COMSOL CONFERENCE INDIA 2012

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Bangalore, India

A study on nutrient mass transport through porous channeled flat sheet membrane & Prediction of scaffold thickness for viable cell culture *(in-vitro)* by 3D modeling for Tissue Engineering application

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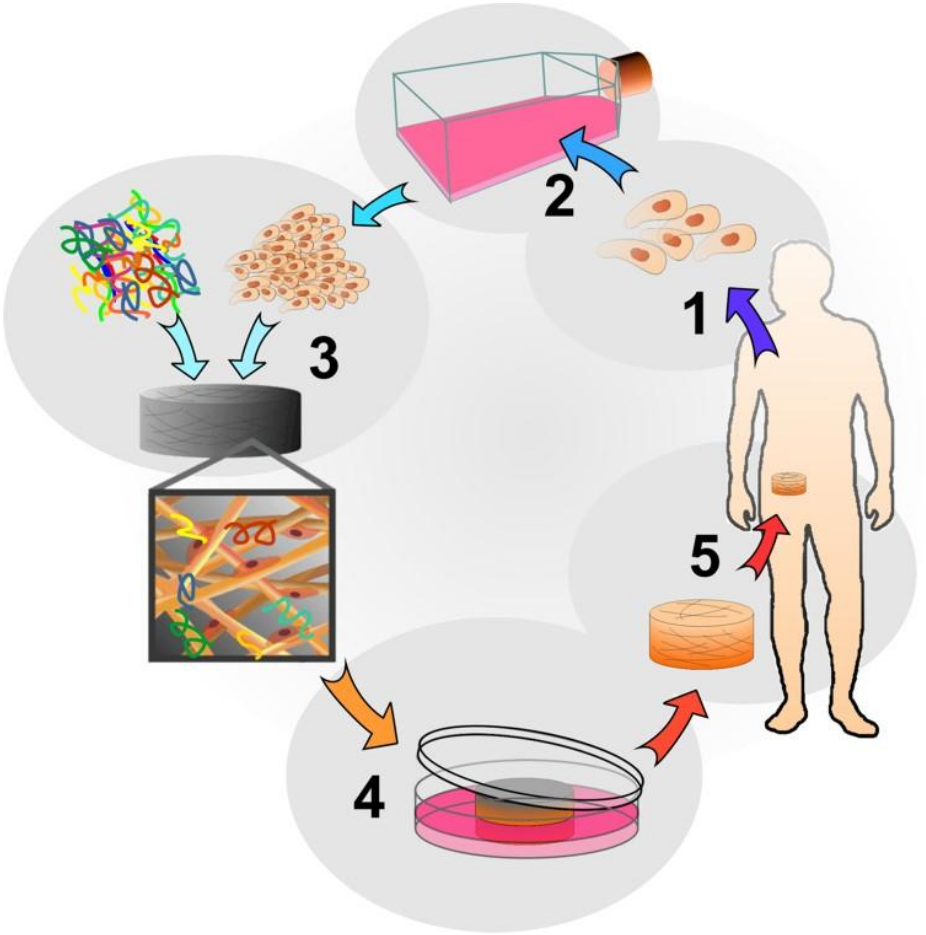
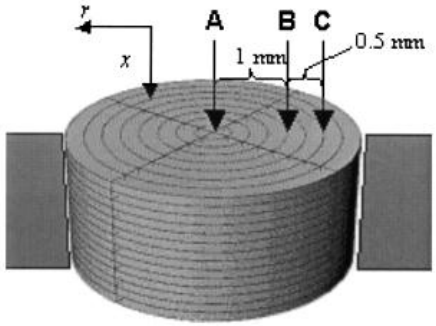
Excerpt from the Proceedings of the 2012 COMSOL Conference in Bangalore

What & Why - Tissue Engineering?

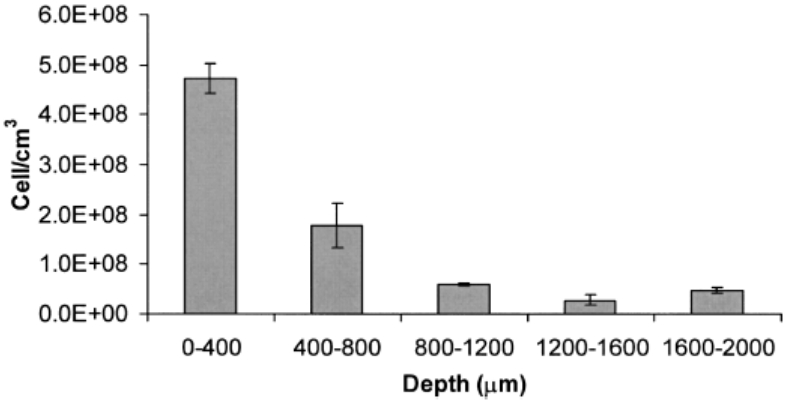


- Demand for donor organs
- Aging population
- increasing surgical procedures, wound care etc.
- *In vitro* toxicity testing to replace animal testing

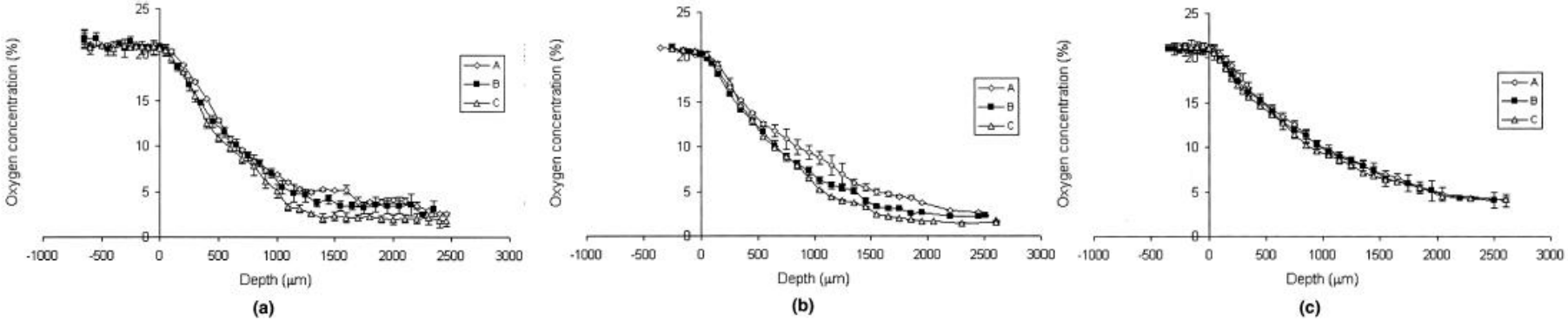
Oxygen depletion in TE 3D scaffolds [*]



