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4D electroactive and microporous polyHIPE-PEDOT scaffolds as a dynamic *in vitro* cell culture platform

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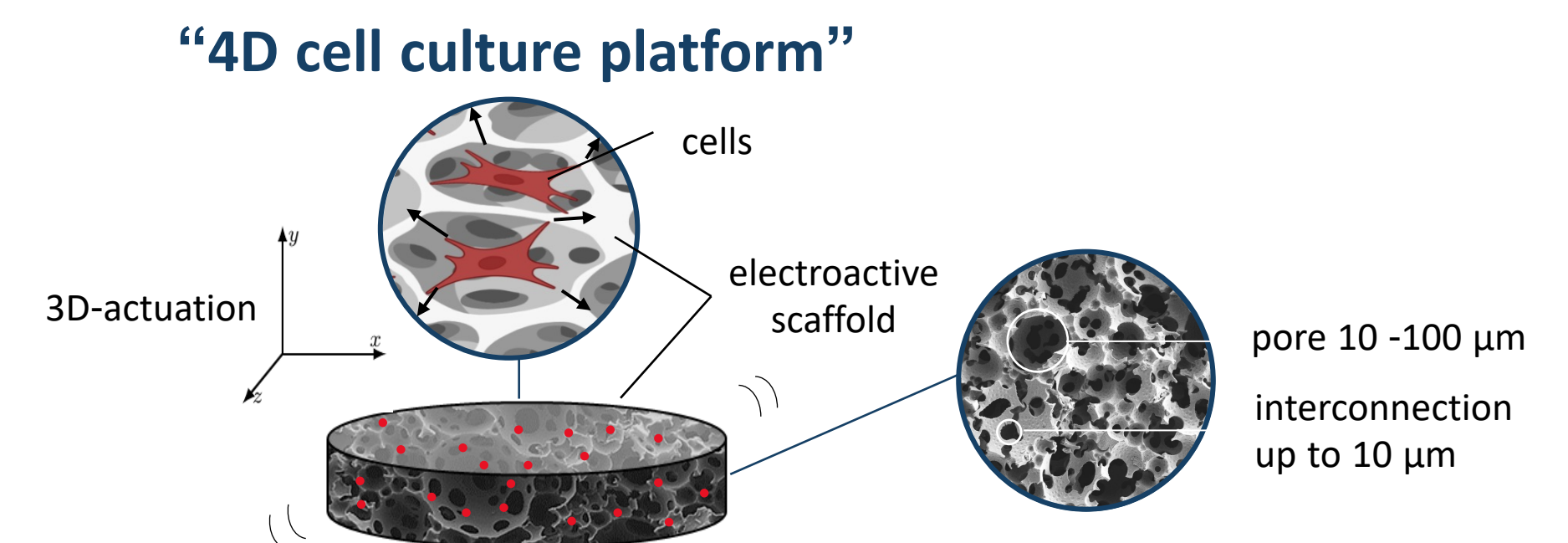
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Introduction

- In vivo*, cells are surrounded by an extracellular matrix (ECM)
- Signals from the ECM such as biochemical or biophysical cues regulate cell behaviour
- 3D cell cultures offer biologically superior structures, but don't transmit dynamic mechanical signals that exist in the cell microenvironment *in vivo*

To better recapitulate the cell microenvironment *in vitro* the aim of this work is to develop a **4D microporous and electroactive scaffold as an innovative cell culture platform:**

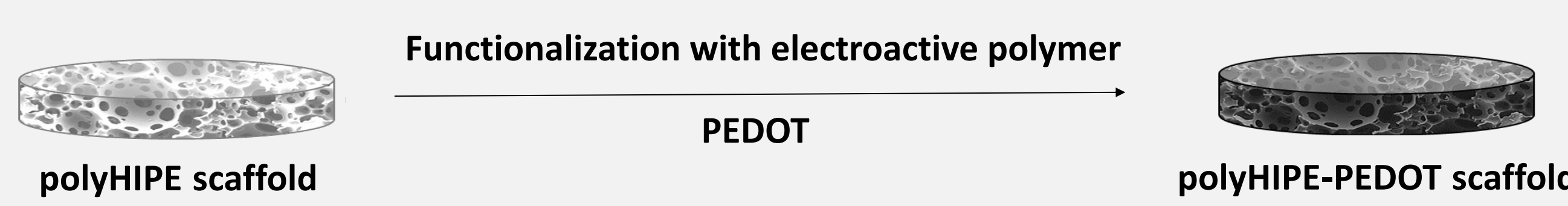
- In situ* electromechanical stimulation of cells
- Monitoring of the cell behavior



