into how biomechanical changes at the skin surface lead to the stimulation of mechanoreceptors in underlying skin and corresponding perception of skin comfort.

The biomechanical response of the stratum corneum (SC) to cleansers and moisturizers is central to combatting skin stress and downregulating neural activity for improved skin comfort. If not properly formulated, cleansers result in an increased skin stress and excessive drying of the SC through, for example, disruption of the lipid bilayer [2]. These can be quantitatively linked to the activation of mechanoreceptors and the perception of skin tightness (Fig. 2). Similarly, while moisturizers provide improved SC hydration [3], they can be engineered to further combat skin stress over extended times for enhanced skin comfort. In both cases, the biomechanical response of the SC to skin care formulations can be quantitatively measured with *ex vivo* models [4,5] and used in predictive computational models of consumer skin comfort.

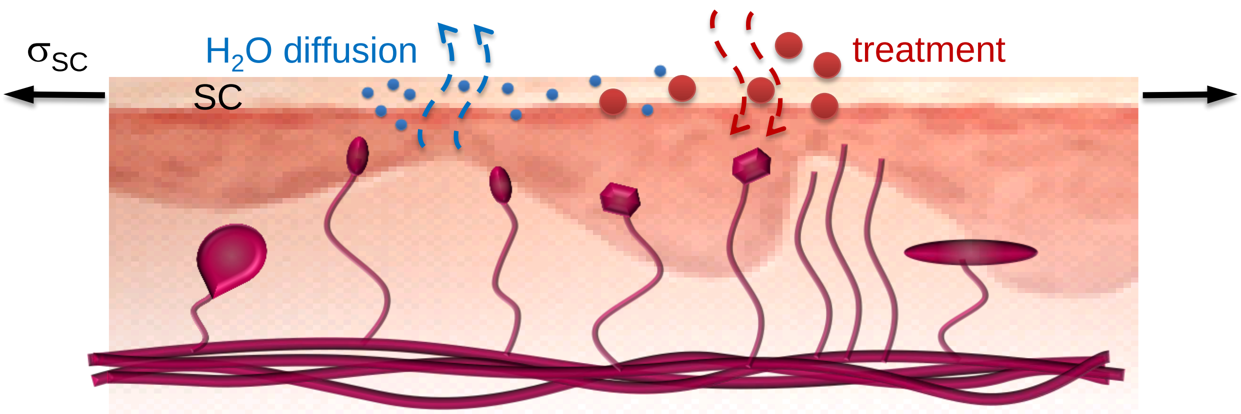

Figure 2: The SC dries as water diffuses into the environment. The resultant shrinking of the SC causes tensile stresses to develop in the SC. SC stresses deform the underlying skin, and these deformations are sensed by cutaneous mechanoreceptors. The magnitude of SC stresses is affected by water loss that is influenced by the treatment, and by diffusion of molecular components of the treatment into the SC.

A system of mechano-sensitive cells known as mechanoreceptors begin appearing near the dermal-epidermal junction and transduce deformation (mechanical strain) of the skin into neural impulses that are sent to and integrated by the central nervous system, comprising a process known as mechanotransduction [6-9]. These neurological signals are interpreted as perceptions and described in vague terms by consumers. For example, an increase in “skin tightness” after using a harsh cleanser or an increase in “softness” from a moisturizer may be reported by a consumer. Quantifying and understanding how to control these sensations through cosmetic treatments is a key aim of consumer cosmetic chemistry.

In this work, *ex vivo* SC models were used to fully characterize the changes in skin mechanical properties resulting from the application of selected cleanser and moisturizer formulations. These properties included the mechanical stresses that develop in the SC under dehydrating conditions. In conjunction, quantitative computational models of the mechanical response of the underlying skin layers were used to predict the stimulation of sensory neurons. The resulting predicted neural activity unveils the link between the skin care formulation and consumer perception of skin comfort.

