

# Bioreactor Cassette for Stem Cell Culture

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BME 400  
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## **Client**

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# Overview

- Background
  - Stem Cell Culture
  - Bioreactor System
  - Current Solutions/Competition
- Design Proposal and Specifications
- Current Status
- Cell Testing
- Future Work
- Acknowledgments

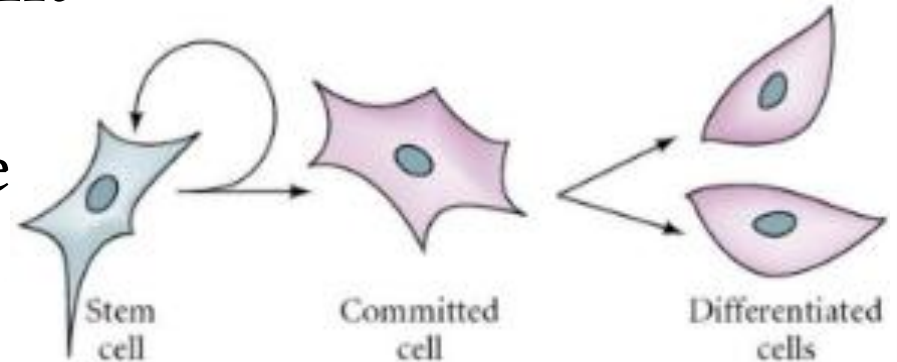
# Problems with Stem Cell Culture

- Sensitive to environment

- Daily media change
- Chemical leaching can cause undesired differentiation

- Clinical limitations

- Desire individualized therapies
- Mass production is not yet feasible



*Pluripotent stem cell* <sup>[1]</sup>

# Current Solutions



Static culture<sup>[2]</sup>



CLINICell Cassette<sup>[3]</sup>

[2] Corning (2010). "Corning® Ultra-Low Attachment 75cm<sup>2</sup> Rectangular Canted Neck Cell Culture Flask with Vent Cap (Product #3814)" *Corning: Life Sciences*. <http://catalog2.corning.com/>

[3] Innomeditch Technologies. "CLINICell Cassette". *Innomeditch Technologies*. [http://www.innomt.com/products/products02\\_02\\_04.htm](http://www.innomt.com/products/products02_02_04.htm)