Schematic representation of the FFF construct, the sample location A,B and C



Cell distribution within construct cultured for 28 days



Oxygen concentration within cartilaginous constructs cultured for (a) 14 (b) 27 (c) 41 days on FFF scaffold

[*] J. Malda, J. Rouwkema, D. E. Martens, E. P. le Comte, F. K. Kooy, J. Tramper, C. A. van Blitterswijk, J. Riesle , ***Oxygen gradients in tissue-engineered Pegt/Pbt cartilaginous constructs: Measurement and modeling*****,** Biotechnology and Bioengineering, 86(1), Pages (9-18)

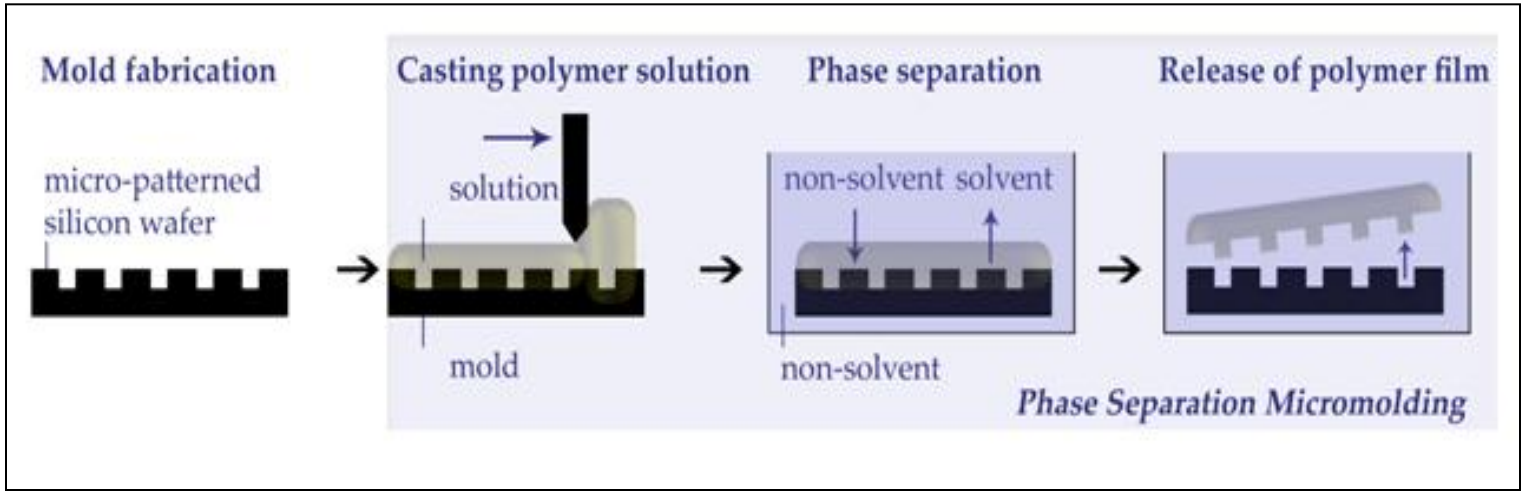
Issues

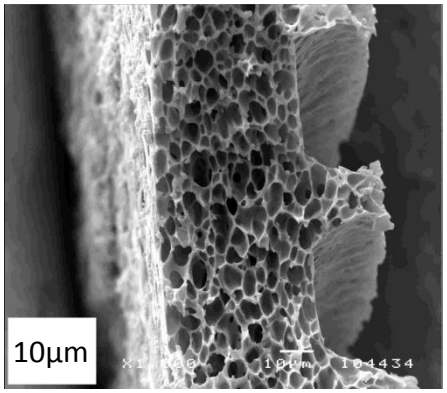
- How can you supply sufficient nutrients throughout the whole scaffold?
- How to mimic natural tissue organization?

Our solution

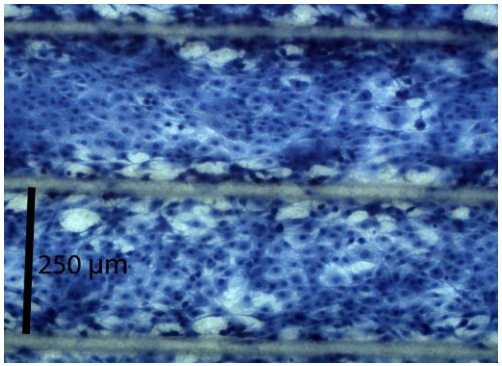
- Method: PSμM - What can it do for TE?
- Stacking /layer-by-layer technology
- Modelling for prediction of maximum 3D scaffold thickness with viable cell culture

PSµM - (Phase Separation Micro-Moulding)



