Bioreactor Cassette for Autologous Induced Pluripotent Stem Cells

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Client

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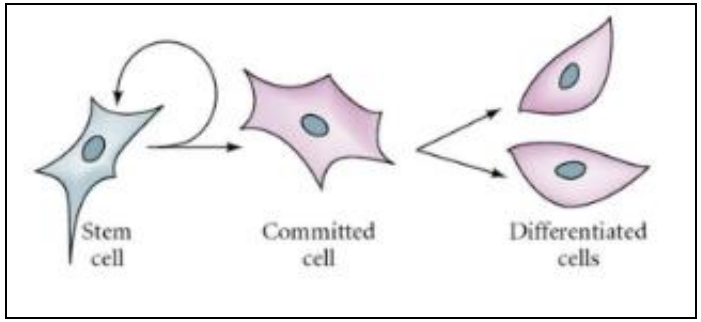
Overview

- Background
- Design Proposal
- Client Specifications
- Design Concept
- Prototype Possibilities
- Future Work
- Acknowledgments, References

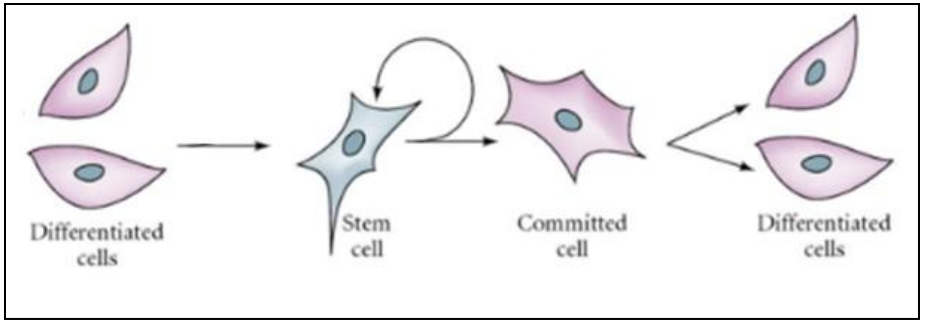
Induced Pluripotent Stem Cells (iPSCs)

Human Embryonic Stem Cell (hESC) [3]



- Derived from blastocyst [5]
- Ethical debate
- Transplant rejection[4]

Induced Pluripotent Stem Cell (iPSC)