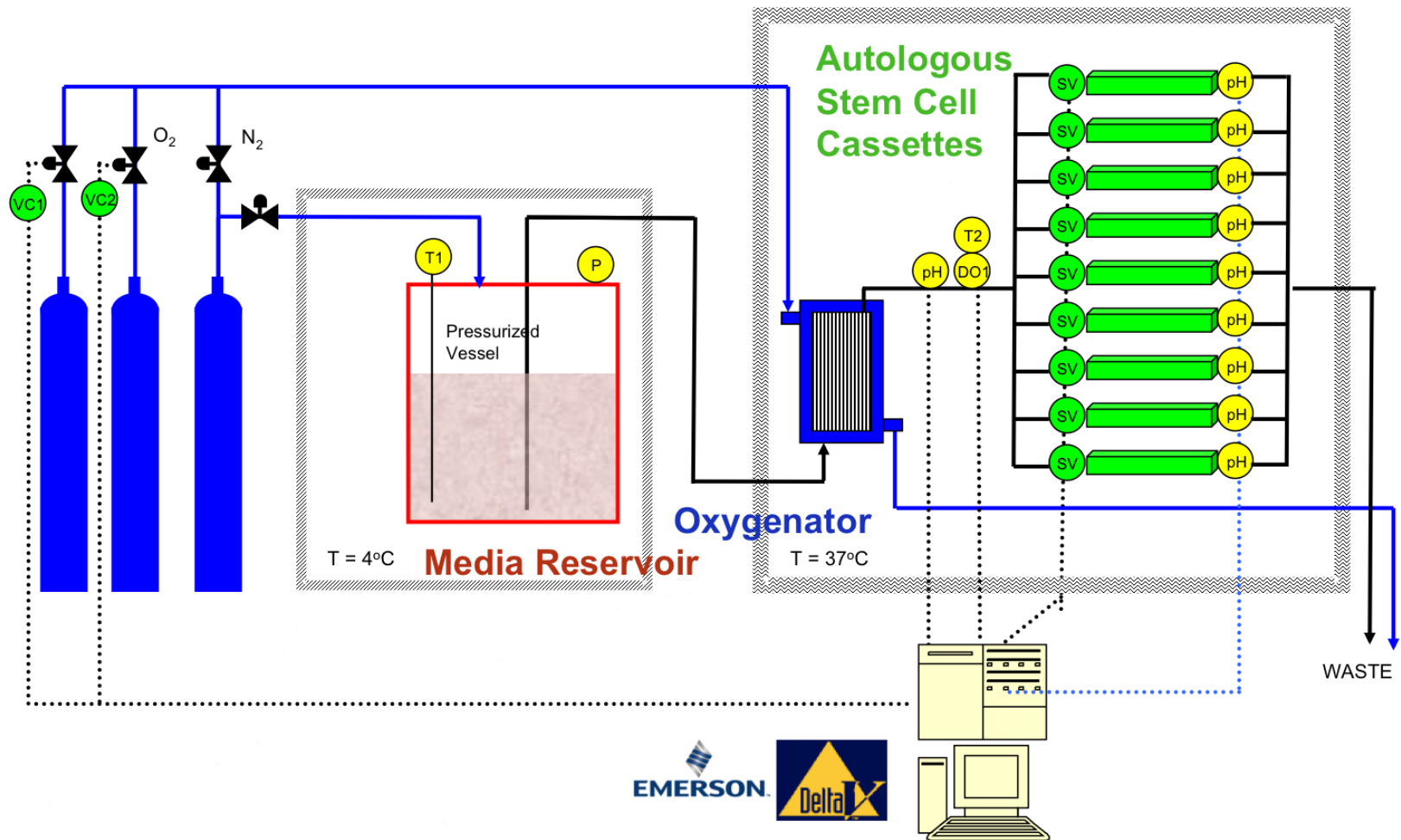
# Design Proposal

Design a cassette system that interfaces with a perfusion bioreactor and provides appropriate conditions to culture several different samples of iPS cells without exchanging media between them.