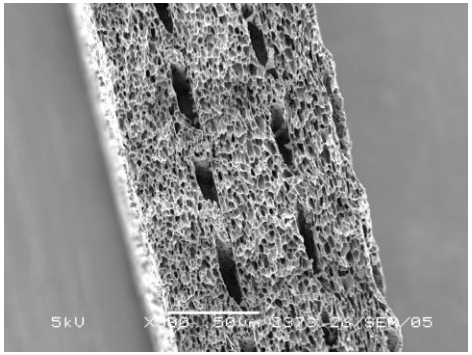


SEM picture of PLLA flat sheet porous membrane



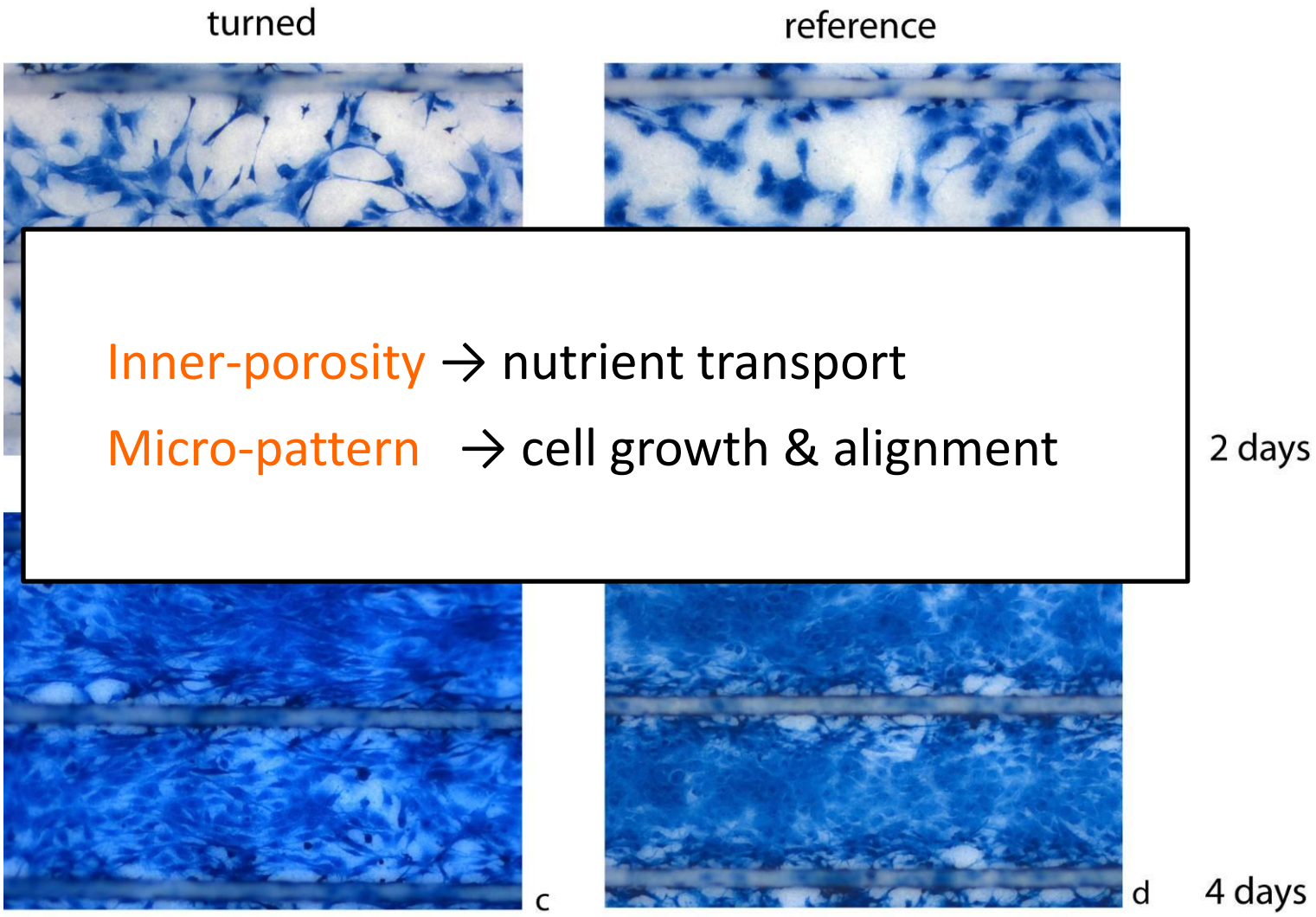
Light microscope picture after 4 days of culturing

(Cell density = 25000cells/cm²)

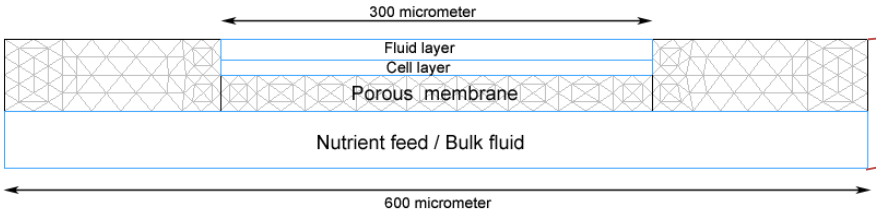


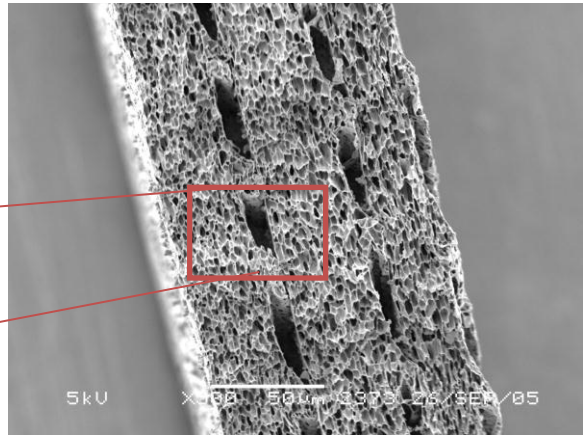
SEM picture of Staked flat sheet porous membrane

Nutrient transport



CFD Modeling using COMSOL



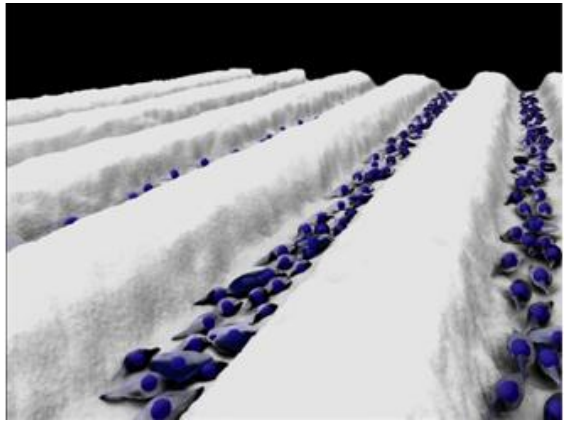


Cell density	80% of channel area
Bulk concentration	0.055 mol / m^3
Diffusion coefficient	8.4 X 10 $^{-11}$ m^2/sec
Consumption rate	3.83 X 10 $^{-16}$ mol/m^3.sec.cell

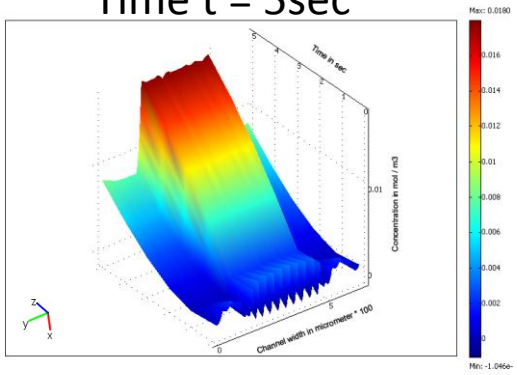
Assumptions

- Spherical cells
- Uniform pore distribution
- No lateral mixing
- Change in nutrient concentration is neglected

