Analyzing Bubble Traps in Organ-on-a-Chip Systems to Improve Efficiency and Reproducibility for Drug Screening

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Abstract

Organs-on-Chips (OoCs), miniature organ systems modeled on microfluidic devices, are used to emulate real tissue and cell environments, allowing for the study of human physiology without the use of live animals or human subjects (1). Currently, a significant concern in OoC systems is the presence of inevitable bubble formation that obstructs flow and increases variability in data collection. To reduce variability, bubble traps can be implemented into the OoCs to capture or divert large bubbles that affect the flow of the media, and therefore, cell interactions (2). *It was hypothesized that the use of lower-pressure channels and a double row of pillars can significantly reduce bubbles throughout the cell flow channels of OoC systems,* offering valuable insights into alternative strategies for bubble mitigation. Using fluid mechanics principles and bubble-trapping architecture, engineered bubble traps diffuse smaller bubbles and block larger bubbles from disrupting the cell's environment. These designs could improve reproducibility in high-throughput testing, allowing OoC systems to have a quicker turnaround in the clinical phase, accelerating drug research and the study of human systems.

Background

- OoCs consist of various polymers, microfluidic channels lined with cells, and membranes to simulate the flow and tissue environment of real organ systems. They are made of multiple layers, varying in thickness and material (1).
- There have been various forms of bubble traps produced: vacuum-based systems utilizing hydrophobic membranes, physical barriers designed to divert gas while allowing liquid to pass, and centrifugal or buoyancy-based devices that separate bubbles through density differences (3). Although, these approaches have design limitations due to the complexity of bubble behavior in fluids. These approaches highlight the ongoing efforts to improve flow consistency and data reliability in OoC systems.

Experimental Methods

Design 1

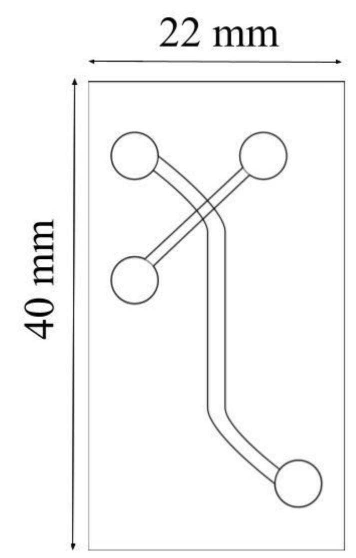
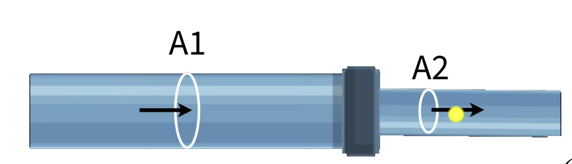


Figure 1: Flow channel layer with high/low pressure trap

$$P_1 + \frac{1}{2}\rho v_1^2 + \rho g h_1 = P_2 + \frac{1}{2}\rho v_2^2 + \rho g h_2$$

$$p_1 - p_2 = \frac{\rho}{2}(v_2^2 - v_1^2)$$

- Secondary channel was implemented
- Bernoulli's principle was used as the basis of creating a lower-pressure liquid
- Venturi equation was used to calculate the pressure difference



(4)

- Without blocking flow, two pillars with a 1.12 mm diameter obstruct large bubbles from traveling into the cell flow channel.
- Due to adhesion, hydrophobicity, and low surface energy, large bubble bind to the PMMA (polymethyl methacrylate) pillars (3).
- External bubble trap interfaces with the tubing and luer lock.
- As flow enters the trap, bubbles ascend to the top of the structure.