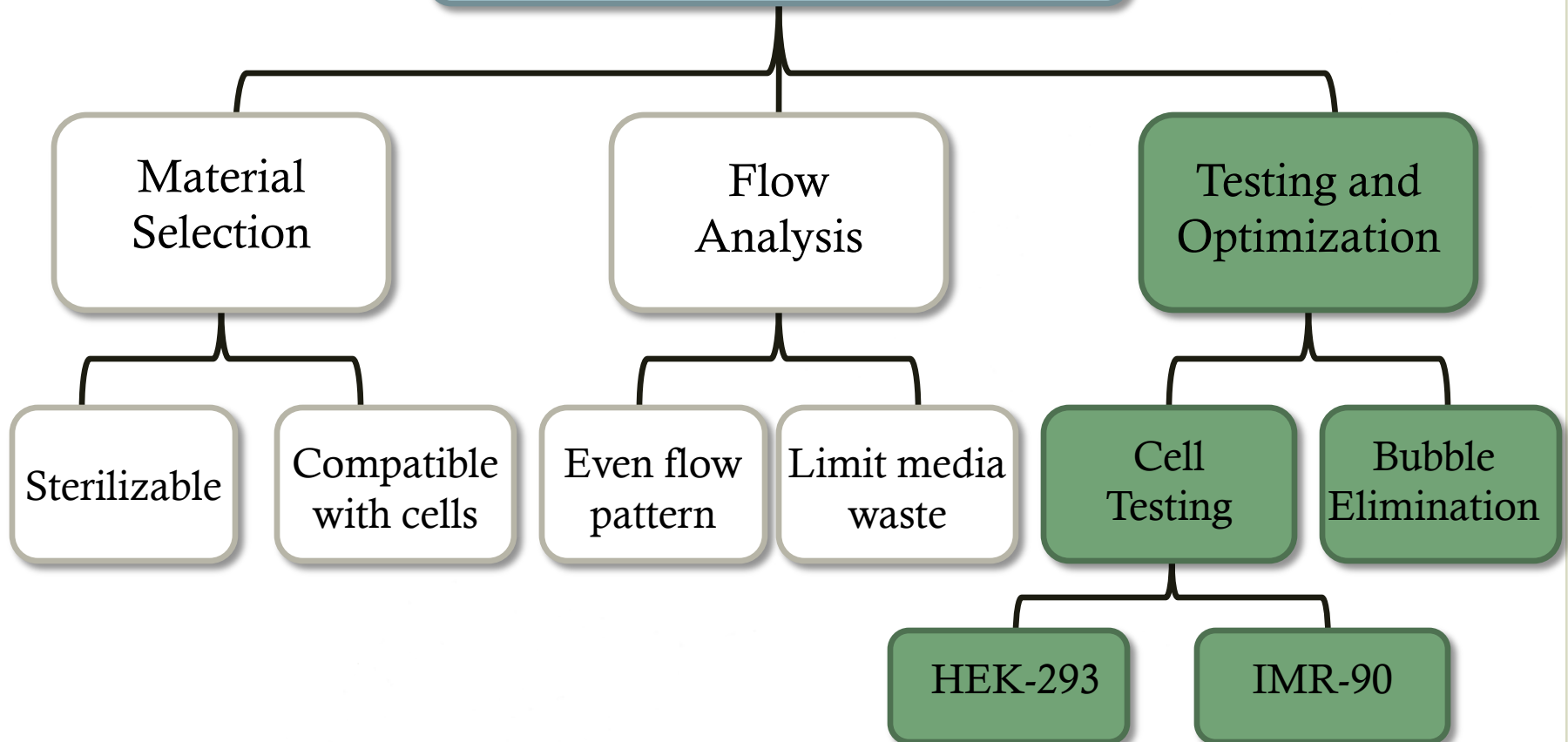
## Specifications

- Use gas-impermeable growth plates
- Be optically transparent
- Allow metabolic monitoring
- Avoid chemical leaching
- Minimize media use

# Bioreactor System<sup>[4]</sup>

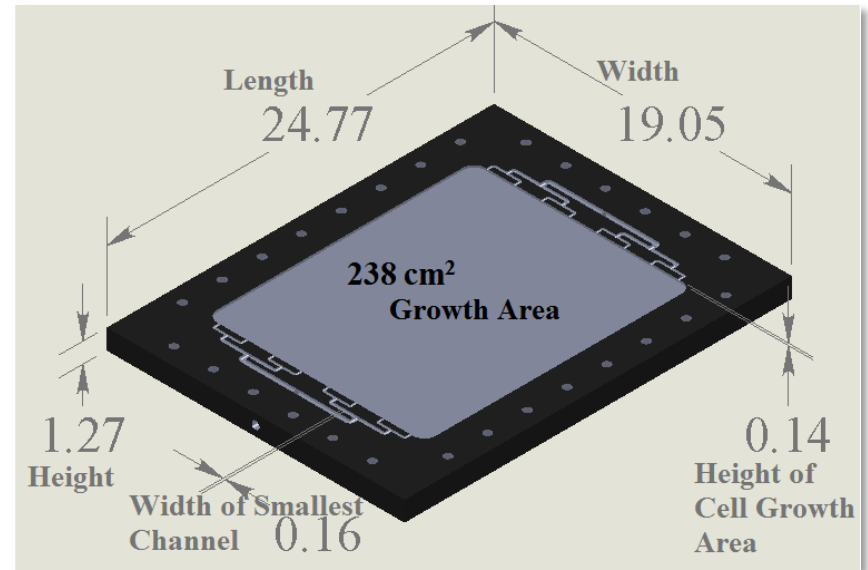
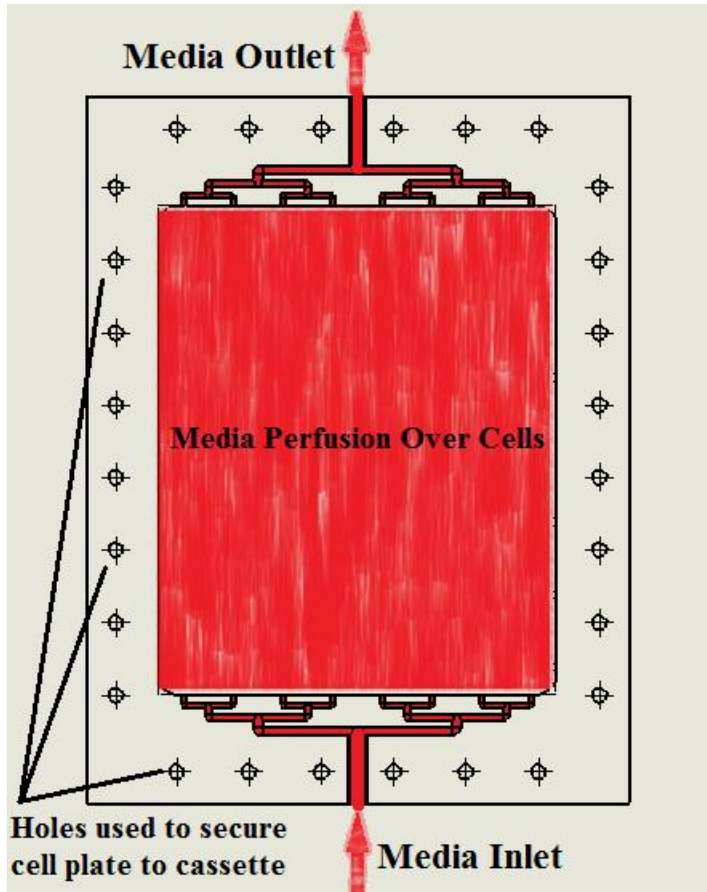