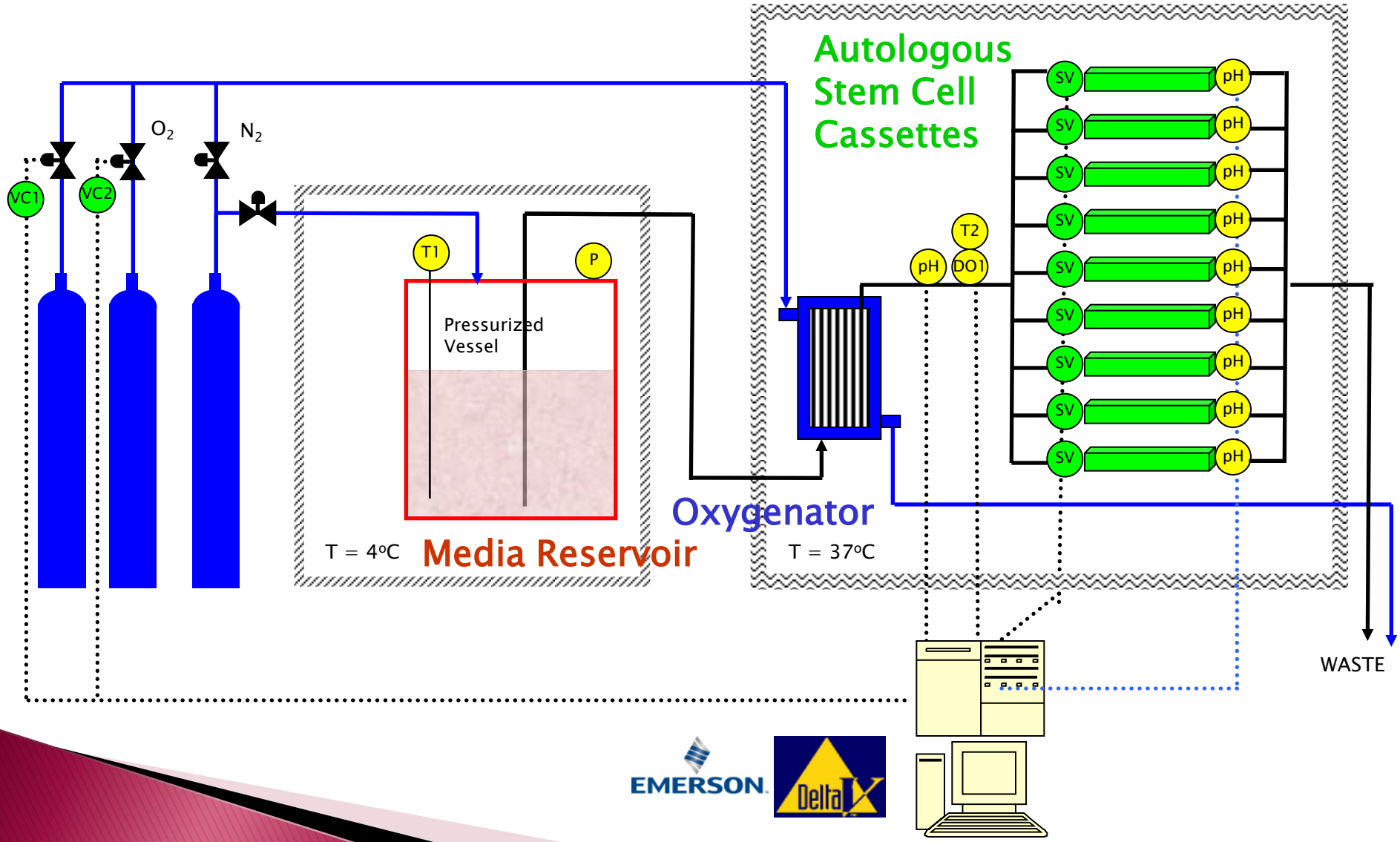


- Derived from mature tissue [4]
- Pluripotency induced [5]
- Individualized nature

Pertinent Characteristics

- Pluripotent [4]
- Require media supply [6]
  - Supply growth factors
  - Wash waste products
- Chemical signals direct differentiation [2]
  - Autocrine, paracrine factors
  - Extractables can mimic differentiation factors

Bioreactor System [2]



Competition and Problems

Current Solutions:

- Static culture
- CLINIcell Cassette

http://catalog2.corning.com/Lifesciences/en-US/Shopping/ProductDetails.aspx?productid=3814%28Lifesciences%29&categoryname=

Problems:

- Emerging field – commercially underdeveloped
- Need to optimize stem cell growth, conditions, and monitoring
- Samples cannot share media

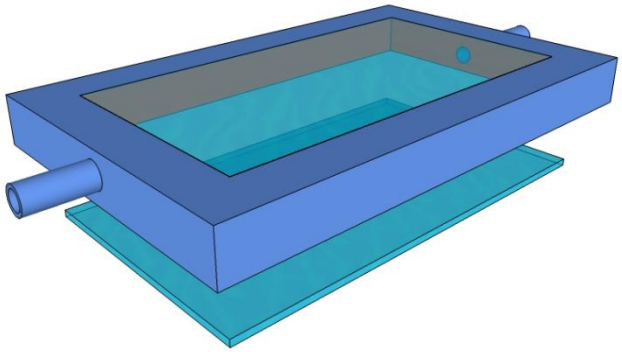
Design Proposal

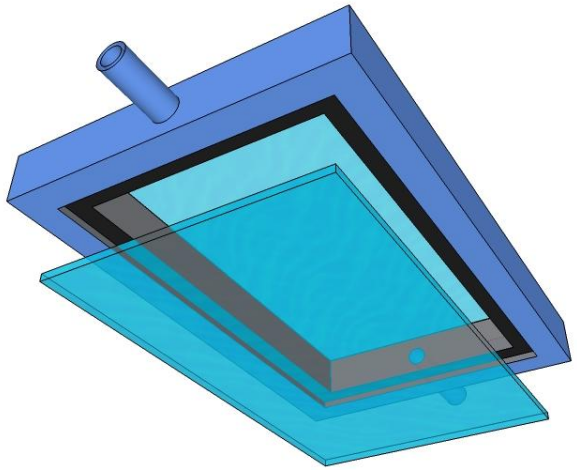
Design a perfusion cassette system to culture several independent samples of iPS cells.