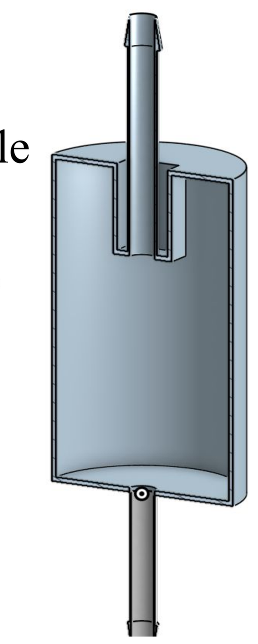


Figure 2: Cross section of tube bubble trap

Design 2

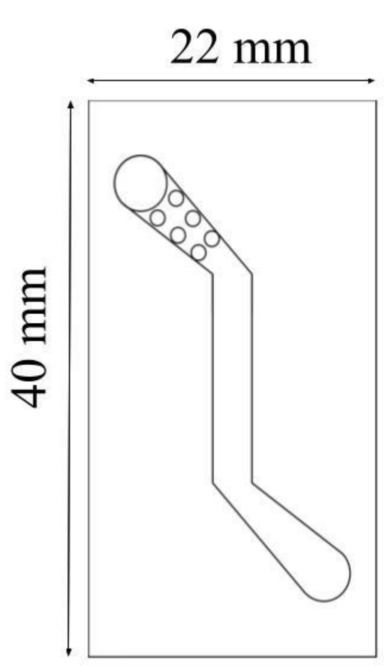
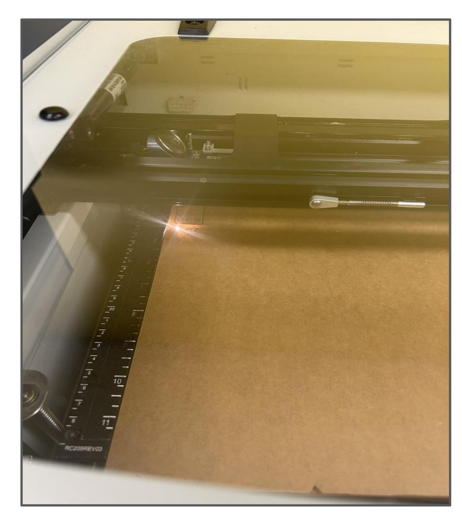
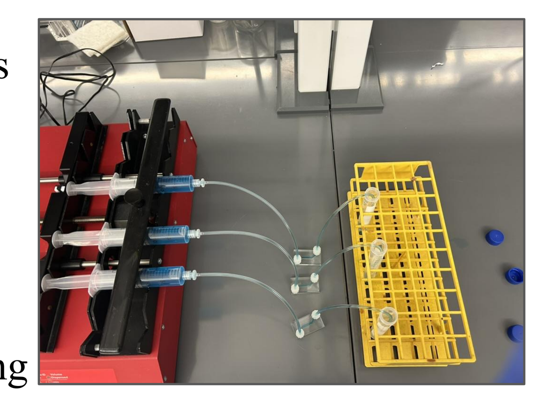


Figure 3: Flow channel layer with pillar trap

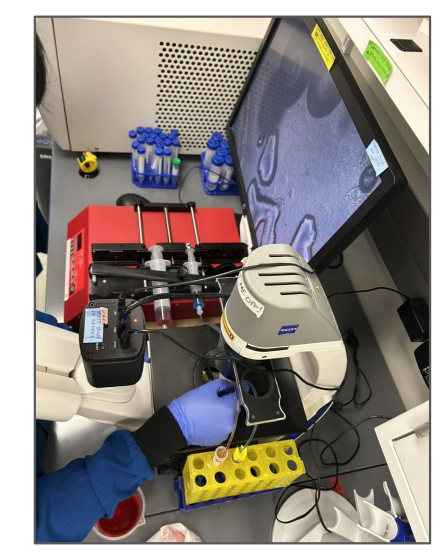
Design and Print → **Run Flow** → **Collect Data**



- Designed layers using Adobe Illustrator
- Printed using Epilogue Zing Laser Cutter
- Assembled using tape layers and heat press



- Pumped dyed water at 2 mL/min using a syringe pump



- Analyzed using inverted microscope
- Collected bubble area and count
- Design 2: collected 1 min intervals 3 times at tubing, pillar area, and cell channel
- Design 1: collected at overlap of channels and cell channel for 10 minutes