# Bioreactor Cassette



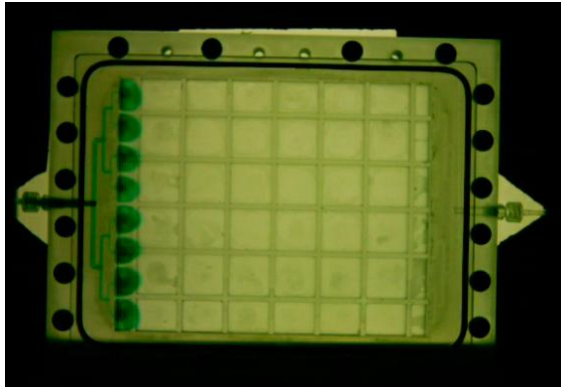


# Project Status: Cassette Design

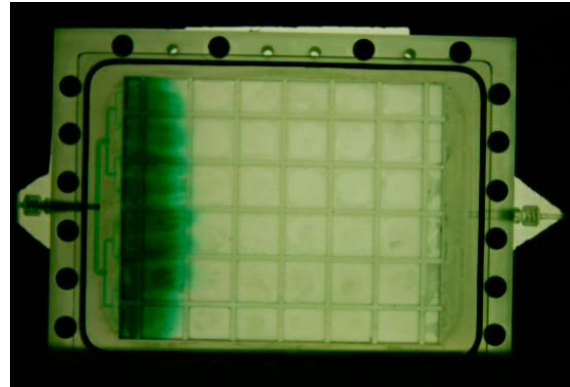


Dimensions in cm

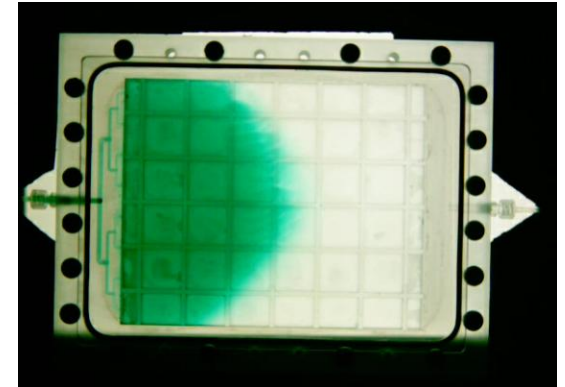
# Project Status: Dye Studies



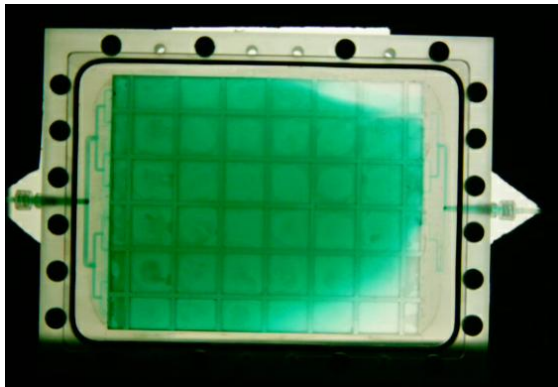