Specifications

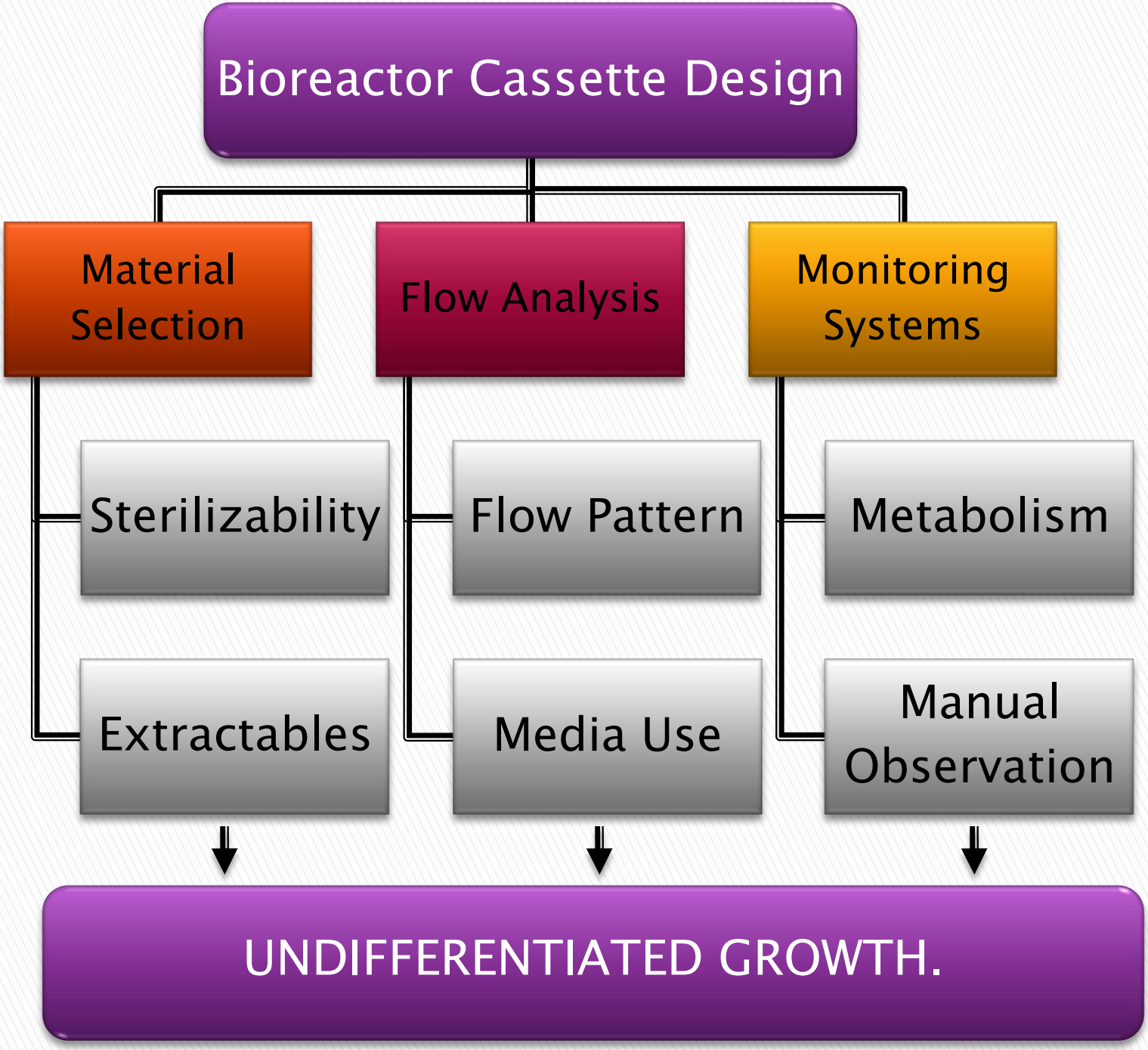
- Optimize growth area
- Undifferentiated growth (no extractables)
- Gas-impermeable growth plates
- Optically transparent
- Monitor pH
- Minimize media use