Materials and Methods: An *in vivo* consumer survey involving several thousand women in two countries repeated in successive years was performed to assess the comfort of a selection of cleanser and moisturizer treatments. Respondents used a product for a week to assess their effect on skin comfort over a daily time by rating how tight the product made their skin feel. A skin tightness perception score was derived for each product by calculating the percentage of women reporting little to no skin tightness perception from using the product in question.

Ex vivo evaluation of each product was performed by measuring stresses that developed in extracted SC several hours after applying each product. To measure SC drying stresses, the SC was first isolated from underlying skin layers using mechanical stripping and enzyme baths. Fully hydrated SC samples were then adhered to a glass cantilever substrate. The cantilever system was placed in a chamber in which the relative humidity and air flow conditions could be controlled to produce a dry environment. As the SC dried over several hours, the cantilever deflected, and the amount of deflection was measured by a capacitive sensor. The deflection was used to calculate the SC stress as described in detail elsewhere [4,10].

The control SC was then fully rehydrated, and either a cleanser or a moisturizer was applied to the SC. The cantilever setup was returned to the chamber, and SC stresses were again measured over several hours as the treated SC was exposed to the drying conditions.

We also sought to understand the effects of applying a harsh cleanser followed by an ideal moisturizing formulation. One of the best formulas from the previous set of moisturizers was chosen. SC stresses were again characterized in a control experiment, and then following the application of a cleanser alone and the application of the cleanser followed by the moisturizer. *In vivo* evaluations involved surveys for reporting perceived skin tightness and dryness before application of a treatment and at multiple intervals up to three hours following the application of a treatment.

For each product, the corresponding measured SC properties informed computational finite element models of skin sections with realistic topography based on skin section images of the cheek and forehead. The models were used to compute the mechanical deformation of underlying skin layers at depths where mechanoreceptors and their corresponding neurons are located. The results of these simulations were used as inputs to numerical models of neural activity, which predict neuron firing rates that result from each of the cosmetic products.

Results: After drying, control SC samples reached stresses between 3-6 MPa. To control for the donor variability in SC samples, measured stresses are normalized with respect to the peak stress in the control SC test for each tissue sample. The application of cleansers generally resulted in elevated stresses compared to the control SC while SC treated with moisturizers experienced lower drying stresses (Fig. 3).

From skin comfort scores in consumer responses, two groups of cleansers became distinguishable (mild and harsh), while three groups of moisturizers were identified (low performing, mid performing, and high performing). A strong linear trend is observed between the relative peak stresses measured in SC treated with cleansers and the corresponding consumer skin tightness perception scores. Similarly, a linear trend was apparent between relative peak stresses measured in SC treated with moisturizers and skin tightness perception scores (Fig. 3).

For SC treated with a harsh cleanser following the application of an ideal moisturizer, the SC stresses were first significantly elevated by ~34% after the application of the cleanser, and then significantly reduced by ~48% following the application of the moisturizer. From the finite element models of skin sections, distinctions in strains that propagate due to SC drying were computed. Strain distributions through the full skin thickness in cheek and forehead locations are shown for untreated skin, skin treated with a cleanser, and skin treated with a cleanser followed by a moisturizer in Fig. 4. The marked differences in the computed strain distributions including at the locations of Merkel cell mechanoreceptors lead to differences in the predicted neuron firing rates. These findings are consistent with self-evaluated tightness and dryness scores obtained in the consumer surveys. Consumers reported increased skin tightness after application of the cleanser and markedly decreased tightness after applying the moisturizer over the 3-hour assessment period.