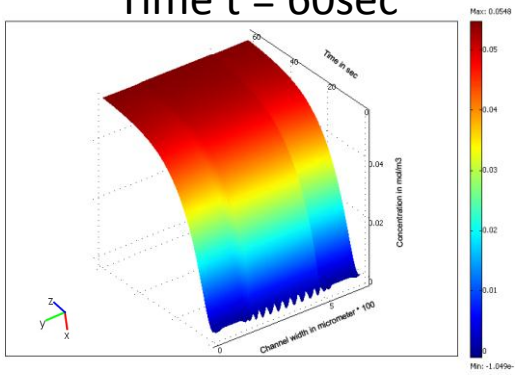
Concentration profile in a channel



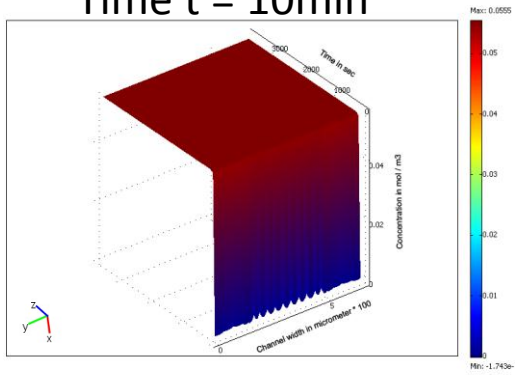
Time t = 5sec



Time t = 60sec

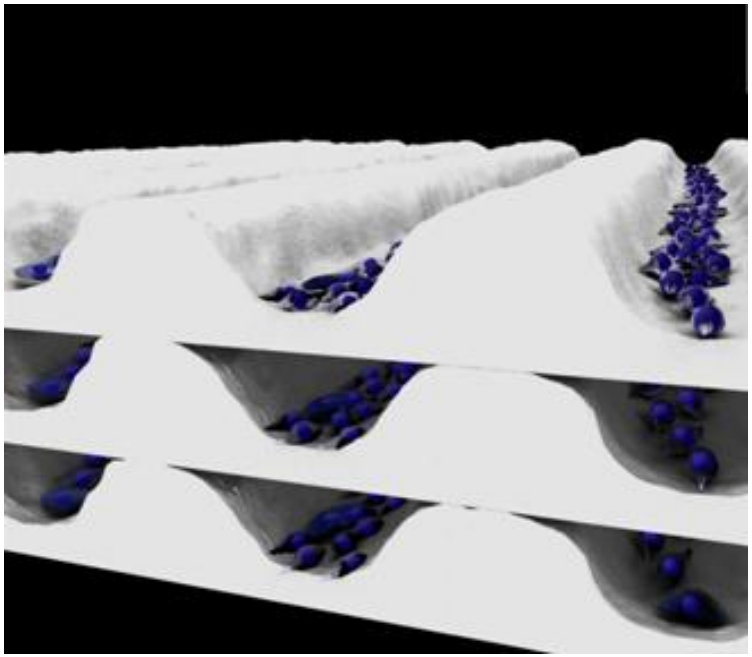


Time t = 10min



Model representing the concentration profile through a single channel at different time intervals

3D Concentration profile



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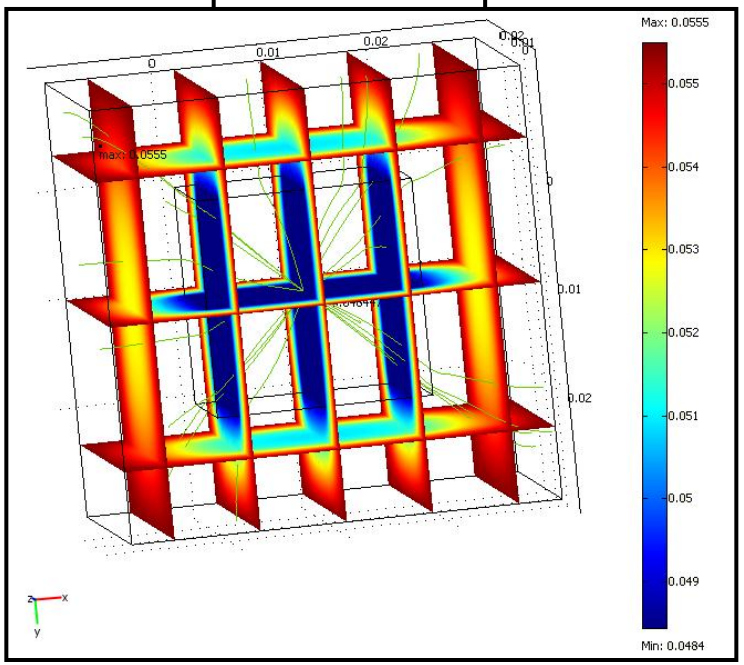

Outcome

- PSμM membranes provide sufficient nutrient transport for cell proliferation
- PSμM can be used to align cells or mimic natural tissue organization
- The model predicts efficient nutrient transfer within the staked flat porous membrane
- Porous 3D scaffold of PSμM membrane stake could be a possibility as TE constructs