20 min



1 hour



4 hours



8 hours



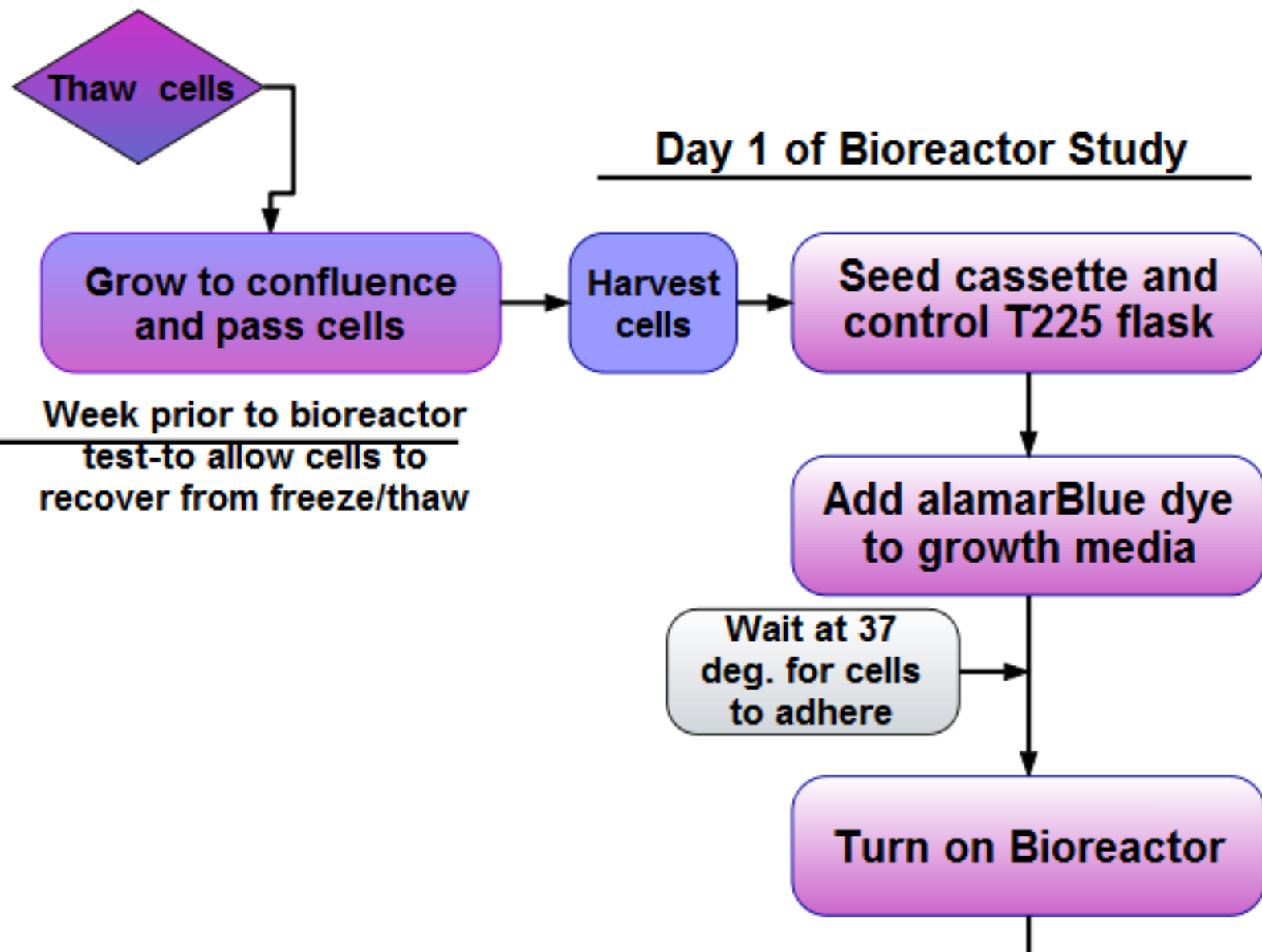
10 hours

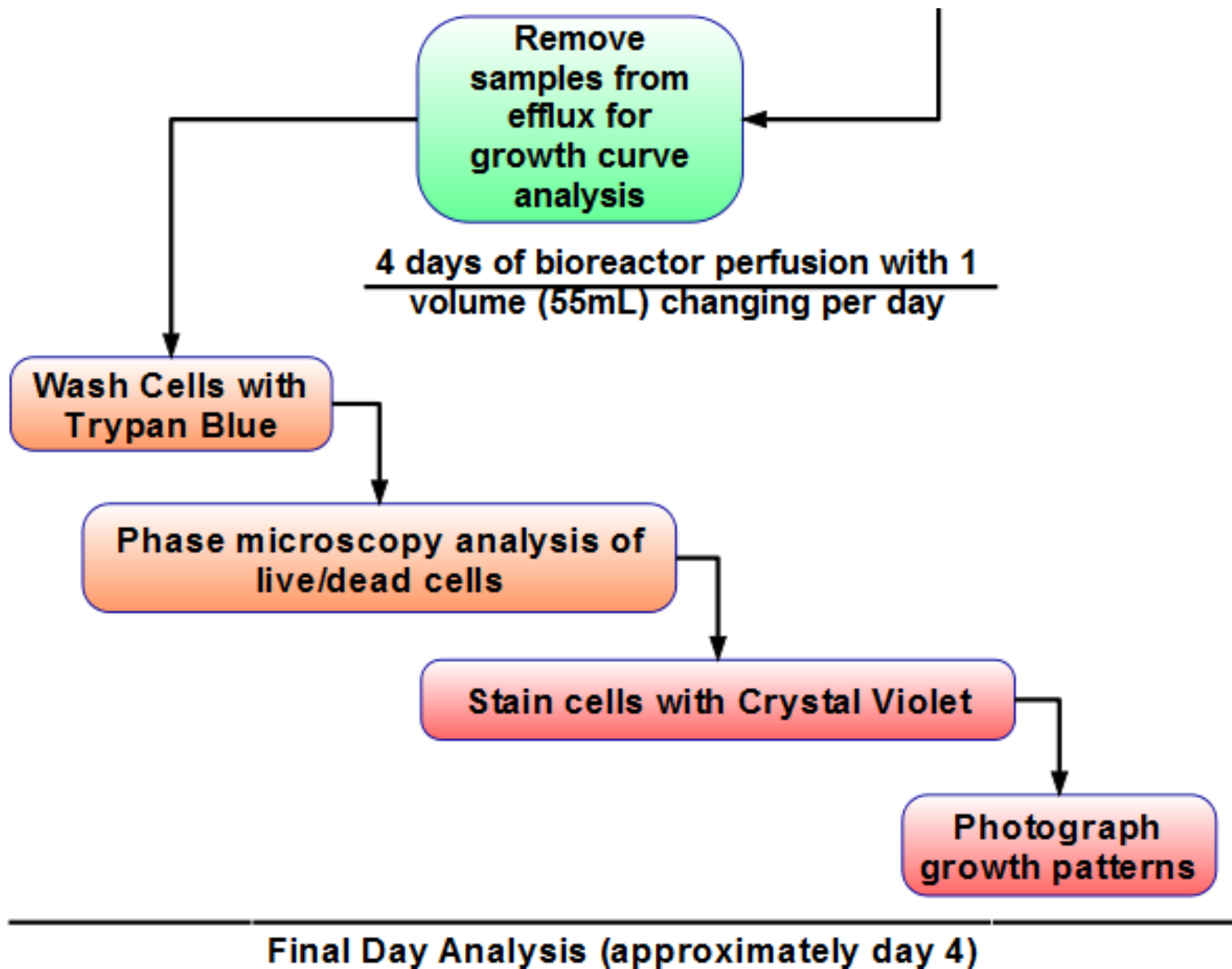


24 hours

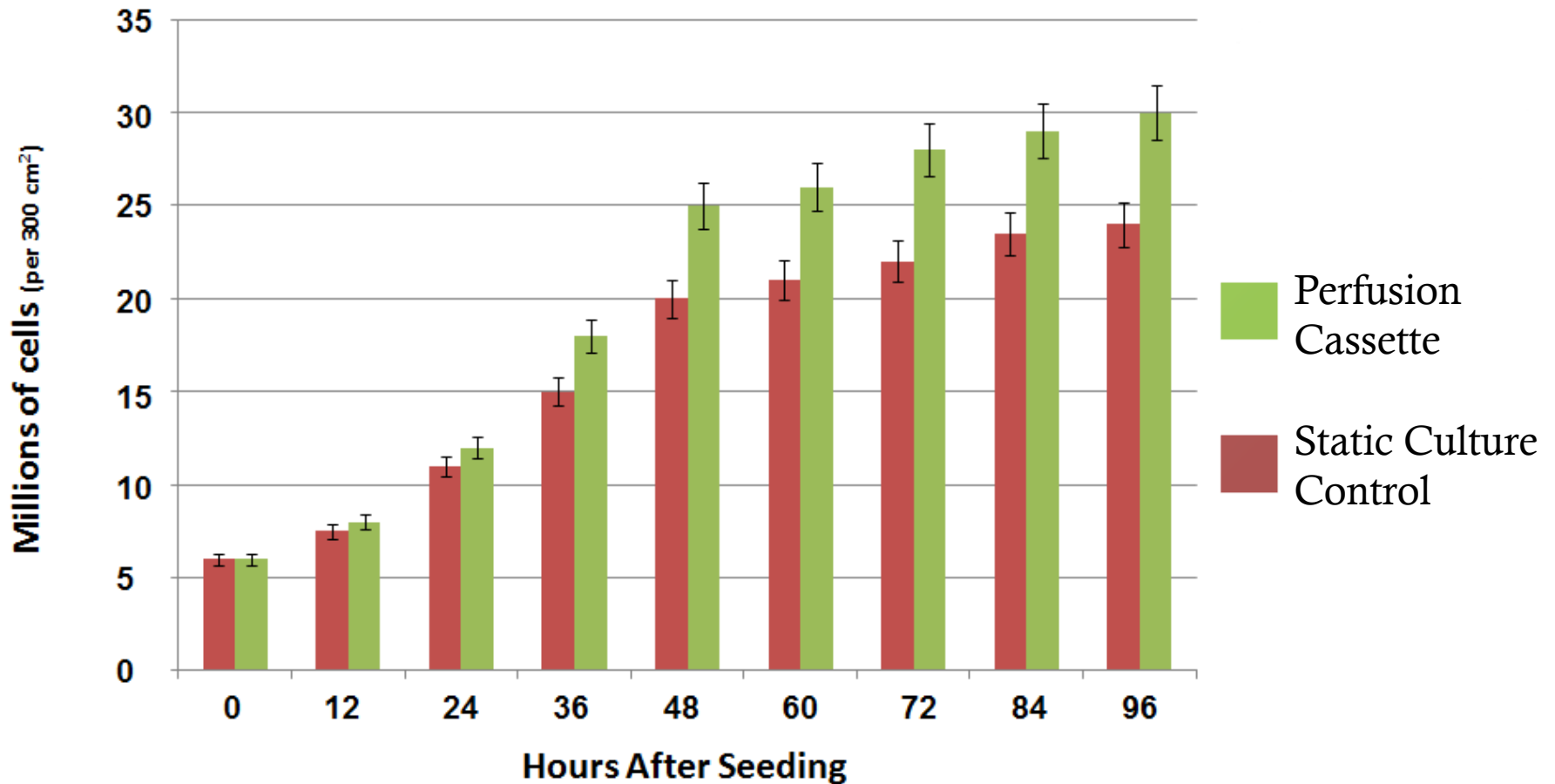
# Cell Testing

- HEK-293: Human embryonic kidney cells
  - Differentiated cells