Results

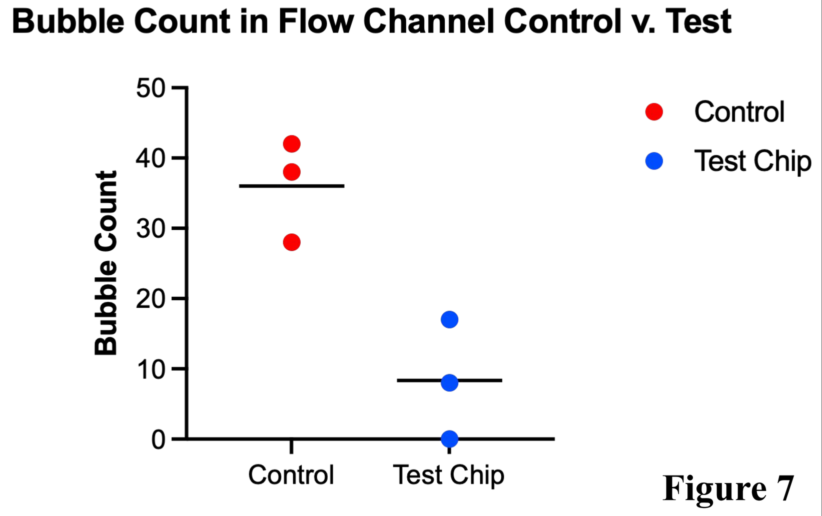


Figure 7

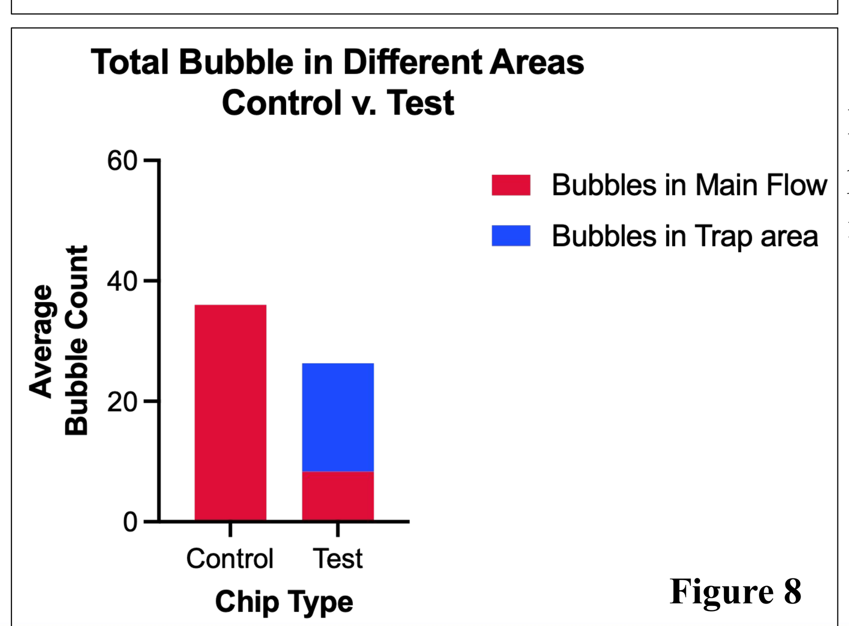


Figure 8

Design 1

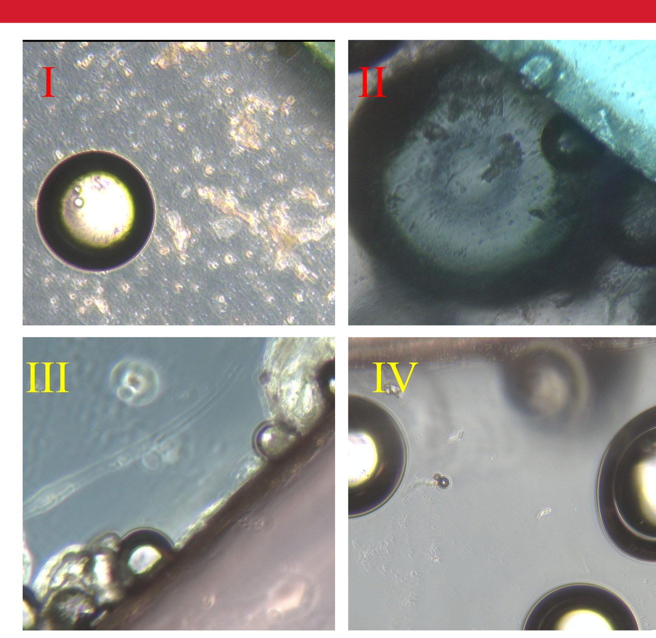


Figure 5: Cross section micrograph of high/low pressure channels (I, II) and micrograph of flow channel in control design (III, IV)