Synthesis of polyHIPE-PEDOT scaffolds

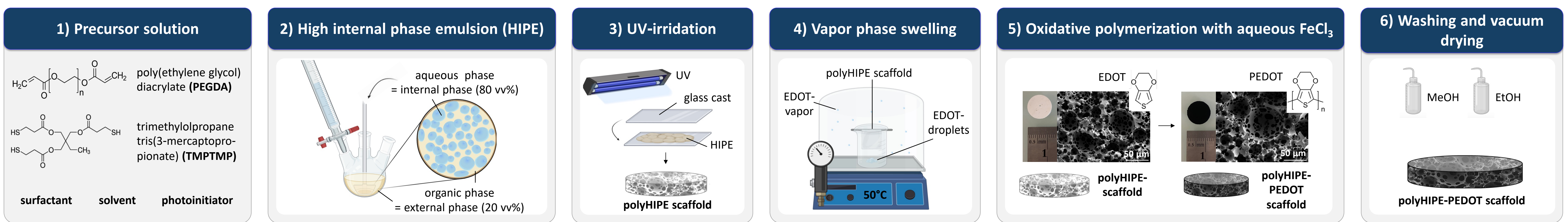
Polymeric scaffold:

- Highly microporous
- Interconnective



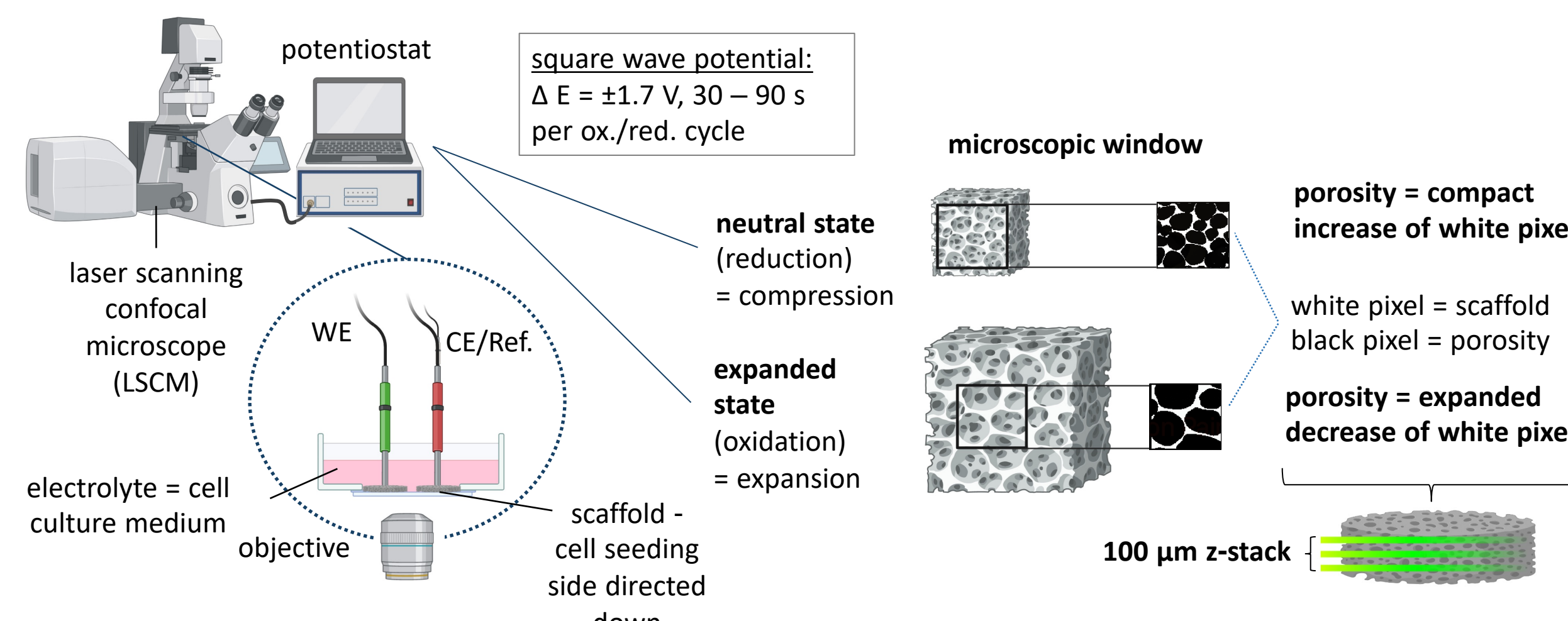
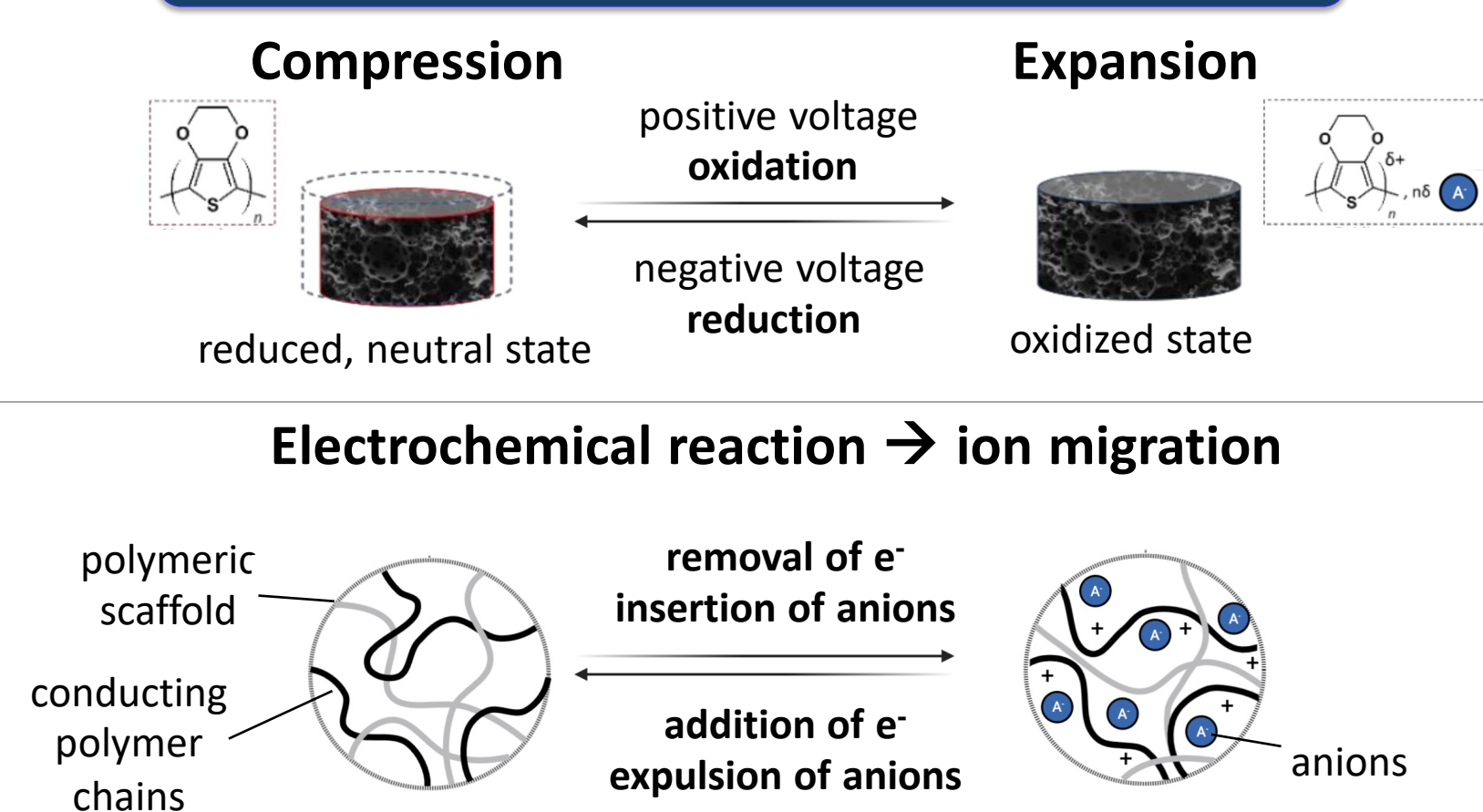
Electroactive polymeric scaffold:

