ON THE MECHANOME OF HUMAN SKIN

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Introduction

We aim at a mechanical characterization of human skin at tissue and cell length scales. Skin provides sufficient compliance to enable body movements but it also forms a mechanically stable barrier against external loads. At cell length scale, the mechanical properties of the extracellular matrix (ECM) determine its "mechanome" [1], influencing cells, e.g. during skin repair or growth.

Methods

Experimental characterization included ex-vivo multiaxial tensile tests, micro- and nano-indentation, in-vivo suction measurements and 3D tissue imaging. Observations were rationalized using a multi-layer poroelastic continuum model [2]. Each skin layer is represented as a bi-phasic material, with the solid part characterized by a fiber network and a compressible matrix, while interstitial fluid flows according to gradients of the chemical potential, as resulting from the fixed charge distribution in the tissue [3, 4].

In order to represent the transition between micro- and macroscale we used a hybrid discrete-continuum model representative of the heterogeneous micro-structure of skin. Fibers are modeled as nonlinear elastic connectors. Multi-phasic continuum elements provide a representation of interstitial fluid, proteoglycans, anions, cations and other non-collagenous ECM components.

Results

The mechanical response in tensile tests indicates an average stiffness akin to a Young's modulus of about 100 kPa, while local indentation leads to a stiffness of few kPa. Model parameters were selected to provide a reasonable fit for experimental data at macro- and micro-scales. The resulting multiscale model representation of skin allows investigating the relationship between tissue microstructure and its deformation and fracture properties.

Moreover, simulation of skin stretch in-vivo provides quantitative information on the associated changes in cues of the "mechanome", which can affect biological processes. Specifically: (i) mean values of cell perceived forces at focal adhesions increase from 25 nN to more than 100 nN for an in-plane stretch of λ=1.1; (ii) such physiologic deformations lead to significant displacement of the interstitial fluid, linked with gradients of its chemical potential. Corresponding average fluid velocities increase by several µm/sec; (iii) resident cells are also exposed to changes in hydrostatic pressure and osmotic pressure of more than 80 kPa and 10 kPa respectively (Figure 1).

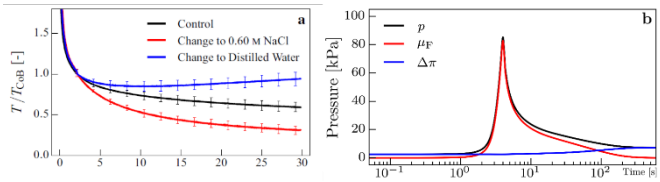

Figure 1: a. Relaxation with change of bath to hyper- or hypotonic solutions leads to force de- and increase. b. Predicted fluctuation of hydrostatic and osmotic pressure for a stretch of λ=1.15.

Fluid flow, gradients in ion concentration and electrical potential determine the movement of mobile charges. As a consequence, skin stretch leads to transient and steady state variations of the local electrical potential and electric field (Figure 2).

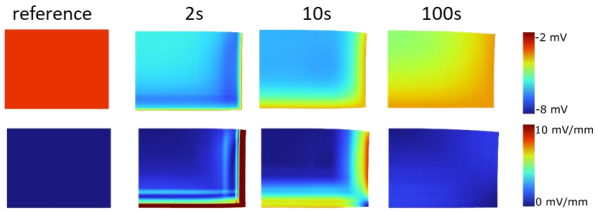

Figure 2: Calculated transient electrical potential (mV) and electric field (mV/mm) in the dermis (cross section, 2x5mm, left symmetry) after in-plane stretch of λ=1.15.

Discussion

Mechanotransduction mainly considers changes of ECM stiffness as well as cell deformation as relevant cues associated with skin stretch. Our results demonstrated the existence of a rich set of physical signals that vary with in-plane tissue loading, constituting the mechanome of human skin. Future studies will focus on the direct measurement of these quantities, on the analysis of the biological processes that they activate, and on possible implications for improving our understanding of skin fibrosis and optimizing mechanotherapies.

References

1. Wang et al, Protein Cell, 5(7):518-532, 2014.
2. Sachs et al, Biomech. Model. Mechanobiol, 20, 969-982, 2021.
3. Wahlsten et al, Biomech Model Mechanobiol, 18, 1079-1093, 2019.
4. Stracuzzi et al, Z. Angew. Math. Mech. 98, 2135-2154 2018.

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