Design Concept



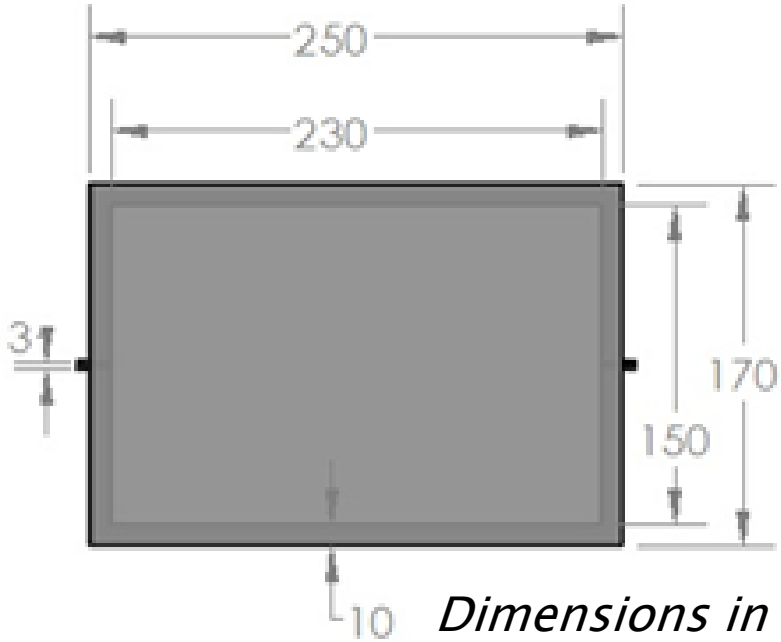


- Recessed frame
- Input, output valves for media exchange
- Transparent plate top
- Polystyrene cell plate inserted, secured from bottom
- Silicone gasket prevents leaks or contamination


Bioreactor Cassette Design
Material Selection
Flow Analysis
Monitoring Systems
Sterilizability
Flow Pattern
Metabolism
Extractables
Media Use
Manual Observation
UNDIFFERENTIATED GROWTH.

Flow Considerations: Geometry

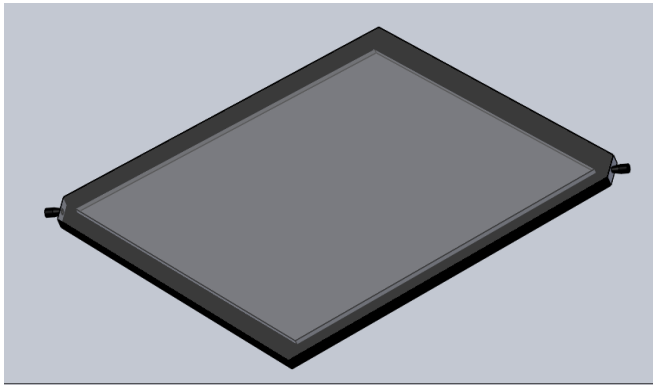
- 2 mm thickness
- 23 cm x 15 cm cell growth plate
- Want consistent flow
- Minimize media use

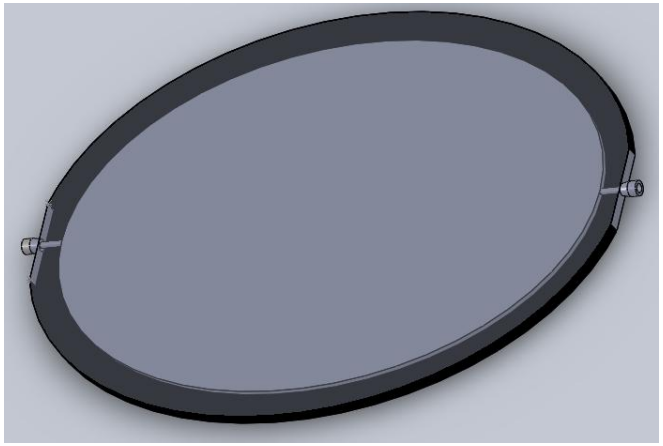


Dimensions in mm

Basic Shapes

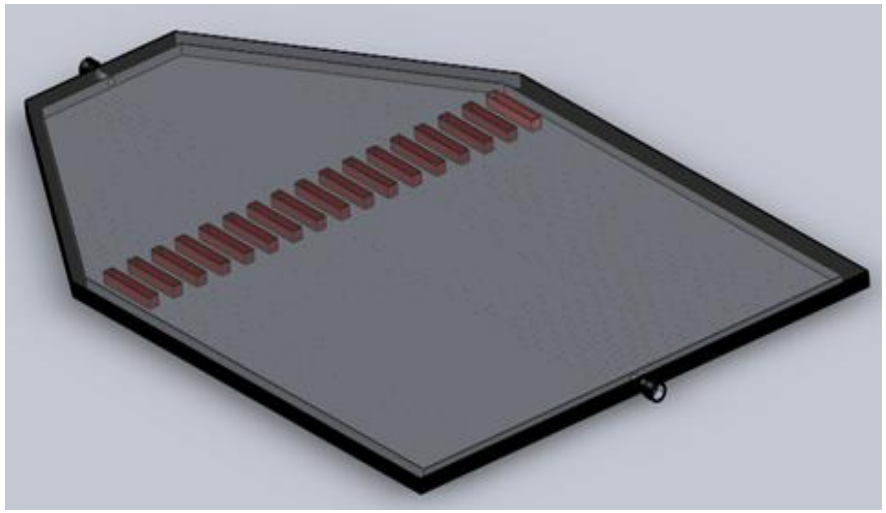
- Rectangle
  - Similar to existing designs
- Diamond
  - Direct flow outward
- Ellipse
  - No corners