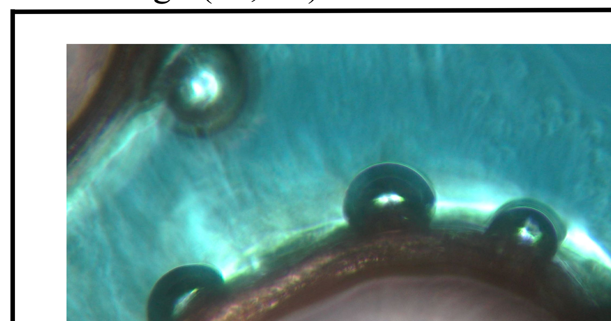


Figure 6: Micrograph of bubbles attached to pillars

Design 2

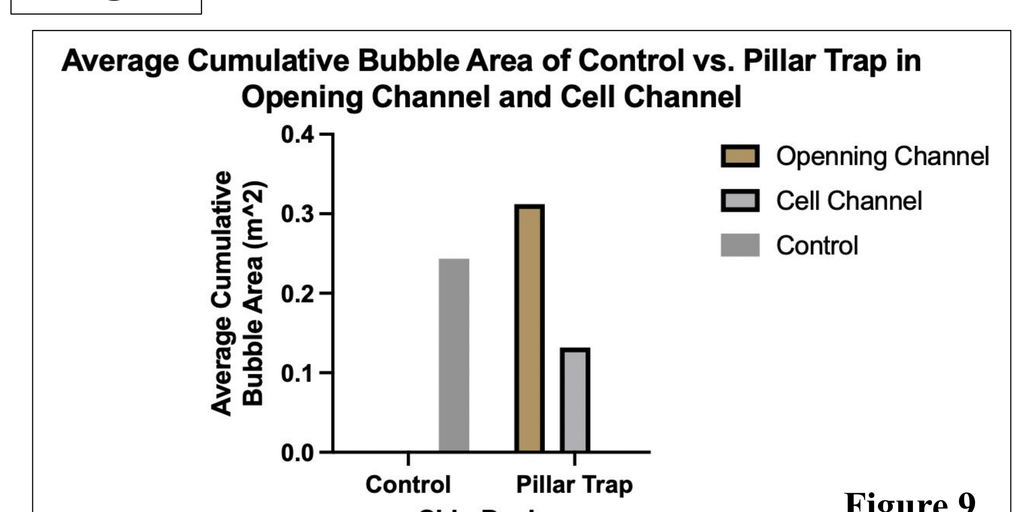


Figure 9

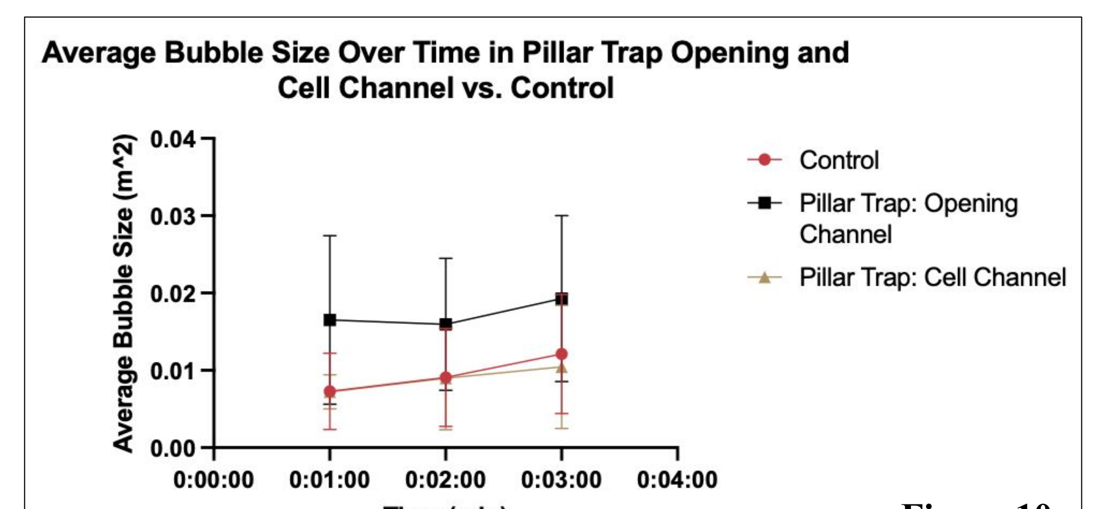
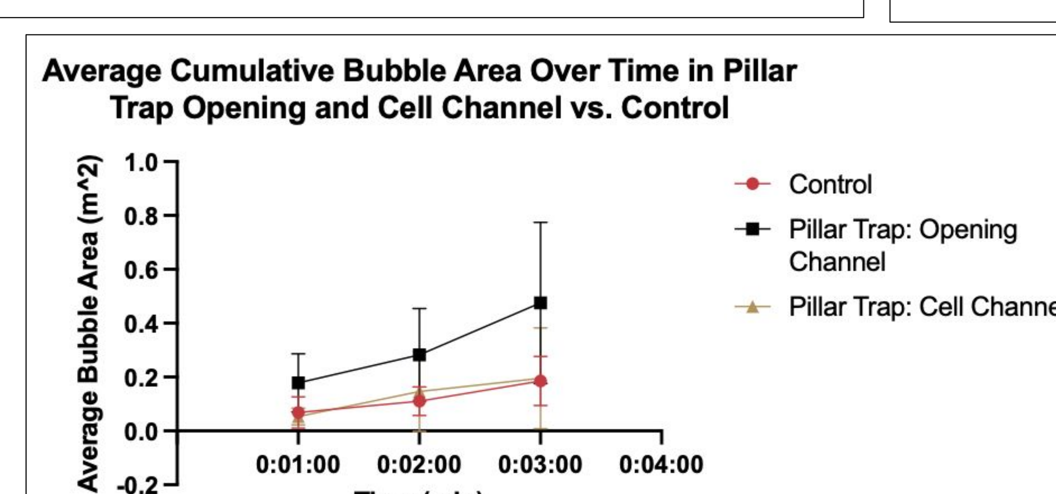