- Preserved polyHIPE morphology

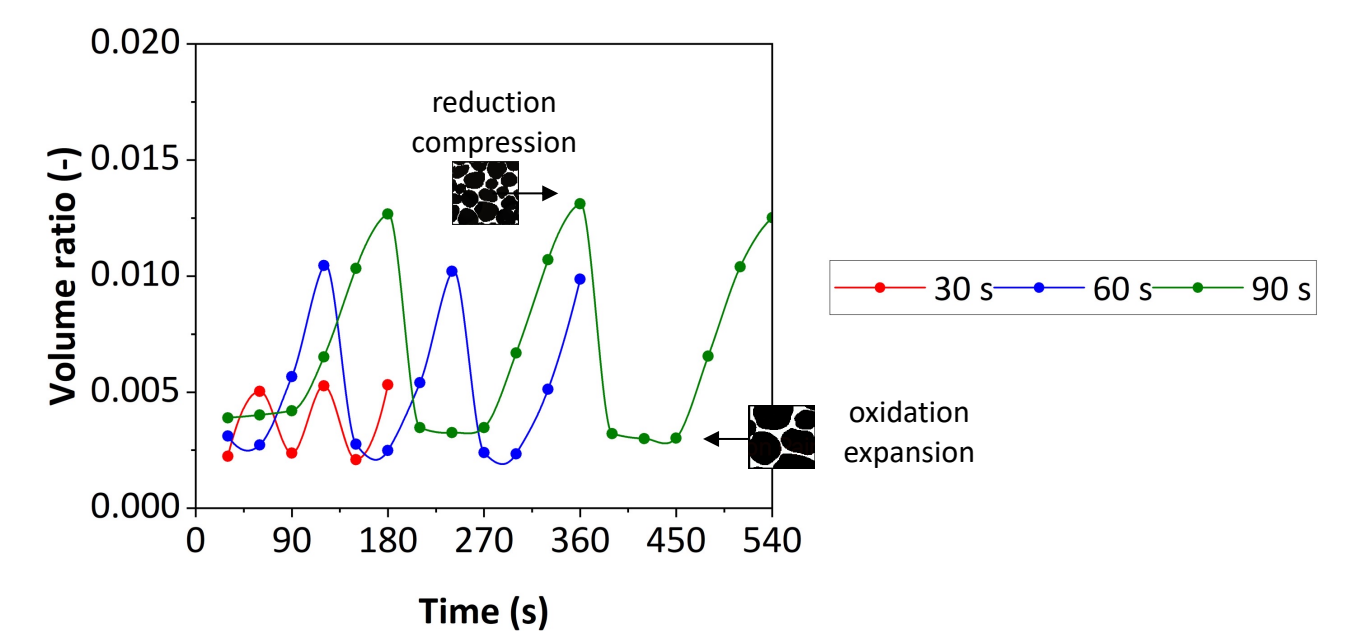


Actuation behavior of polyHIPE-PEDOT scaffolds

Mechanism



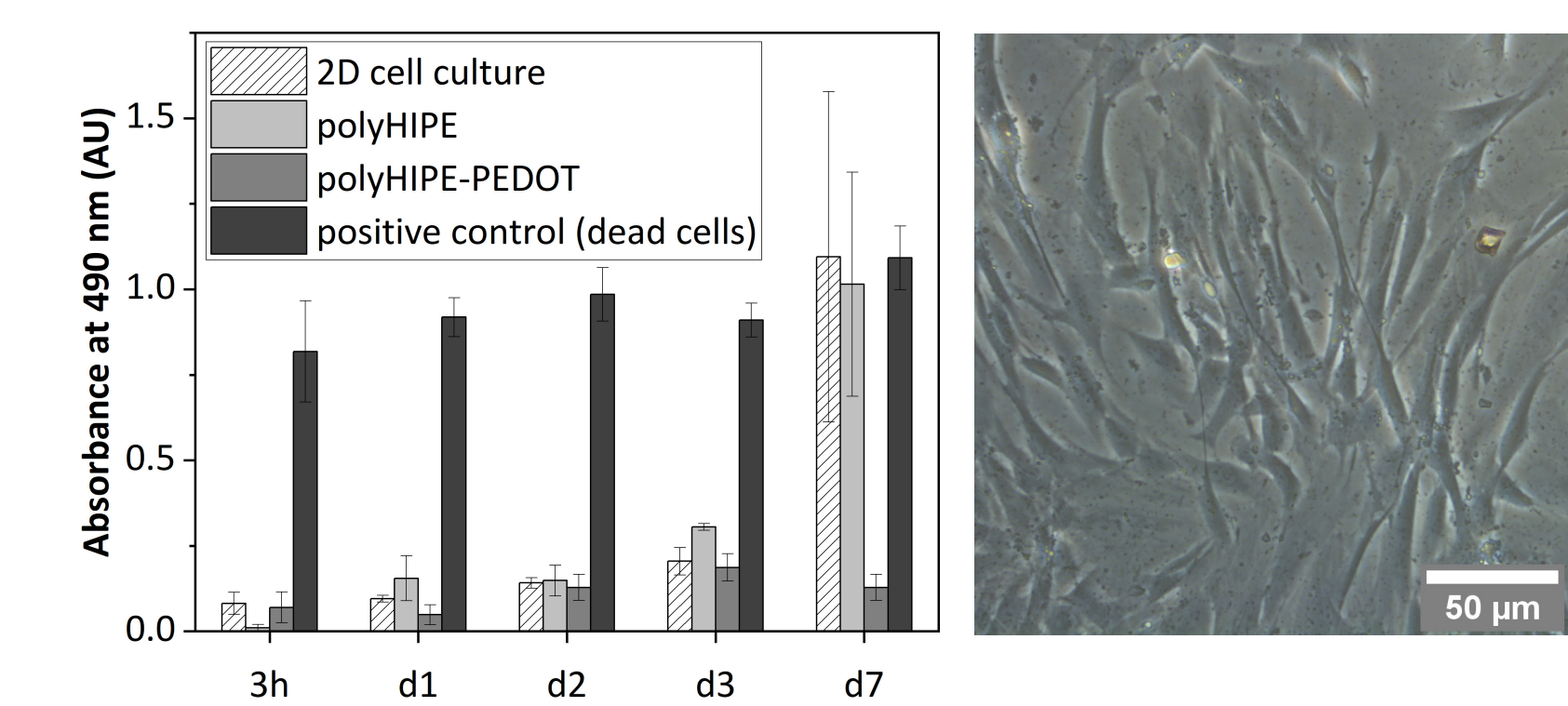
Actuation response of polyHIPE-PEDOT scaffolds to electrochemical stimulation



- PolyHIPE-PEDOT scaffolds showed direct response to electrochemical stimulation
- Reduction/oxidation time determines actuation frequency and volumetric expansion