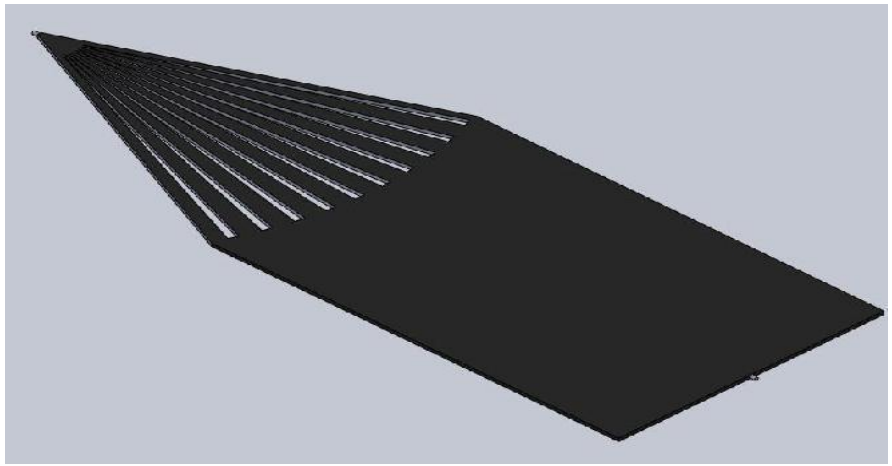




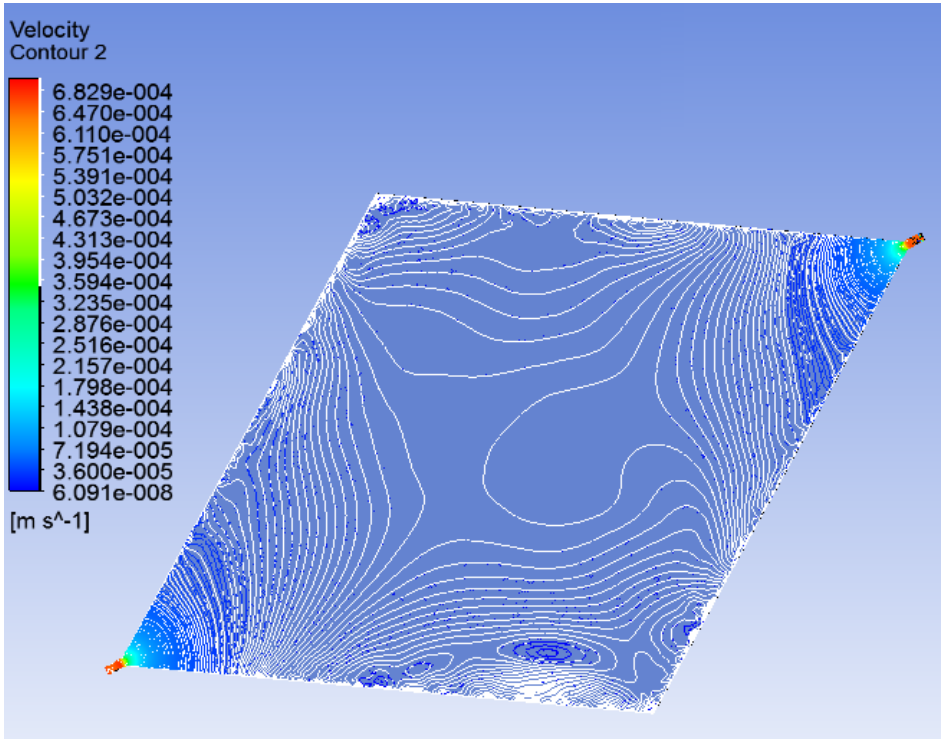
Complicated Shapes

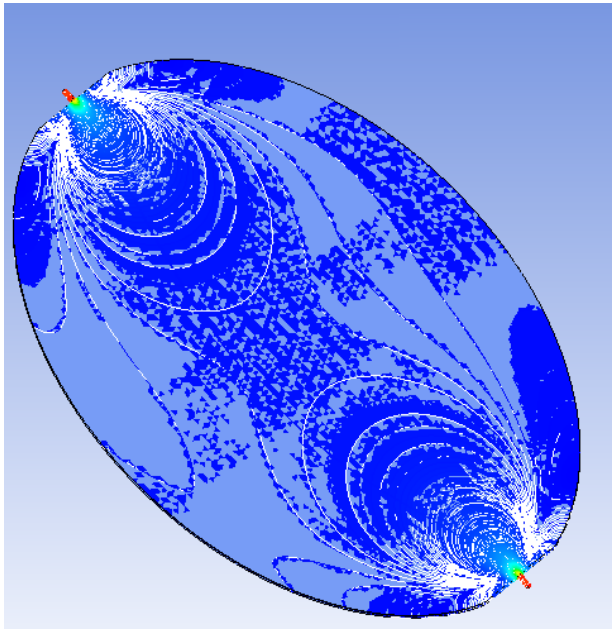
- Fan with Straighteners
  - Straightens flow after directed outward
- Fan with Guides
  - Evenly directs flow