Figure 10



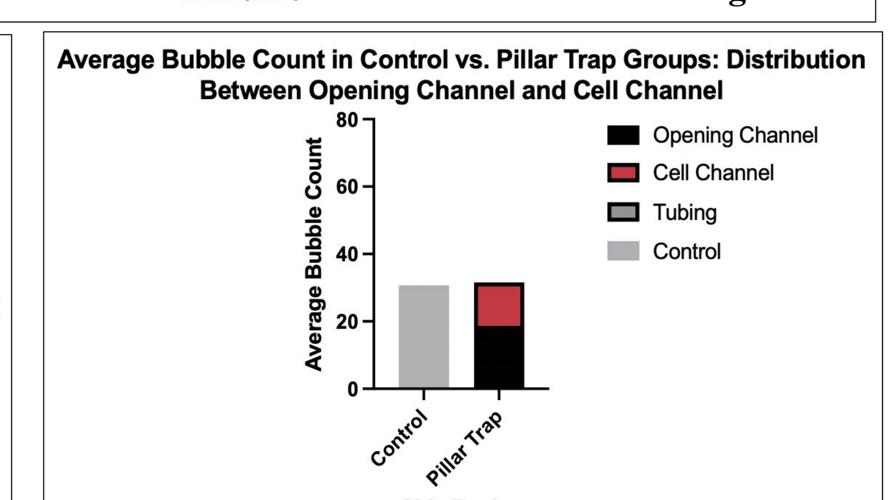


Figure 12

Conclusion and Future Steps

Design 1

- High/low pressure chips had significantly lower average bubble count in the main channel (8.33) than the control chip (36.0) (**Fig. 8**).
- Individual trials with the test chip showed decreased bubbles in the main channels (**Fig. 7**).

Design 2:

- Pillar chip opening channel (OC) had a significantly larger average total area (0.312 m^2) than cell channel (CC) (0.132 m^2) and control (0.243 m^2) (**Fig. 9**)
- Pillar trap OC had a higher average bubble count (18.7) than CC (12.9) (**Fig. 12**)

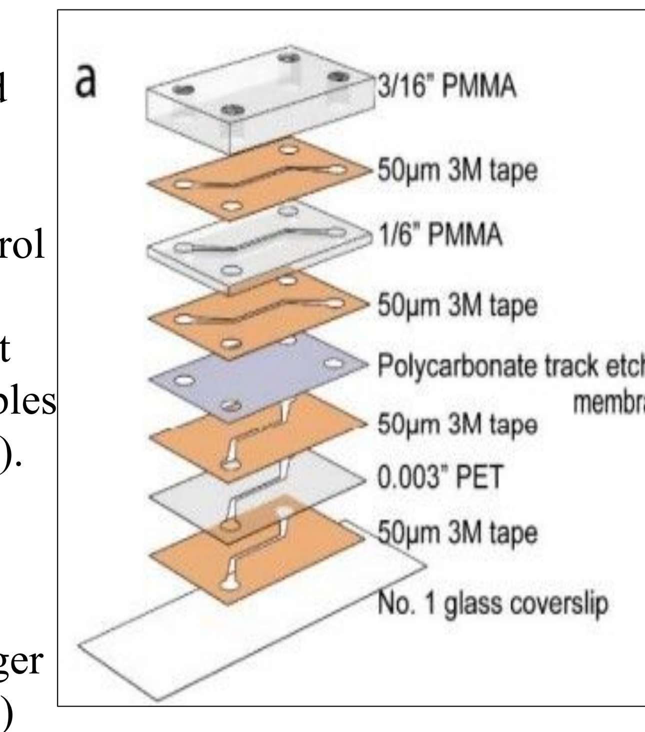


Figure 4: Exploded view of OoC

Future Steps:
Future steps include collecting additional data on bubble formation and passage in the chips to evaluate bubble trap efficiency, using cells, and integrating a double flow channel setup.

References

1. Leung, C. M., de Haan, P., Ronaldson-Bouchard, K., Kim, G.-A., Ko, J., Rho, H. S., Chen, Z., Habibovic, P., Jeon, N. L., Takayama, S., Shuler, M. L., Vunjak-Novakovic, G., Frey, O., Verpoorte, E., & Toh, Y.-C. (2022). A guide to the organ-on-a-chip. Nature Reviews Methods Primers, 2(1). https://doi.org/10.1038/s43586-022-00118-6
2. Gao, Y., Wu, M., Lin, Y., & Xu, J. (2020). Trapping and control of bubbles in various microfluidic applications. Lab on a Chip, 20(24), 4512–4527. https://doi.org/10.1039/d0lc00906g
3. (2019, September 25). *Bubbles in Microfluidics: How They Form and How to Avoid Them*. The MicroFluidic Circle. https://www.ufluidix.com/circle/bubbles-in-microfluidics-how-they-form-and-how-to-avoid-them/
4. Khan Academy. (2023). Khanacademy.org. https://www.khanacademy.org/science/ap-college-physics-1/xf557a762645cccc5:fluids/xf557a762645cccc5:fluid-flow/v/fluid-flow

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