Lung-Alveoli-on-Chip:
Mechanical Characterization of a New Biological Membrane

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Introduction

Lung-on-chips (LOCs) are advanced in-vitro models, aiming at reproducing the complex microenvironment of the alveolar basement membrane. Since the lung extracellular matrix (ECM) is known to influence cellular behavior, it is essential for membranes to closely mimic composition and mechanical properties of the air-blood barrier. However, the currently used membrane is made of polydimethylsiloxane (PDMS), which poorly mimics the in-vivo chemical and physical properties. Hence, biological membranes were developed to replace this synthetic material. The aim of this study was to characterize their stiffness, to evaluate their possible integration into an in-vivo-like LOC generation. The ultimate goal was to reduce their Young's modulus, to approach the material properties found in-vivo.

Materials and Methods

The 8 µm thin biological membranes were made of collagen and elastin (CE membranes), and were supported by hexagonal gold meshes, mimicking the physiological structure of the lung alveoli. Mechanical characterization was performed via bulge test, a non-destructive method based on the measurement of the maximal deflection reached by thin films when subjected to uniform pressure (Fig. 1). A fit was then applied to the experimental data, to extrapolate the Young's modulus using a relation between deflection and pressure. Membranes made of various PDMS types were analysed as reference, to prove the reliability of the implemented bulge technique.

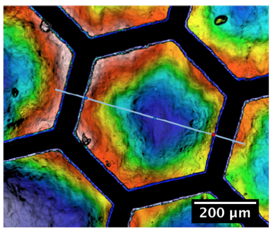

Fig. 1 Bulged shape of CE membranes, supported by hexagonal gold meshes and subjected to a pressure of -1 kPa. The picture was acquired using a 3D optical profiler.

Results

Membranes made of PDMS (Dow Corning, Sylgard 184) were found to be stiffer (E = 334 $\pm$ 129 kPa) than CE membranes with a 1:1 collagen to elastin ratio (E = 173 $\pm$ 37 kPa). A simple method to tune the stiffness of biological membranes was presented by adapting their composition. The Young's modulus was effectively reduced by gradually decreasing the collagen content in the material, reaching a value of 75 $\pm$ 43 kPa (Fig. 2).

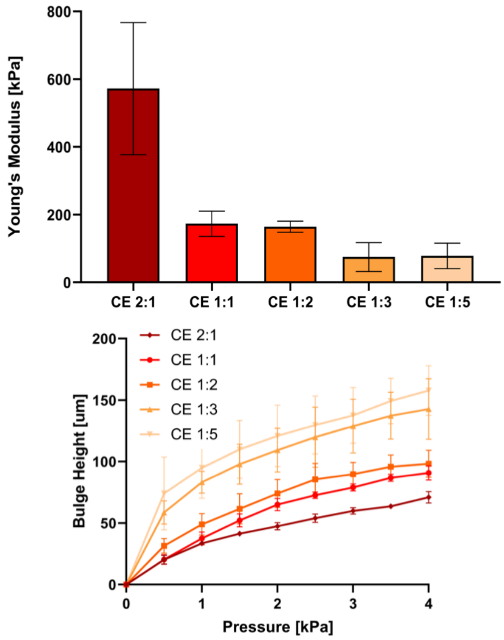

Fig. 2 Young's modulus and deflection obtained for CE membranes by varying their collagen and elastin content.

Discussion

To our knowledge, bulge test was performed for the first time at the micrometer scale, hence not allowing a direct comparison of the results with previous findings. However, as expected, the increase of elastin to collagen ratio allowed to obtain a more stretchable and softer material. Since the tuned stiffness was still far beyond that of lung ECM (E ≈ 2 kPa), the material still needs to be optimized to better mimic the cellular microenvironment of the lung alveoli. To conclude, bulge test was shown to be a promising method for mechanical characterization. It will allow further investigation of future biological membranes.

References

P. Zamprogno et al. Second-generation lung-on-a-chip array with a stretchable biological membrane. BiorXiv, 2019

Acknowledgements

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