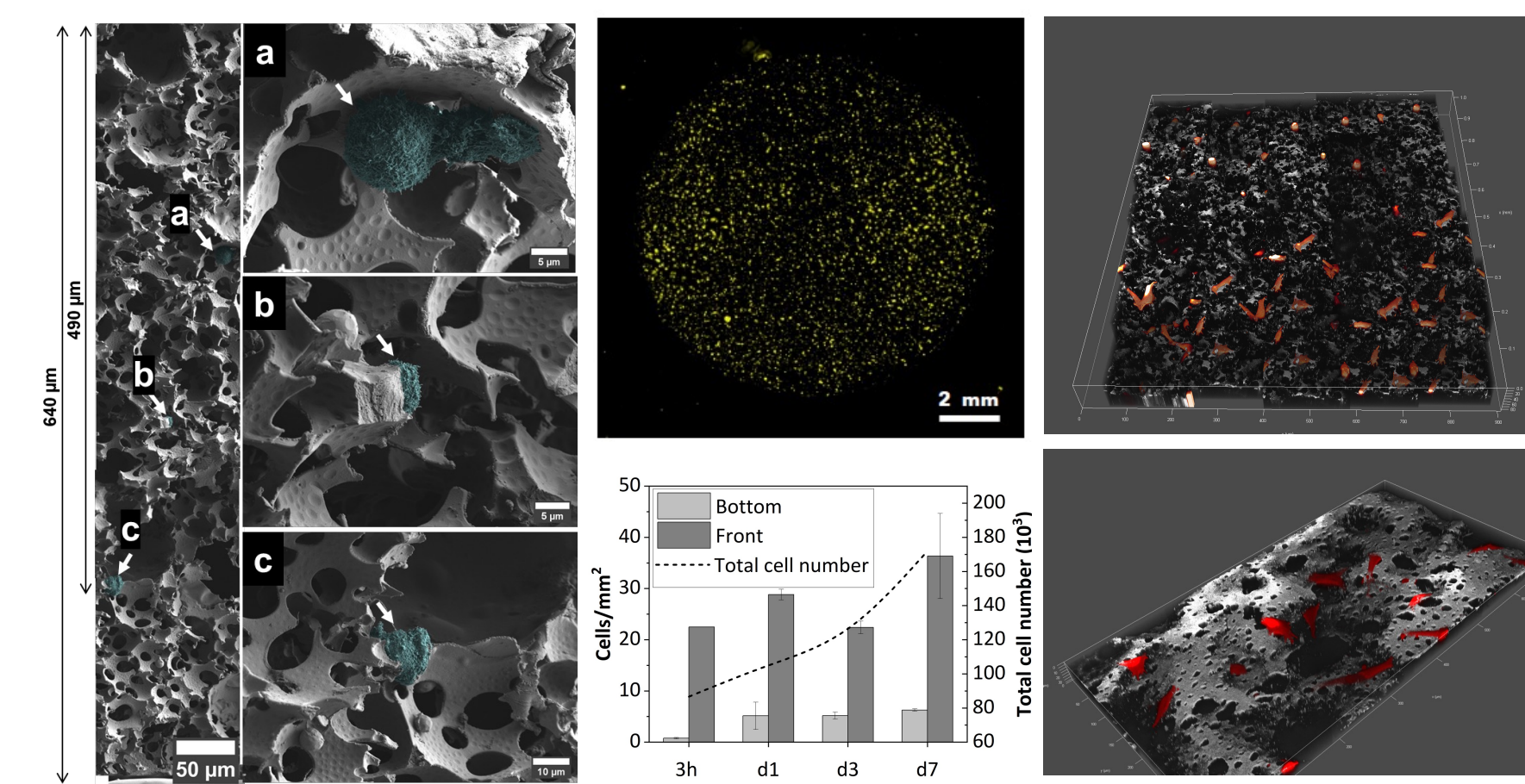
Cytocompatibility

Cytotoxicity via LDH-activity



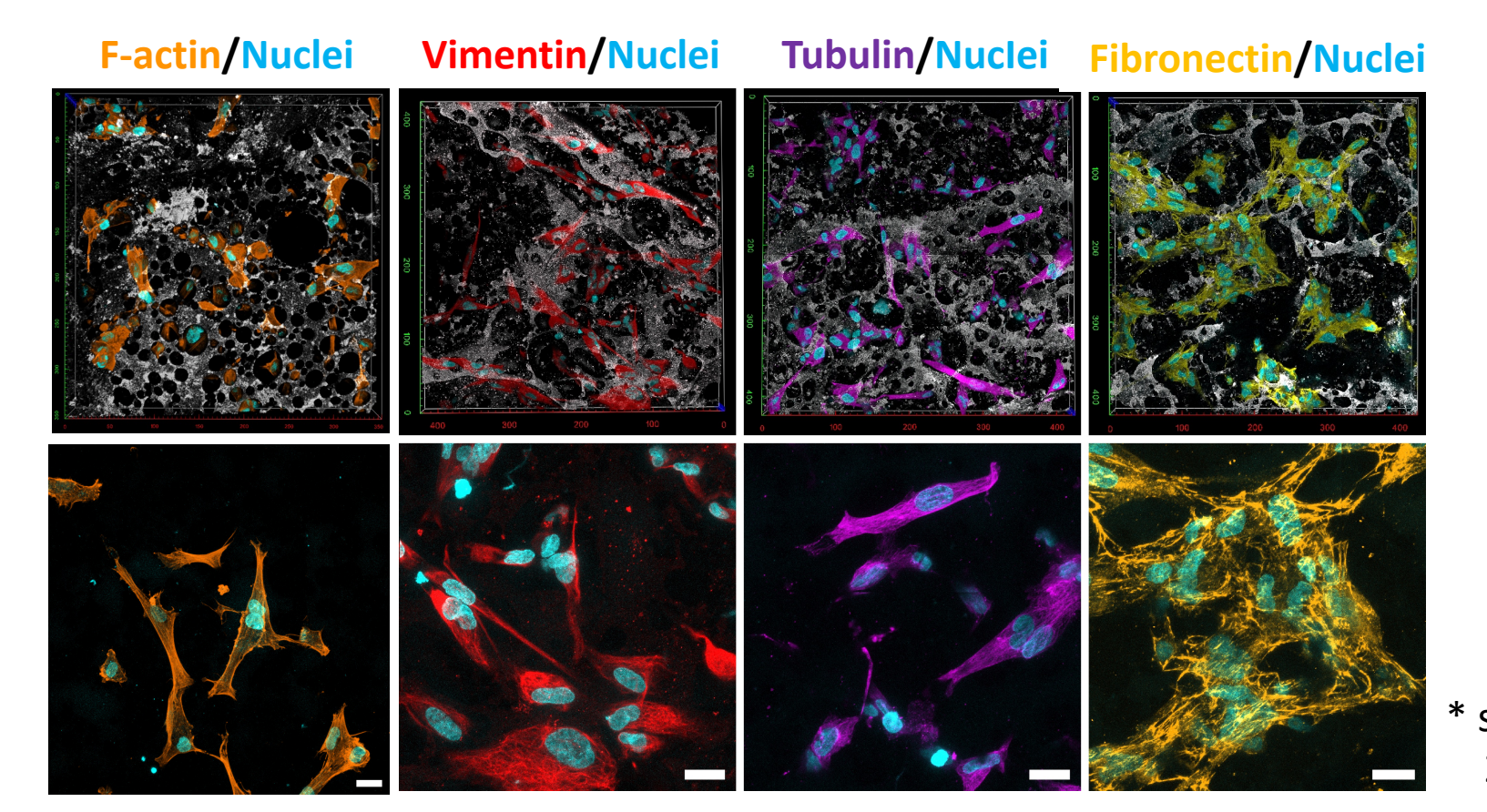
- PolyHIPE-PEDOT scaffolds showed no cytotoxic effect over time for human dermal fibroblasts

Cell colonization



- PolyHIPE-PEDOT scaffolds allow cells to adhere, spread and migrate into the microporous structure