  - **Test:** General cell viability and growth, spatial variations
- IMR-90: iPS cell line
  - Undifferentiated
  - **Test:** Ability to maintain cells in undifferentiated state



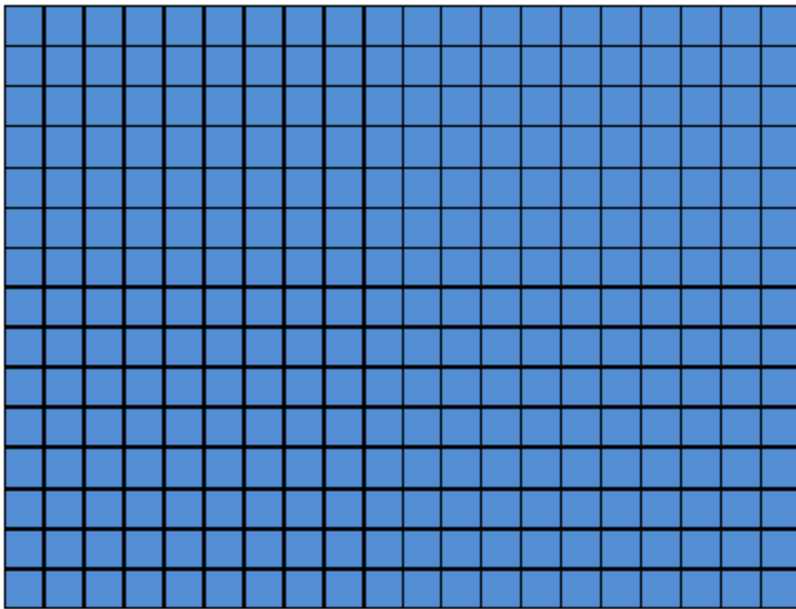


# Expected Results: Proliferation Dye Study

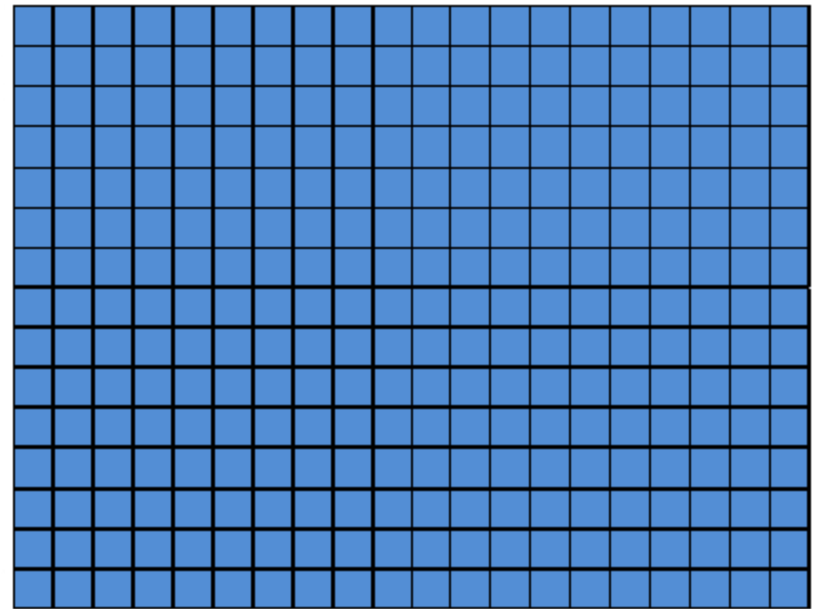


# Expected Results: Crystal Violet Stain

- Evaluation of seeding uniformity
- Compare crystal violet stain in 1 cm<sup>2</sup> sections at Day 4
- Analyze with chi squared test
- Expect no statistical difference between control and perfusion cassette