Acknowledgement

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MIRA INSTITUTE FOR BIOMEDICAL TECHNOLOGY AND TECHNICAL MEDICINE

stw Technologiestichting

for financial support

Colleagues at,

University of Twente The Netherlands

MTG

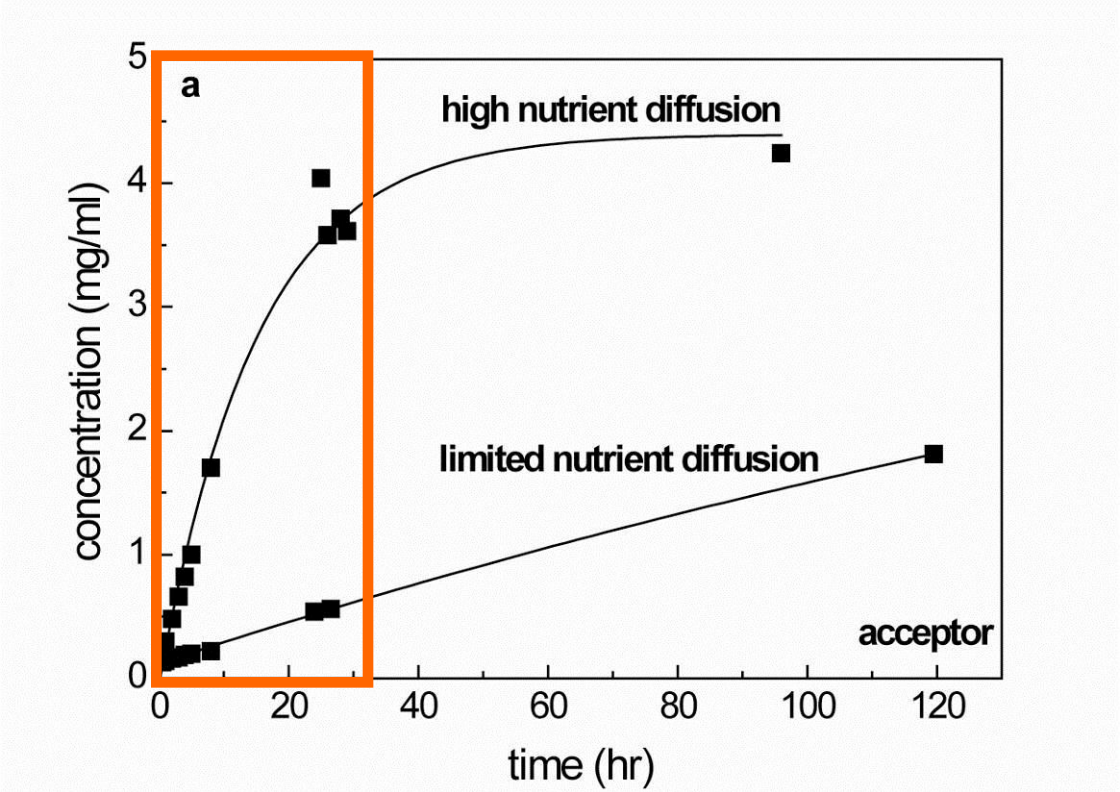
for continuous support


Thanks for your attention……
…..Questions / suggestions

Glucose diffusion

PLLA - dioxane, 5 wt%, EtOH, $T_{non\text{-}solvent}$ decreased

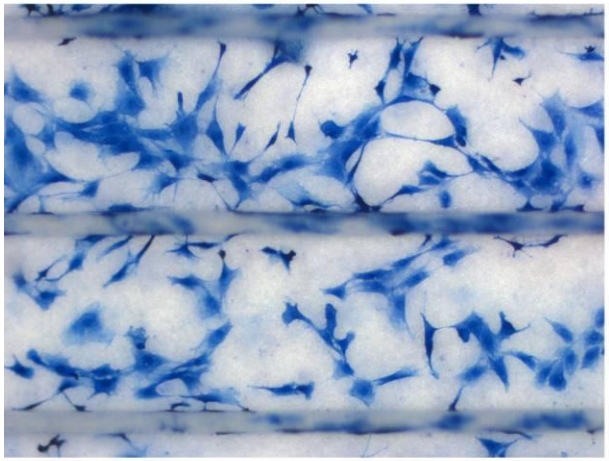
- Porosity ~ 84%
- Glucose diffusion (after 24 hr): 88%



