# Development of a Surface Tension Driven In-Situ Biofabrication Pipeline for Biomimetic Lung basement Membranes

Johannes Fehr

Supervisors: Prof. Dr. Olivier Guenat, MSc. Tobias Weber
Institution: University of Bern, ARTORG Center for Biomedical Research
Examiners: Prof. Dr. Olivier Guenat, MSc. Jan Schulte

## Introduction

Lung disease remain a major cause of death and the development of new drugs is slow due to inadequate in-vitro models. Lung-on-Chip (LoC) focuses on understanding alveolar (patho)-physiology and drug response and the effect of respiratory motions on cells due to mechanical stimuli. To increase the relevance of LoC, better membranes are needed. The first generation of LoCs used porous PDMS membranes, second generation LoCs vitrified protein membranes. Both generations could not match the in-vivo membranes either in terms of thickness, stiffness or composition. The aim of this project is to produce hydrogel membranes that provide a cell-friendly environment and more closely match the alveolar basement membrane in terms of thickness, stiffness and protein composition.

## Materials and Methods

Gold grids were dip-coated in protein solutions and crosslinked to form thin hydrogel membranes within the pores of the grid. To investigate the influence of protein concentration on membrane thickness, three concentrations of a collagen - elastin solution, 1.75 mg/mL, 3.5 mg/mL and 5.0 mg/mL, were used. To investigate the influence of protein composition and concentration on attachment of A549 cells, different bulk solutions containing collagen I, elastin and fibronectin as well as a fibronectin coating, were tested.

## Results

The described protein concentrations resulted in thicknesses of (14.6 ± 2.3) µm, (15.5 ± 2.5) µm and (16.1 ± 2.9) µm, respectively.

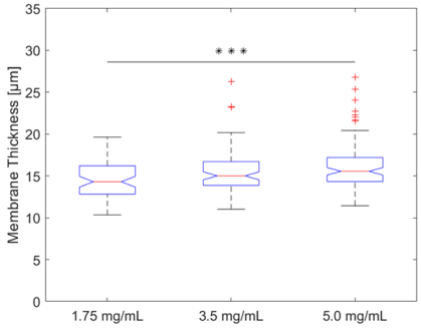


*Fig. 1 Thickness as a function of protein concentrations of CE 1:1 hydrogel membranes.*

Due to unknown reasons, the used cell line did not perform as expected and the results have to be taken critically. Two general trends were observed. Hydrogel membranes containing fibronectin or coated with fibronectin increased cell adhesion and proliferation. Pure collagen I membranes improved the cell environment compared to membranes containing elastin.

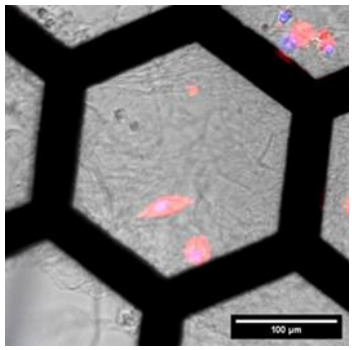


*Fig. 2 Limited cell adhesion, proliferation and actin secretion of A549 cells on a collagen – elastin – fibronectin hydrogel membrane with fibronectin coating. Blue: nuclei, red: actin. Scale: 100 µm.*

## Discussion

It has been shown that it is possible to produce thin hydrogel membranes by surface tension controlled filling of dip-coated gold grids. It can be concluded that the mechanical stability of the hydrogel membranes is sufficient for cell culture and first trends in cell adhesion and proliferation could be observed.

## References

P. Zamprogno *et al.*, 'Second-generation lung-on-a-chip with an array of stretchable alveoli made with a biological membrane', *Commun Biol*, vol. 4, no. 1, Dec. 2021, doi: 10.1038/s42003-021-01695-0.

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