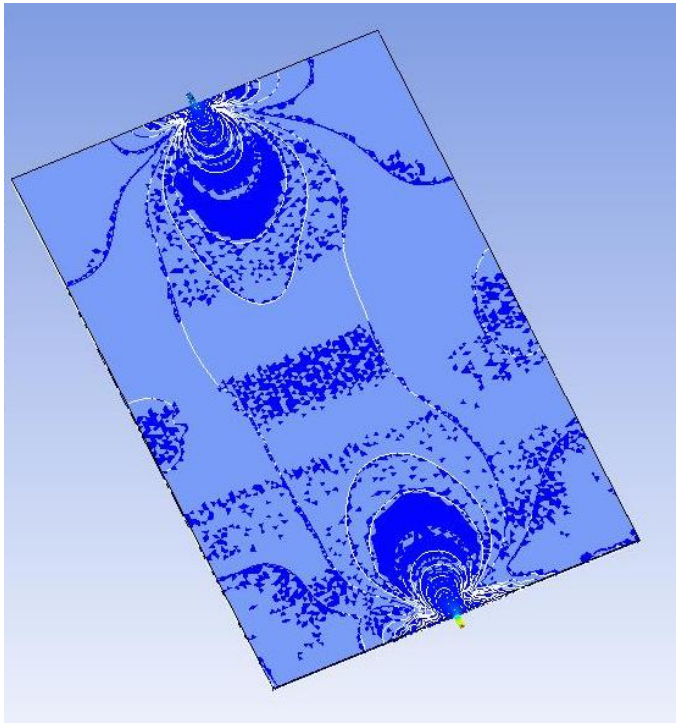




CFD Analysis: Contours







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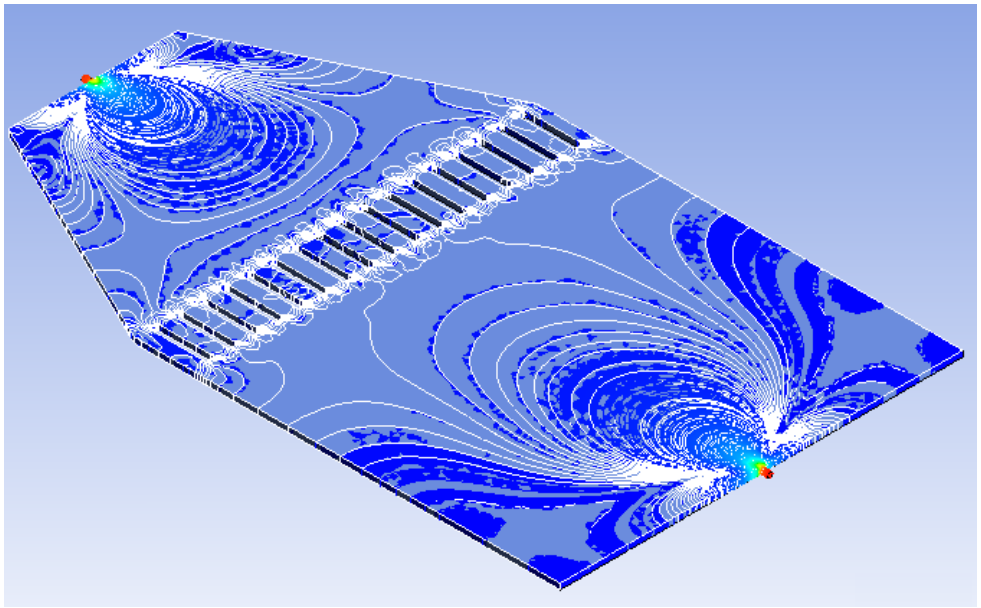
