Microfabrication of a Device for Measurement of Tissue Contractile Forces in High Throughput Screening (HTS)

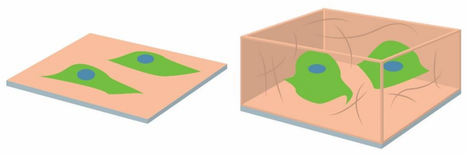
S. Dubois, L.Zhao, C. Moraes

Introduction

The cost of drug screening has grown exponentially, as only small percentages of potential hits lead to clinically effective products. Emphasis **in High Throughput Screening (HTS)** has shifted from **increases in capacity to improvements in quality**.

This suggests a need for **more realistic (3-dimentional) HTS-compatible microenvironment** to improve the screening process.

2D vs 3D Cell Cultures	
Flat morphology Monolayer Rigid Surface	Structurally complex Physiologically realistic Diffusion limited



Representation of a traditional 2D cell culture (left) versus 3D (right)

Objective

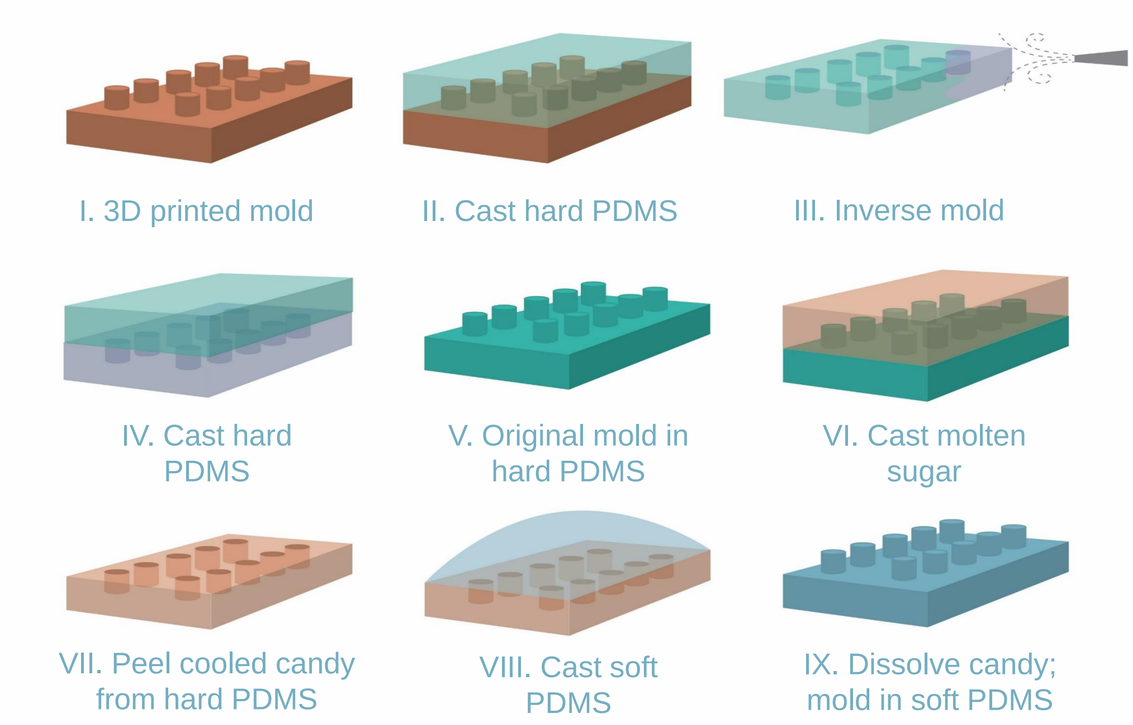
Fabricate a 3-dimensional tissue arrays with interact in **mechanically and physiologically realistic culture systems.**

Characterize microtissue mechanics through mechanical analysis.

Evaluate the **relevance** of microenvironmental parameters on the design of drug discovery.

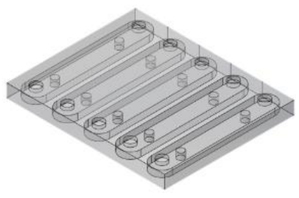
Methodology

Super-soft lithography will be used to fabricate the device from soft **polydimethylsiloxane (PDMS).** The device is a close-faced device to reduce microtissue failure, or slipping from the pillars.



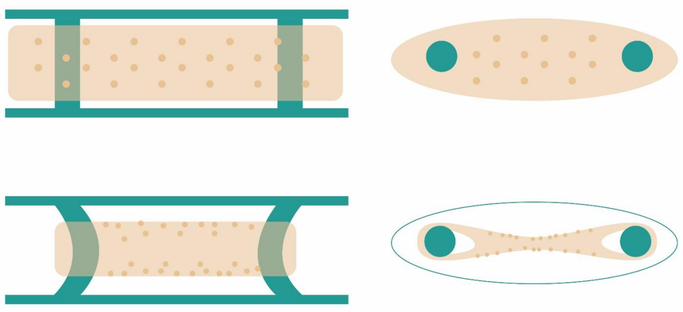
The microfluidic device encloses the fluid, cells and tissues make it easily compatible with HTS, allowing for segregation of each sample for drug testing.