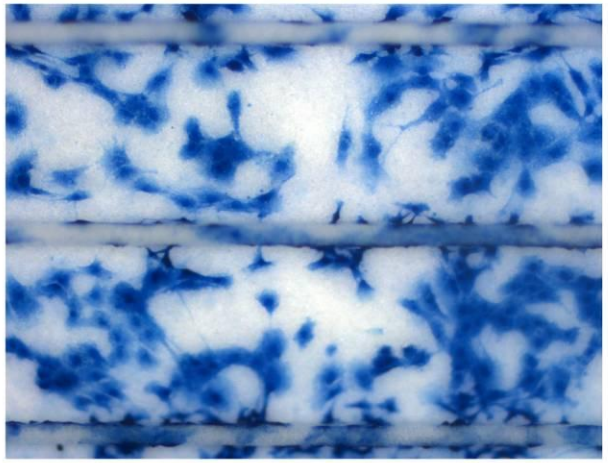
Nutrient transport

turned

reference

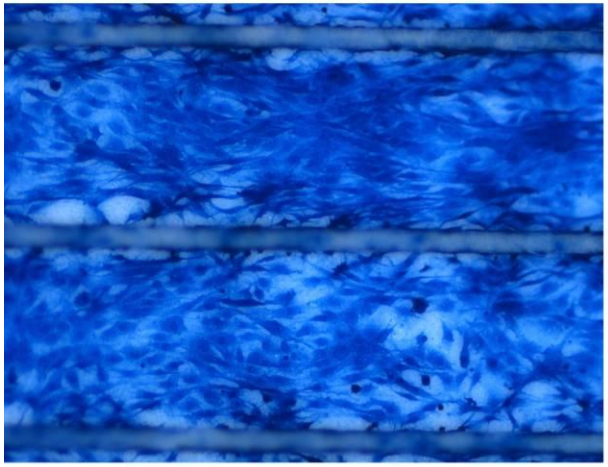


a

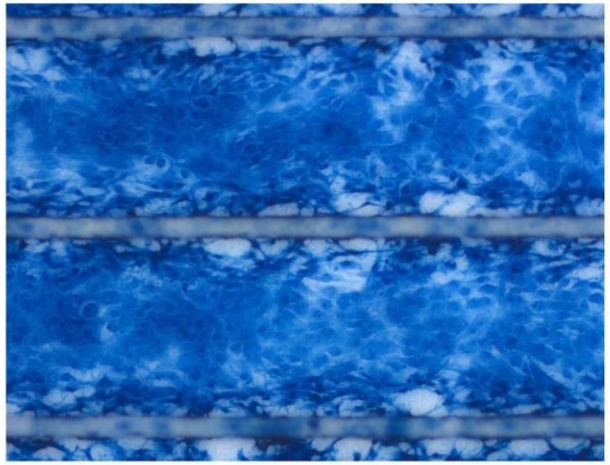


b

2 days



c

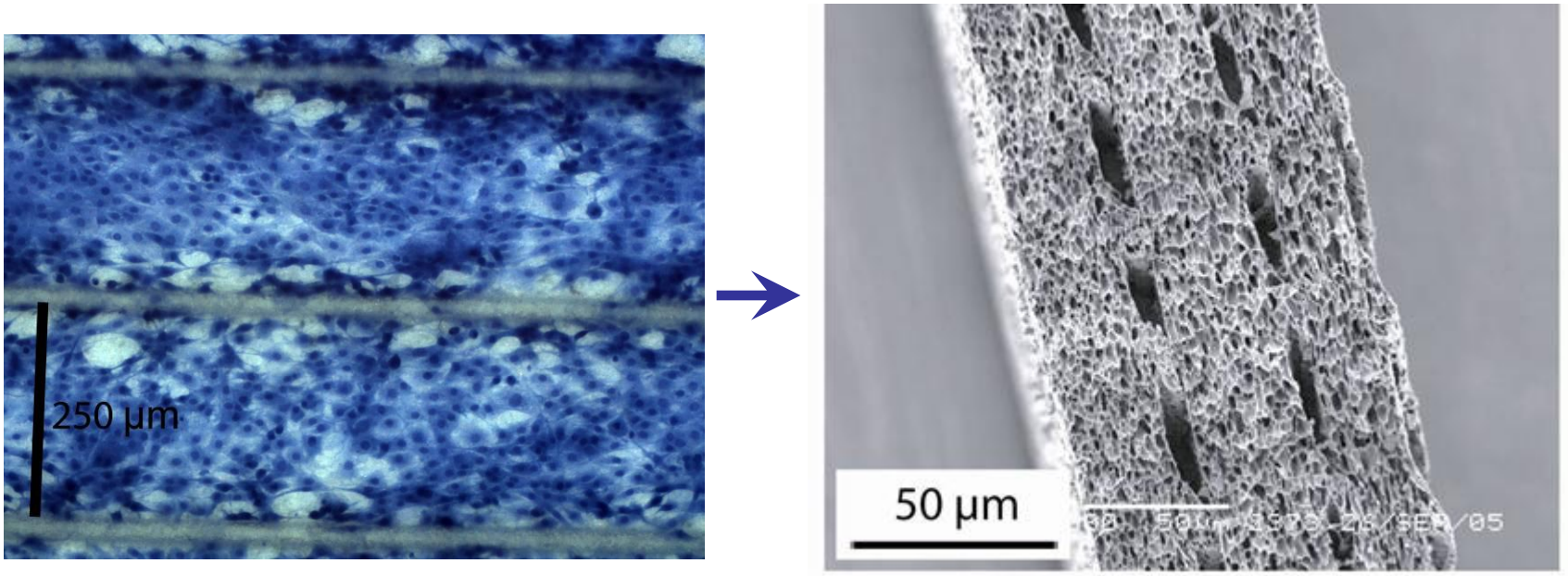


d

4 days

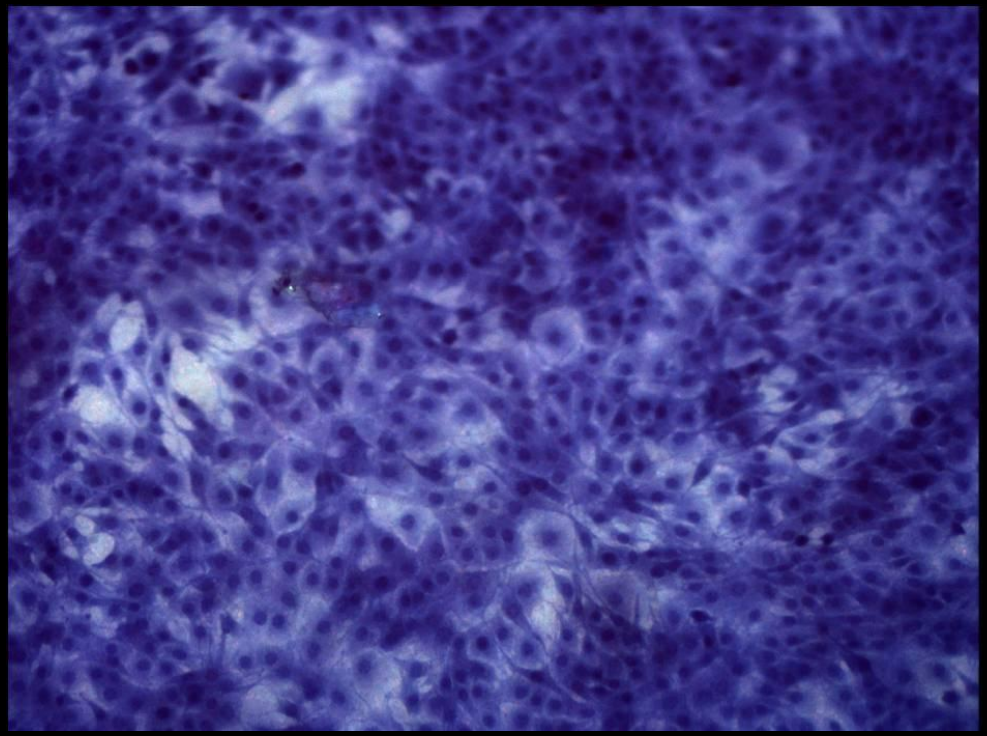
Concept for 3D cell culture