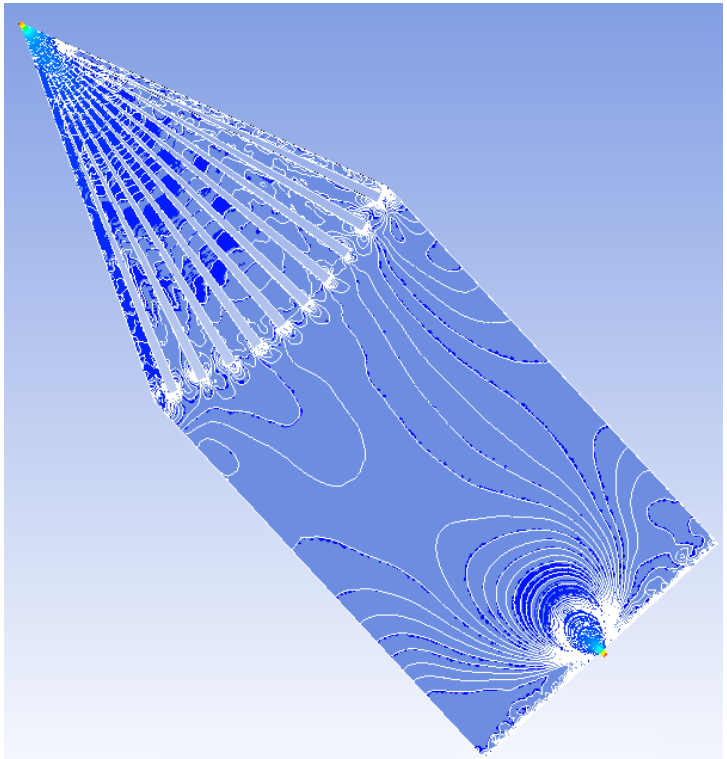
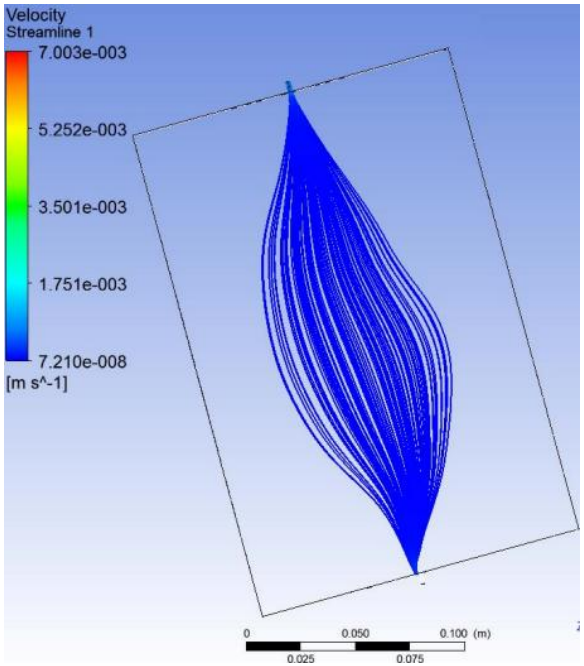
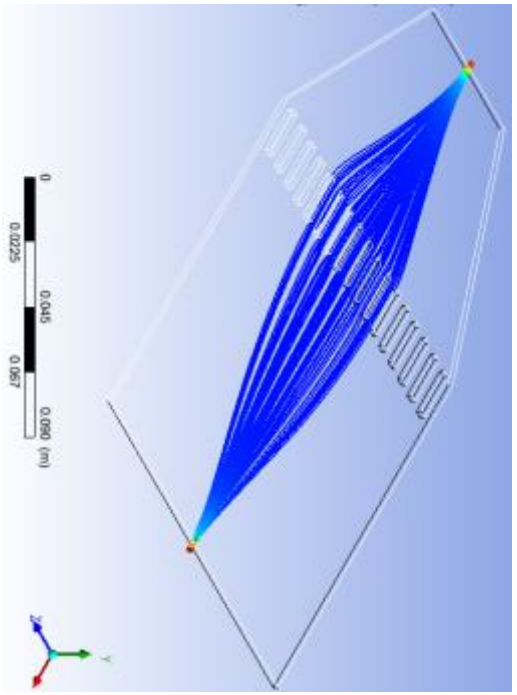
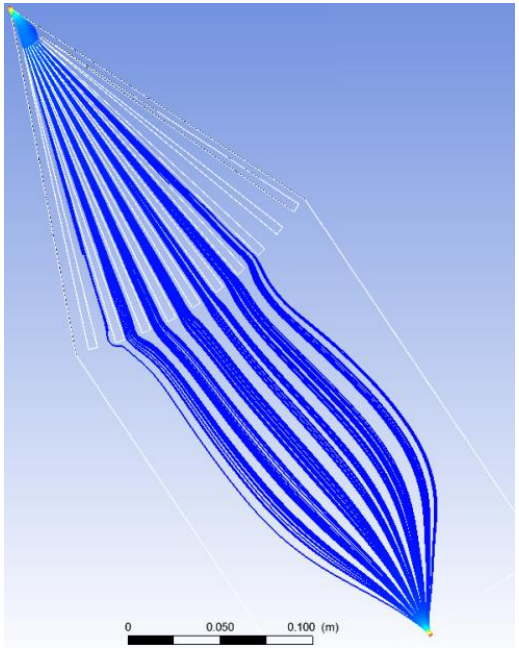