Final closed-face design

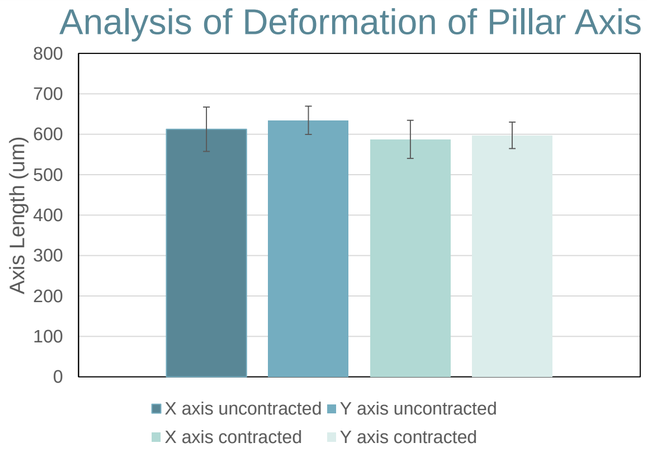


Results

Hypothesized Contraction of Gel

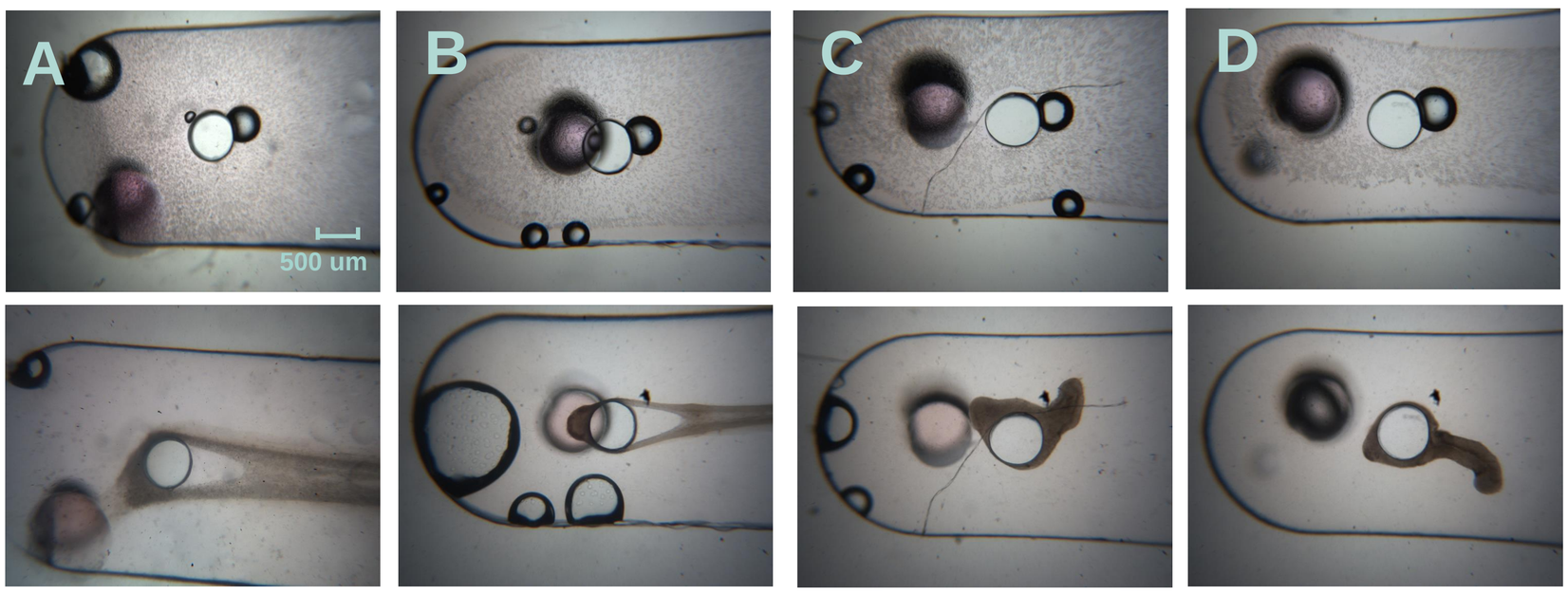


Analysis of Deformation of Pillar Axis



Successful Microtissue

Microtissue Failure



Through image analysis of the contracted and there uncontracted states (A,B,C,D) it was shown that **no significant pillar deformation occurred**.

Microtissue formation occurred successful and **as predicted** (A,B) within 48 of gelllation. **Microtissue failure** also occurred (C,D). The rate of failure suggests a need for a more flexible pillar design.

Conclusion

Supersoft lithography was **successfully** incorporated in the microfabrication of the device. The data collected shows **no significant deflection** of the pillars, nor was any significant deformation of the pillar measured. This suggests a need for a **change in design** to more flexible pillars, however proof of concept was shown through the microtissue formation.

Future Work

Pillar Dimensions
- Increased length or decreased diameter will allow for greater deflection
- Increase distance of injection site to reduce interaction

Mechanical Stretching
- Mount on a cyclic stretching platform
- Characterize the general rigidity of tissue as well as contractile force

Comparative testing
- Test against traditional 2D culture
- Evaluate relevance of microenvironment

References

[1] Legant W, et al. *Proc. Natl. Acad. Sci.* (2009)
[2] Moraes C, et al. *Lab on a Chip* (2015)
[3] Adams & Branter, *Health Econ* (2010)
[4] Zhao, et al. *Adv. Mater.* (2013)
[5] Moraes C, et al. *Ann. Biomed. Eng.* (2012)

Acknowledgements

Moraes Lab Group
Thank you to Selina Liu for 3D printing.

NSERC CRSNG

McGill