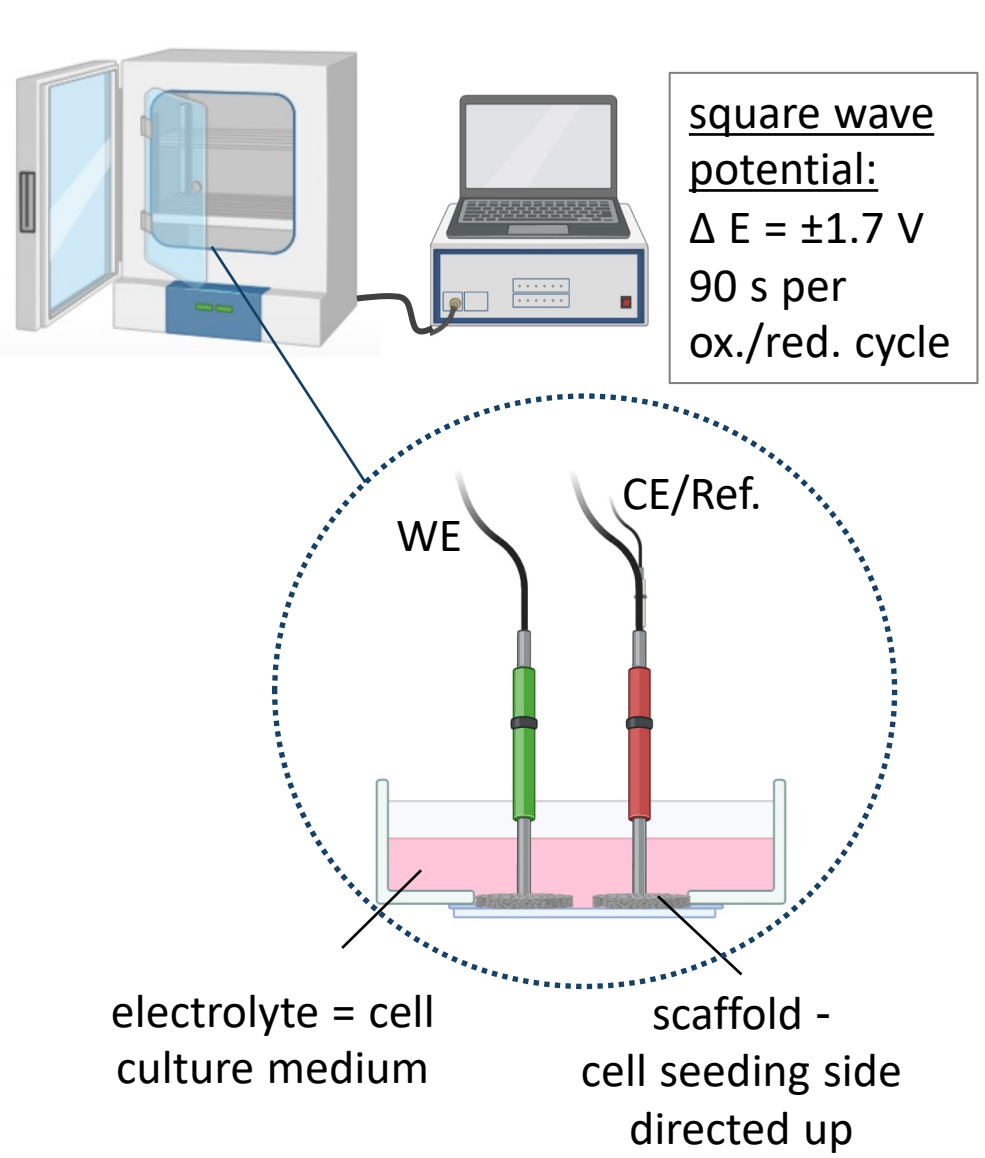
Cell morphology and ECM



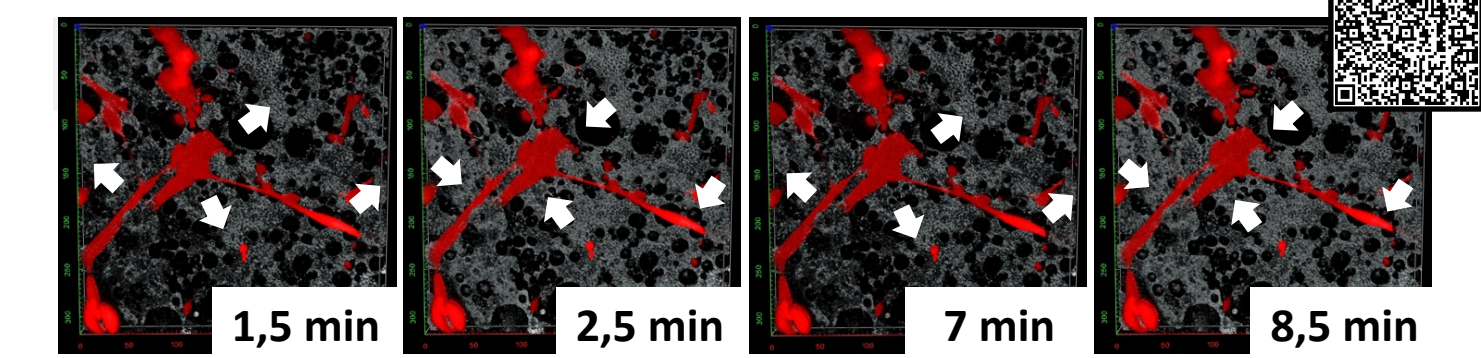
- Fibroblast cells show typical spindle shaped cell morphology on polyHIPE-PEDOT scaffolds and secrete and organize fibronectin

