Mechanistic Modelling of Interstitial Fluid and Protein Extraction via Hypobaric-Induced Skin Deformation

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Dermal interstitial fluid (ISF) has emerged as a promising alternative to blood for diagnostic monitoring due to its rich chemical composition; however, most existing ISF extraction methods remain invasive. Experimental evidence indicates that applying hypobaric pressure can induce sufficient skin deformation to drive ISF to the surface, offering a pathway toward truly non-invasive sampling. This study combines human experiments and in silico modelling to investigate how skin stretching under hypobaric loading influences ISF extraction dynamics and to quantify the relationship between deformation, extracted ISF volume, and total protein content.

Experimental data were generated using a vacuum-driven skin-stretching device with a central post applied to the forearm skin of healthy volunteers. These data were used to calibrate and validate a computational model in which skin is represented as a hyperelastic material to capture hypobaric deformations. Fluid transport within the dermis is described using the unsaturated Darcy law, while protein transport is modelled as convection dominated. Sodium concentration served as a surrogate for ISF volume, and total protein content was quantified using a bicinchoninic acid assay.

The model was calibrated using time-series data collected at -4.5 PSI, which exhibited a non-linear increase in ISF extraction over time. At 20 minutes, the calibrated model predicted 2.46 μL of ISF and 40.08 μg of protein, closely matching experimental measurements of 2.33 ± 1.31 μL and 37.11 ± 12.06 μg, respectively. The validated model was then used to predict ISF and protein extraction across pressures from −2.25 to −6.75 PSI at 10 minutes. Predictions fell within experimental 95% confidence intervals, with root-mean-square errors of 0.44 μL (ISF) and 5.82 μg (protein) and reproduced the observed nonlinear dependence of extraction on hypobaric pressure.

This combined experimental–computational framework provides a physics-based understanding of how mechanical loading modulates ISF availability and protein yield in human skin. It enables in silico optimisation of pressure/time protocols without extensive human experimentation, informing safe and efficient device operating windows. Furthermore, it sets a foundation for future studies for tailoring protocols to disease states like eczema, where dermal hydration and the porous structure differ.