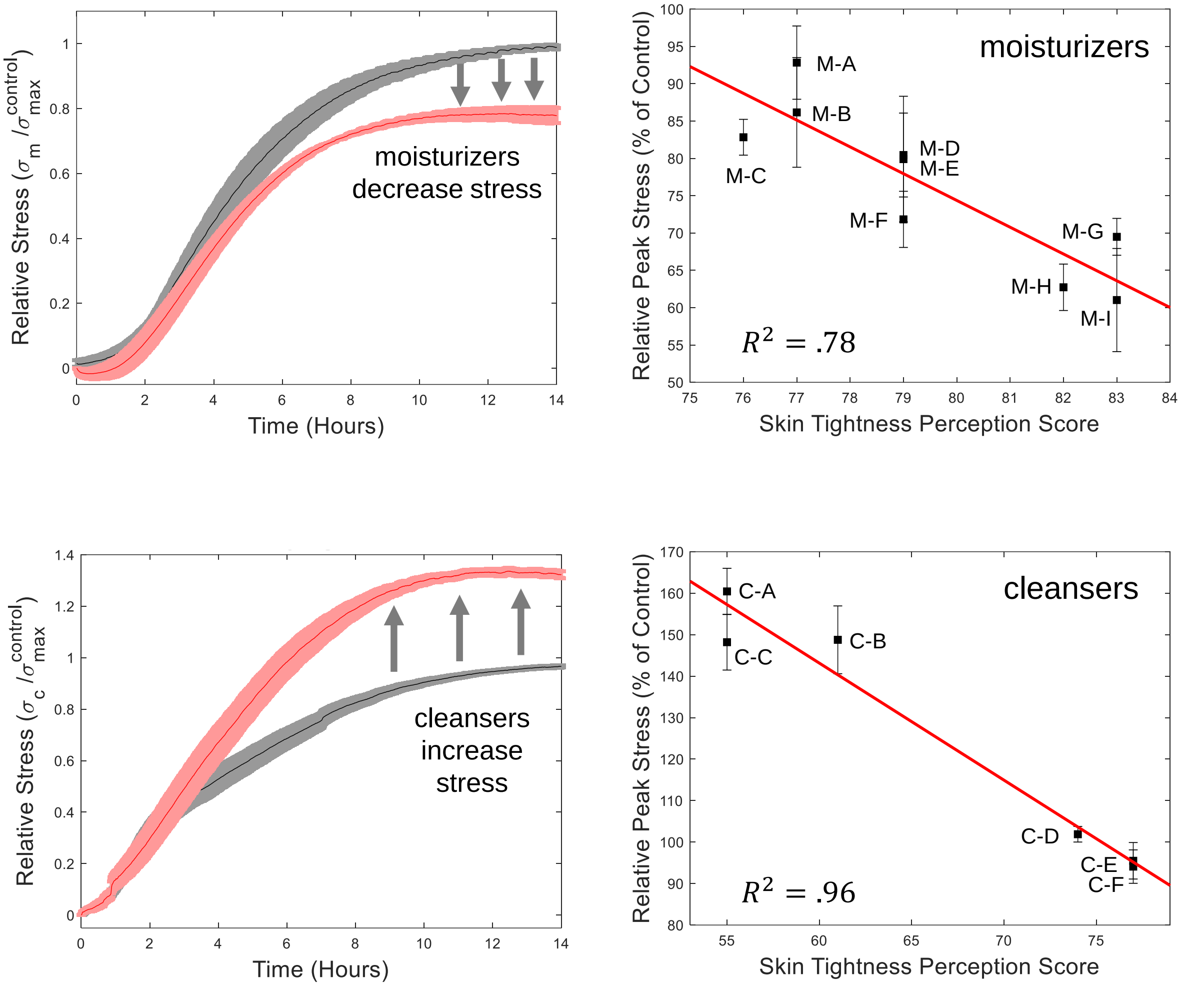

Figure 3: Effective moisturizers significantly reduce the stresses that develop in the SC compared to control SC while harsh cleansers significantly increase stresses that develop in the SC. From evaluating the performance of several moisturizer and cleanser treatments, distinct groups emerge for both treatment types—low, mid, and high performing moisturizers and harsh and mild cleansers.

More extensive computations indicated that the predicted neuron firing rates showed a strong linear correlation with the skin tightness perception scores for all of the cleanser and moisturizer treatments.