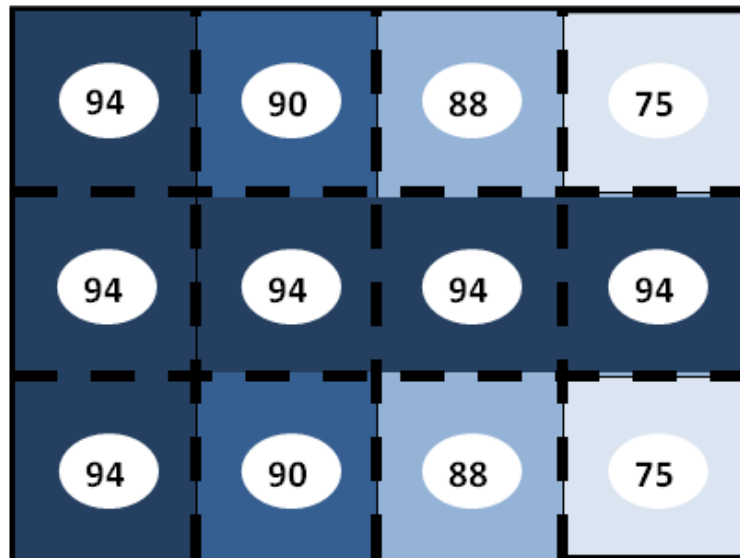
Perfusion Cassette



Static Culture

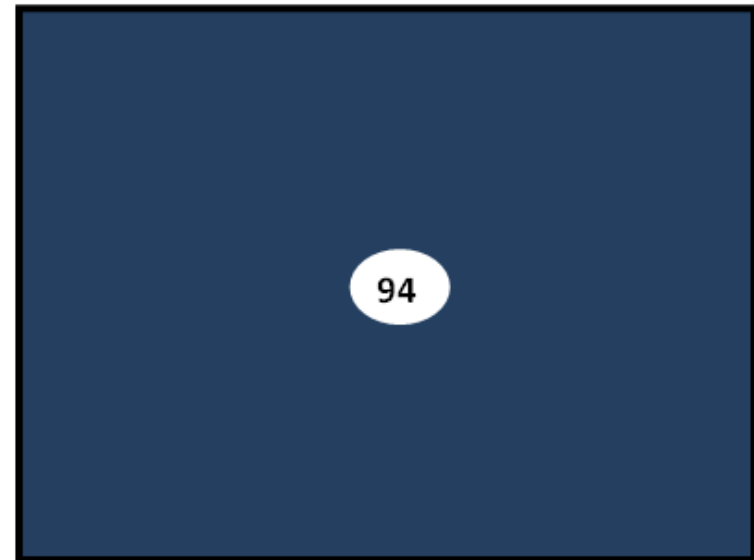
# Expected Results: Trypan Blue Viability Stain

- Evaluation of viability with respect to location
- Compare viability between zones and systems at Day 4
- Analyze with unpaired, independent Student t-test
- Expect viability differences between zones and systems



Perfusion Cassette,  
Percent Live Cells

n=3



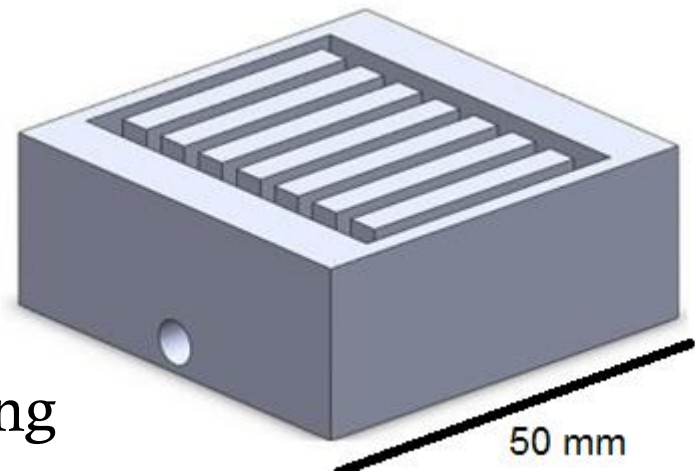
Static Culture,  
Percent Live Cells

n=3



# Future Work

- Testing with IMR-90 cells
- Bubble regulation
  - External bubble trap
  - Modify design
- Testing with efflux pH monitoring



Possible external bubble trap

# Acknowledgements

- Dr. Hei, Bill Kreamer, Diana Drier
- Kyle Ripple, Carol Elmer
- Dr. Mackie, Dr. Hancock
- Sheku Kamara, Vince Anewenter

Questions?