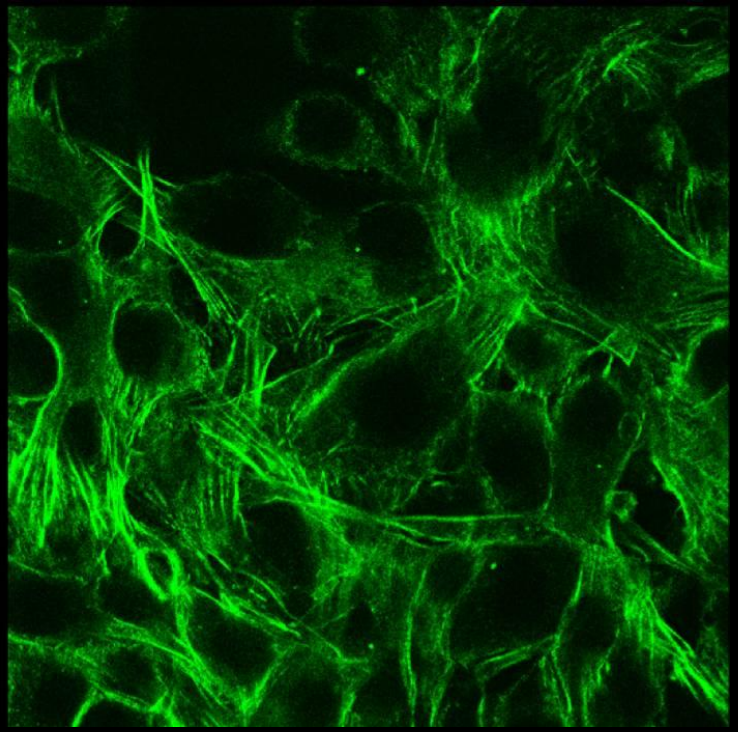
Stacking porous micro-patterned sheets

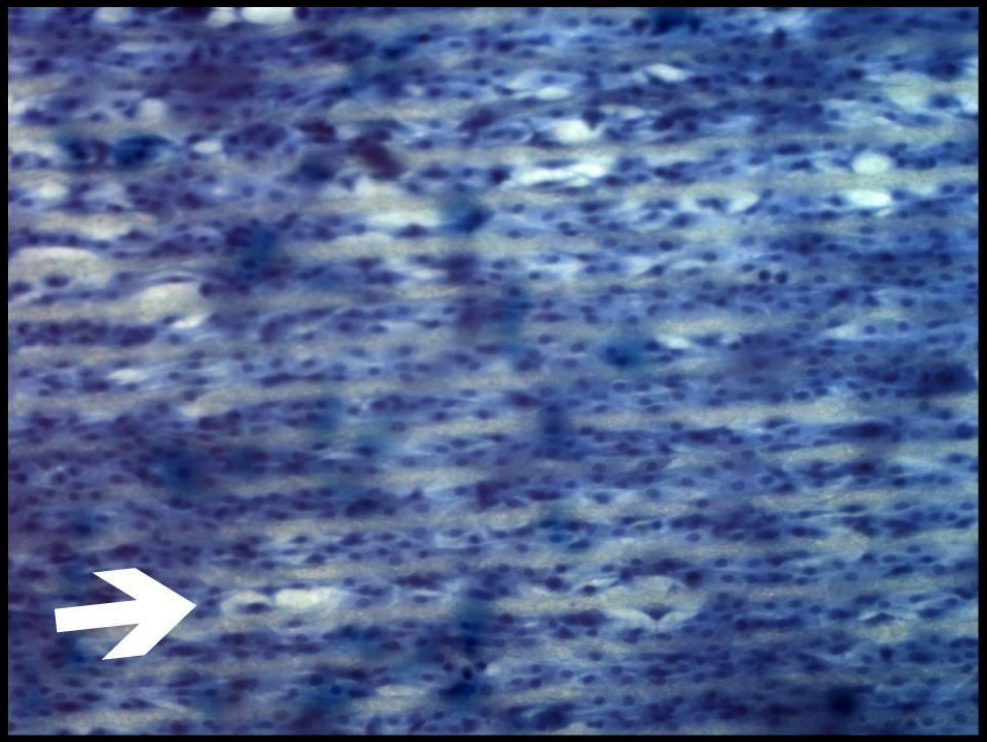


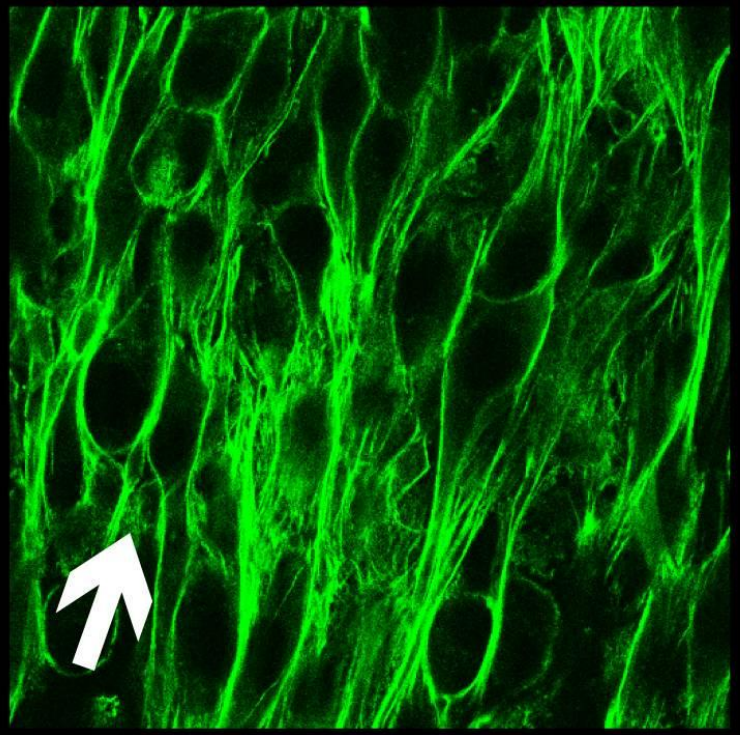
Micropattern → cell growth & alignment

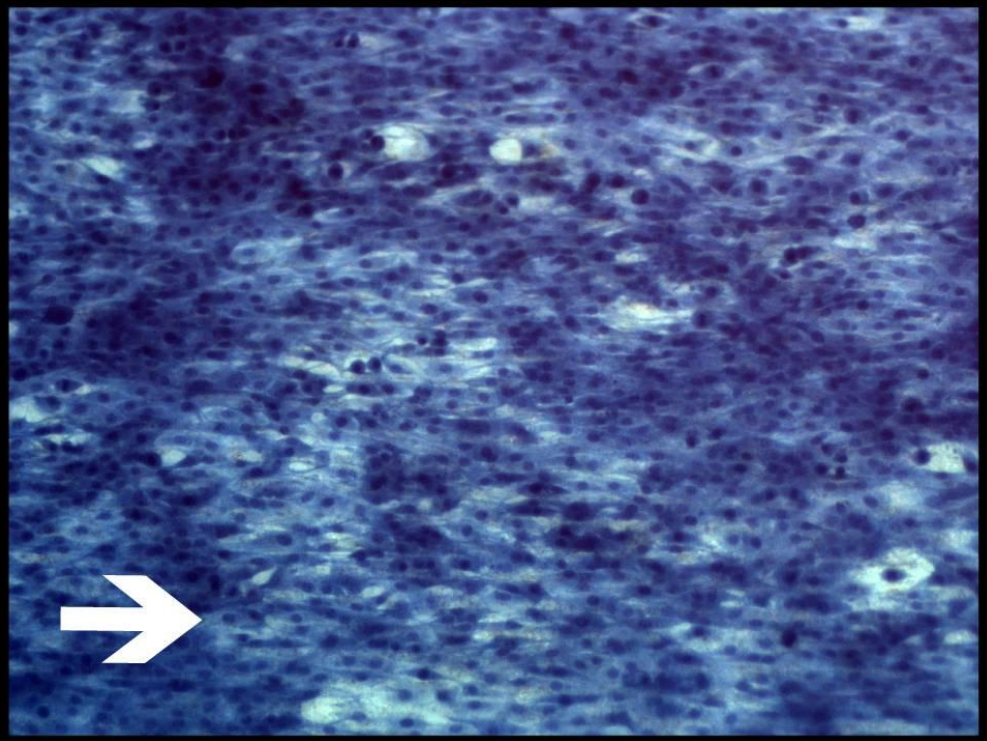
Inner-porosity → nutrient transport