Discussion: In this work, we demonstrate a clear and robust connection between the SC's biomechanical state as influenced by cleanser or moisturizing formulations and reported skin comfort. More specifically, we investigated the relationship between SC film stresses measured *ex* *vivo* in a laboratory and consumer scores of tightness sensations recorded *in vivo* in a clinical trial. This strongly suggests that the perception of skin tightness is the result of mechanical changes in the SC, specifically the formation of tensile drying stresses in the SC that occurs with *ex vivo* drying or *in vivo* during the day under normal use conditions.

We also described the mechanism by which drying stresses at the surface of the skin propagate to underlying skin, stimulating cutaneous mechanoreceptors and triggering a sensorial perception of skin tightness. This mechanism is elucidated from finite element modeling. Differing magnitudes of stresses in the SC result in distinct magnitudes of strains at the depths of mechanoreceptors. This, in turn, affects the firing rate of sensory neurons and explains why there are a range of skin tightness perception scores corresponding to the cleansers and moisturizers analyzed in this study. Additionally, as observed in Fig. 4, the strains that develop in skin layers beneath the surface of the skin are dependent on the surface topography of the skin.

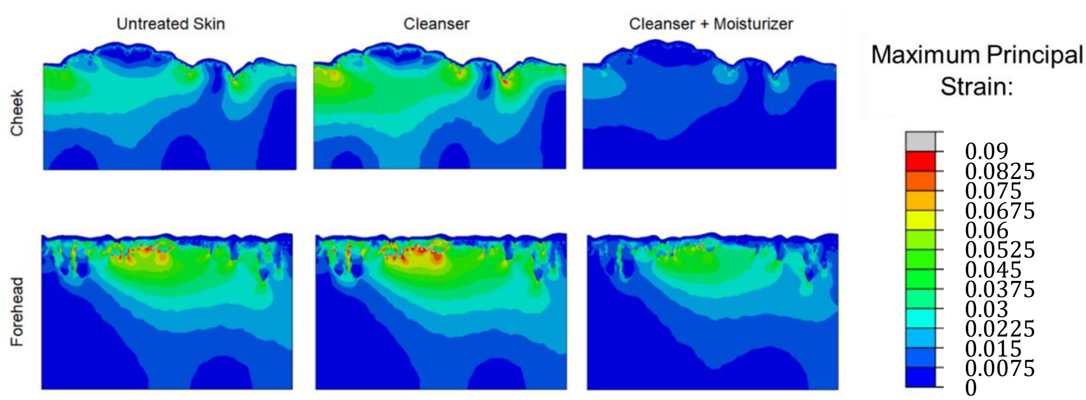

Figure 4: Strain contour plots from SC drying for untreated skin, skin treated with a harsh cleanser, and skin treated with the harsh cleanser followed by an ideal moisturizer are shown for skin sections from the cheek and the forehead. SC stresses from cleanser treatments increase the strains that develop in underlying skin compared to untreated skin which causes them to be perceived as relatively uncomfortable. Skin treated with a cleanser followed by a moisturizer has lower magnitudes of strains in skin layers beneath the surface compared to untreated skin which explains why moisturizers are generally perceived favorably.

A more focused study of factors that are observed simultaneously with the perception of skin tightness suggests methods for relieving skin tightness and improving skin comfort. Since following cleanser application with the application of a moisturizer both improved the perception of skin tightness and dryness, the moisturizer can be considered as a highly effective treatment for enhancing skin comfort. The measured reduction in SC stresses is indicative of the ability of the moisturizer to also combat skin stresses.

Conclusion: Measured skin stress involving the response of the SC to cleanser and moisturizer formulations are useful predictors of skin comfort. The connection is validated by finite element computational simulations of skin sections and numerical models of neural activity that show quantitatively how skin stress translates to a nervous system response. Additionally, studies combining clinical and consumer evaluation studies with laboratory and computational data are an avenue to new findings in the field of emotional perception and well-being.

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Conflict of Interest Statement: BL, GSL, and AP are employees of L'Oréal. JP, SHR and RHD received funding from L'Oréal.

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