Electromechanical stimulation *in vitro*

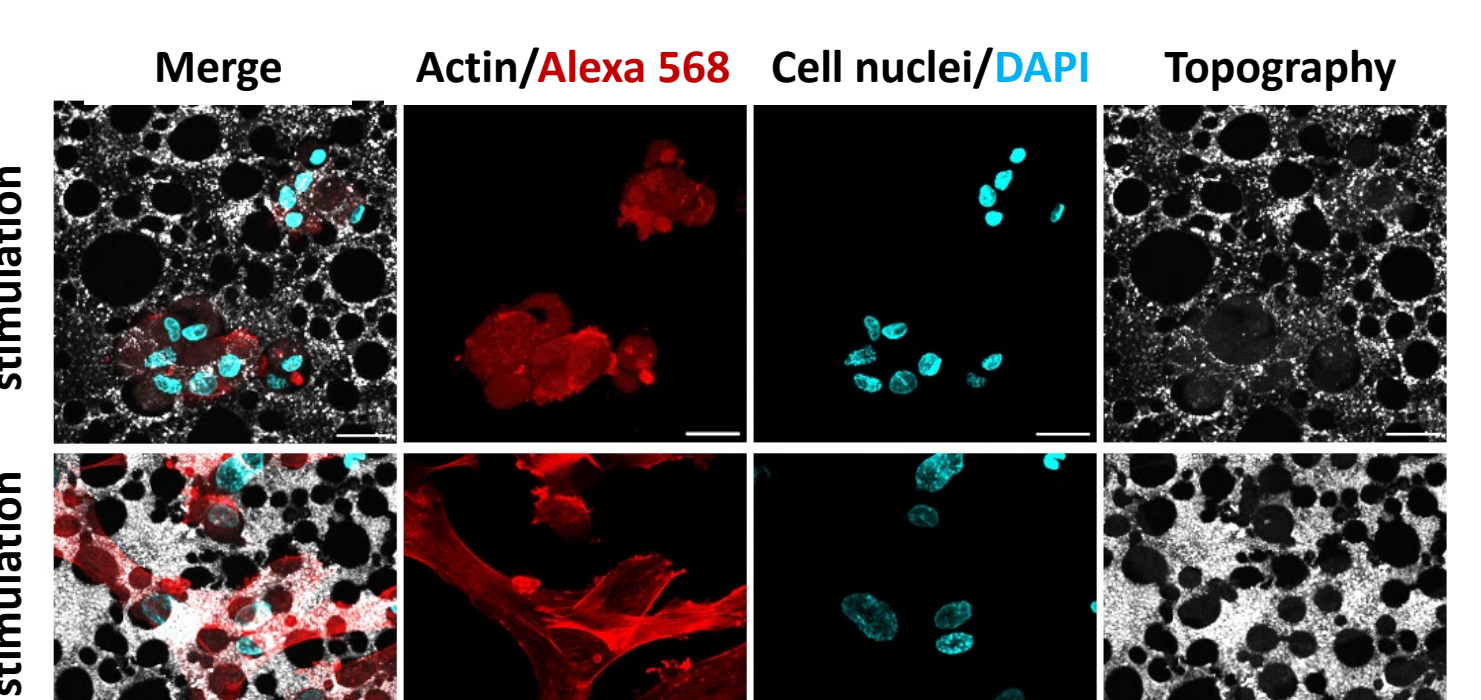
Electromechanical stimulation setup



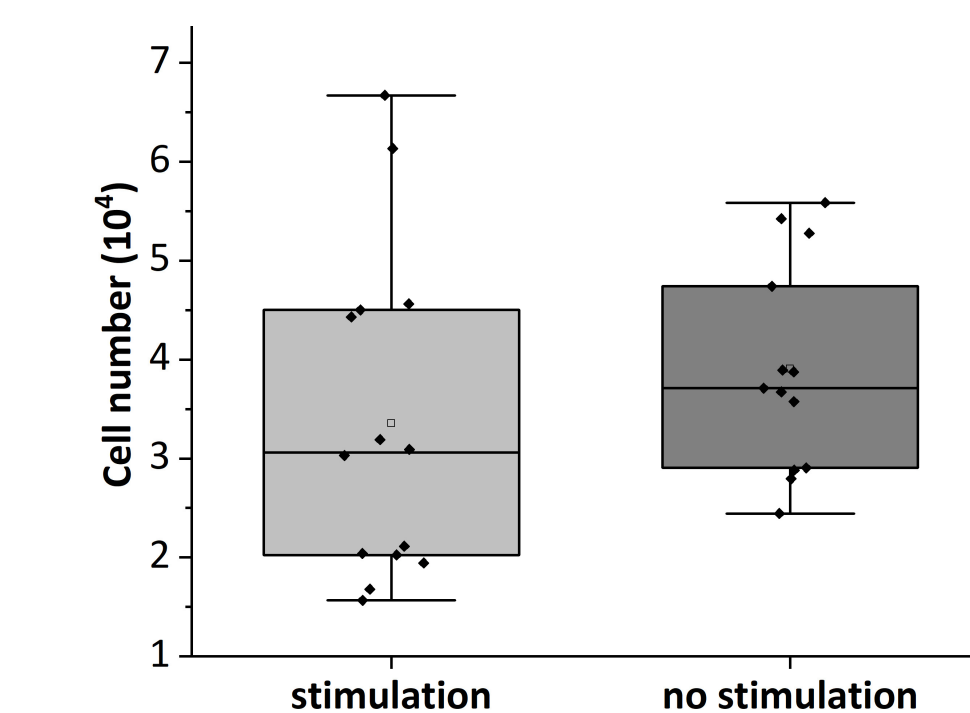
In situ and real-time monitoring



Cell behavior after 5h of electromechanical stimulation



Cytotoxicity after 5h of electromechanical stimulation



- 5h of electromechanical stimulation had no cytotoxic effect on cells
- Stimulated human dermal fibroblasts showed membrane deformation and changes in their morphology

Conclusion

- 4D microporous and electroactive scaffolds were successfully processed by the functionalization of a polyHIPE-scaffold with the conducting polymer PEDOT
- PolyHIPE-PEDOT scaffolds comply with the requirements of cell culture and allow cell adhesion, spreading and migration inside the microporous structure
- Typical 3D cell morphology and ECM production on polyHIPE-PEDOT scaffolds were found
- Electromechanical stimulation setup was designed and implemented for a CLSM and allowed the *in situ* and real-time monitoring of cells during stimulation
- 5h of electromechanical stimulation had no cytotoxic effect on human dermal fibroblasts
- Electromechanical stimulation leads to changed cell phenotype of human dermal fibroblasts, which remains to be explored

References

A. Ferrández-Montero, B. Carlier, R. Agniel, J. Leroy-Dudal, C. Vancaeyzele and C. Plesse, 4D smart porous scaffolds based on the polyHIPE architecture and electroactive PEDOT, *J. Mater. Chem. C*, 2021, 9, 12388-12398

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