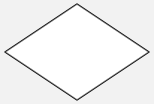
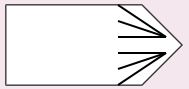
CFD Analysis: Streamlines







Design Matrix

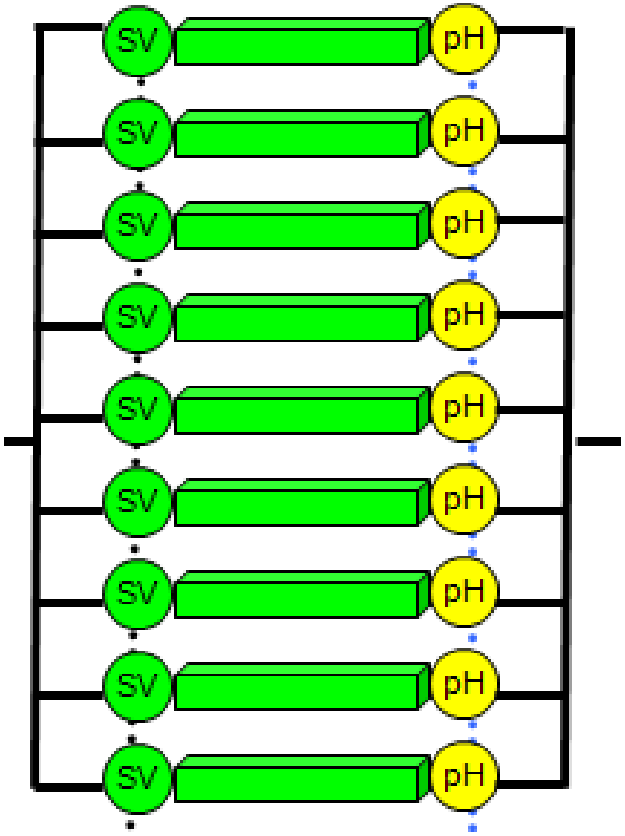
	Weight					
Fluid Analysis	0.60	4	7	6	8	9.5
Feasibility for prototype	0.15	10	9	4	9	9
Mass-Production	0.05	9.5	9	9	9	9
Maximize Cell Production	0.10	10	9	9	10	10
Efficient Media Use	0.10	8	8	8	7	7
	Score	**6.18**	**7.70**	**6.35**	**8.30**	**9.20**

Scale: 1 – 10 (1 poor, 10 excellent)

Future Works

- Further optimize geometry using CFD
- Finalize material selection
- Fabrication and testing
  - Dye
  - Salt gradient
  - Stem cell growth
- Output pH
- Flow adjustment at input

[2]



Acknowledgements

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- Sheku Kamara, Vince Anewenter, Issac Reifschneider
- Professor Willis Tompkins

References

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- [2] Hei, Derek (2010). "Bioreactor Perfusion Design" *Waisman Clinical Biomanufacturing Facility, University of Wisconsin-Madison.*
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Questions?