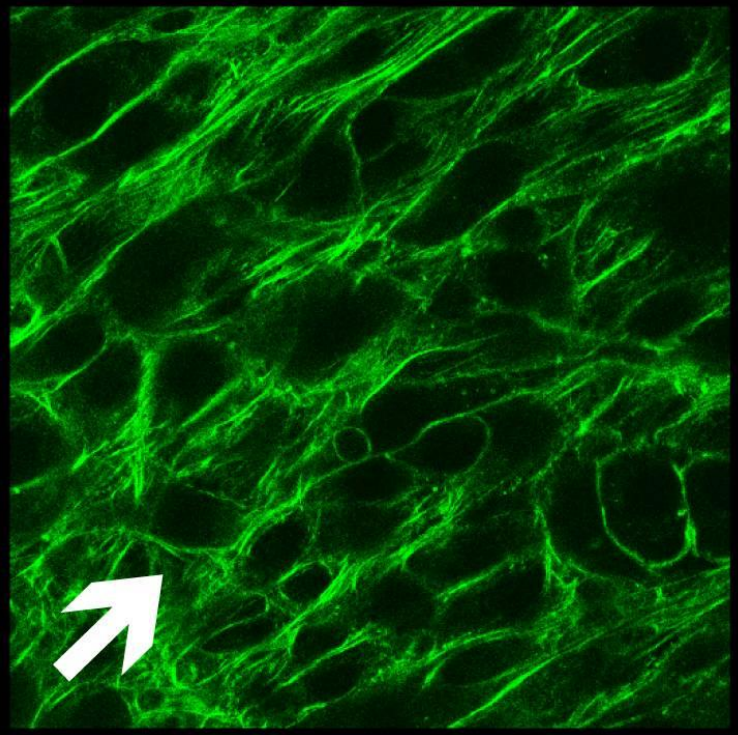


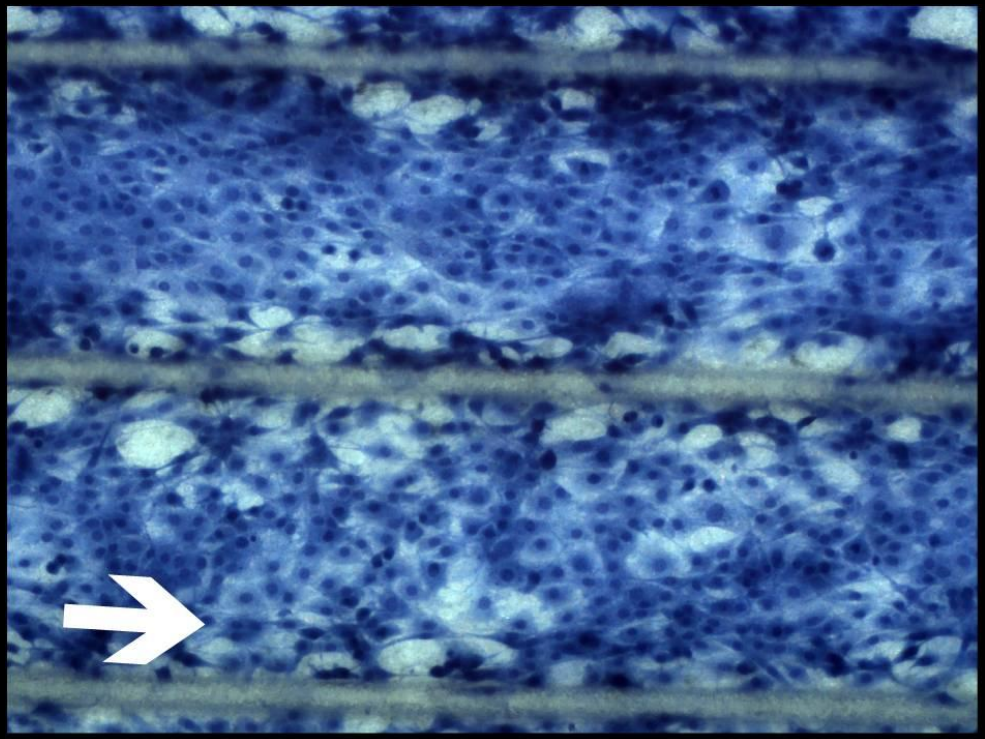


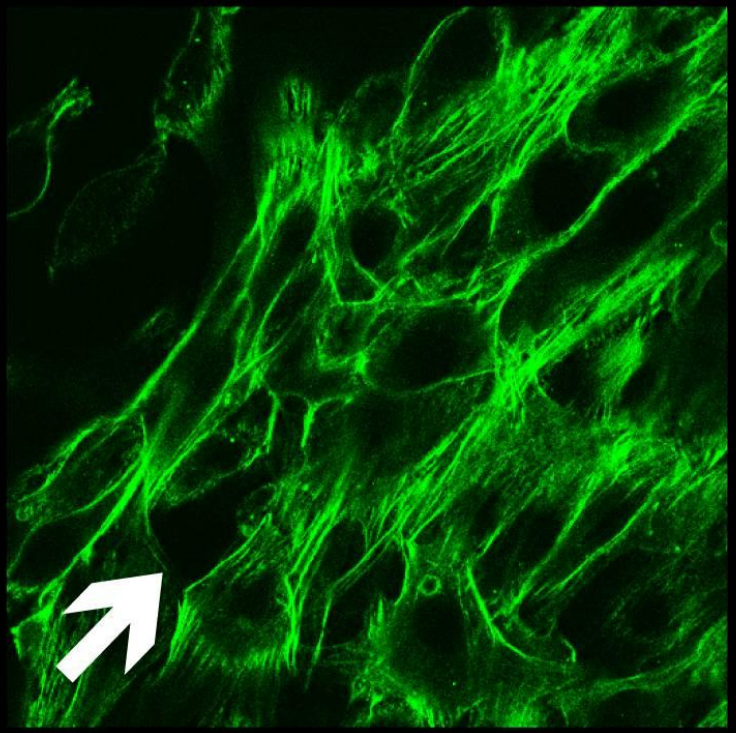


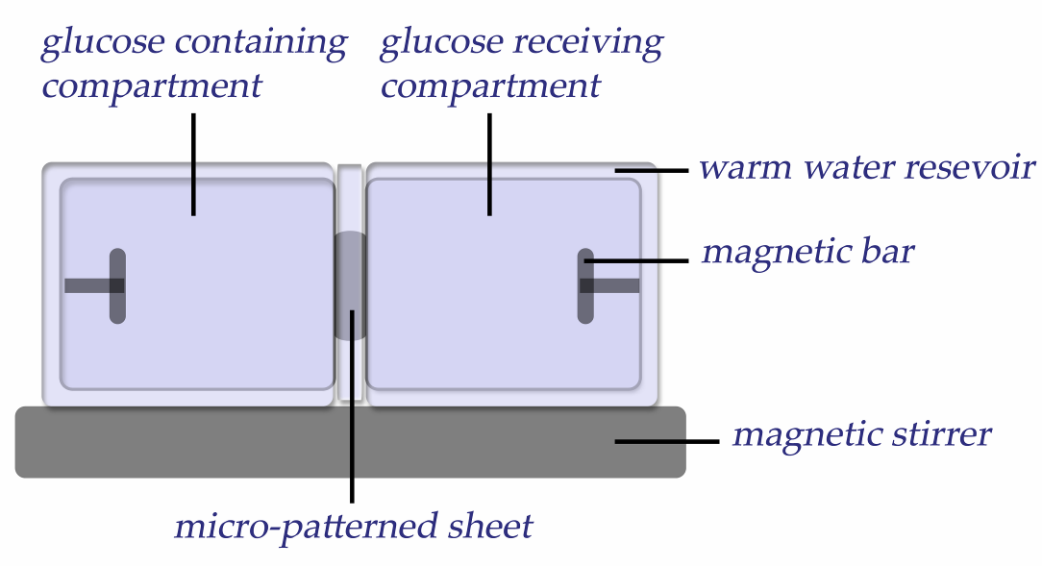











glucose containing compartment
glucose receiving compartment
warm water resevoir
magnetic bar
magnetic stirrer
micro-patterned sheet