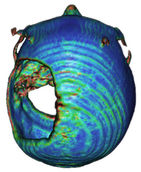

OSTEO ENGINEERING LAB

Department of Plastic Surgery | OSU

Analysis of Bioreactor Flow through Tissue Engineering Scaffolds through Computational Fluid Dynamics and Bioreactor Systems

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Introduction

The Osteo Engineering Lab is investigating the use of 3D printed biodegradable scaffolds on regeneration of craniofacial skeletal tissue.

In tissue engineering, bioreactors are used to give control over cell and tissue proliferation and differentiation. The variables that can be controlled include temperature, pH, gas concentration, media flow rate, shear stress, hydrodynamics and mechanical force.[1] This can help with cell seeding, used to promote bone growth within the system once implanted. And allow for full seeding of scaffolds by delivering nutrients and taking waste products away.

By using a bioreactor, 3D printed porous poly(propylene fumarate) scaffolds can be seeded with dynamic culture, **eliminating the necrotic core** problem of static cell cultures. This system can be modeled using computational fluid dynamics accounting for flow in and out of the bioreactor as well as scaffold size and velocity flow.

Hypothesis:

By controlling factors of the bioreactor detailed in a computational fluid dynamics model, a modelled perfusion bioreactor can be validated for the seeding of cells onto 3D printed scaffolds.

Objectives:

- Investigate factors affecting flow distribution and velocity in a bioreactor system
- Develop a perfusion bioreactor system that is small, easy to sterilize, disposable, and efficient.

Materials and Methods

- **Scaffold Creation:** The scaffolds were initially made with a Triply Periodic Minimal Surface Gyroid Structure in MathMod for a specific diameter and length, shown below. The scaffold was processed using Meshlab and GMSH to close holes and reduce the amount of faces, shown above.

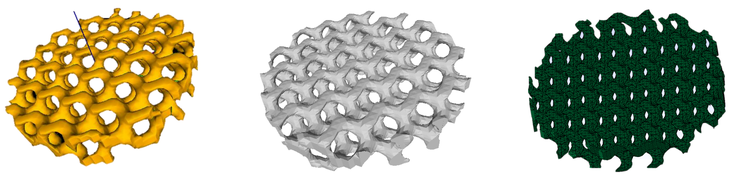

Figure 1. From left to right, the Gyroid Structure in MathMod, Meshlab, and GMSH

- **Design of Experiments**: The bioreactor chamber was designed with a chamber replicating a syringe tube, placing the scaffold within the chamber. Controlled variables include the inlet velocity, inlet/outlet shape, inlet diameter, and outlet diameter were changed in COMSOL.
- **Bioreactor parts:** All of the bioreactor parts coming in contact with the scaffolds come or can be sterilized, including the tubing. Parts were 3D printed to fit the peristaltic pump and stepper motor. Most of the system was placed within the incubator to promote cell growth, with only the electronic controls lying outside the incubator.

Results

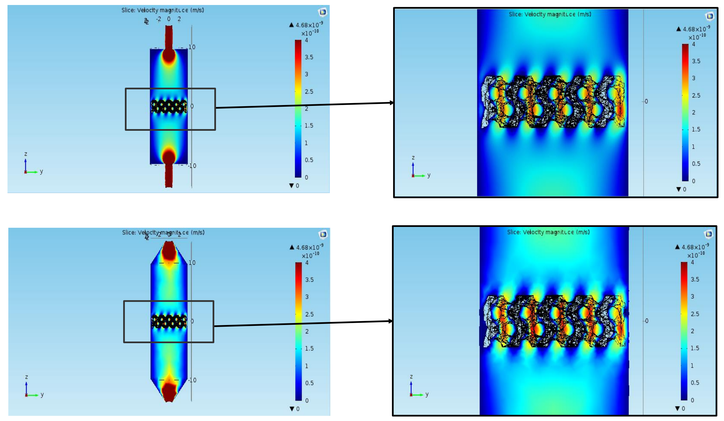

Figure 2. The difference in models of a cylindrical (top) design and a conical (bottom) design and their effects of their rate of flow exiting the scaffolds. A conical model allows for a more even velocity distribution.

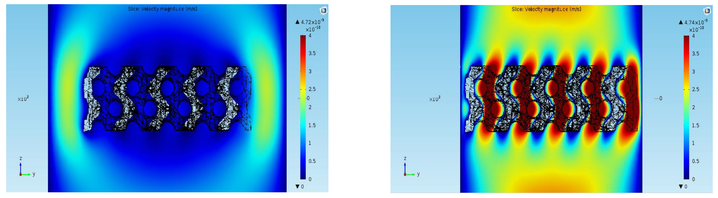

Figure 3. The difference in models of diameter of the cylinder. The left shows an excess of space on the sides, where flow goes around the scaffold. The right shows how a smaller diameter increases flow distribution through the scaffold.

Bioreactor Inputs			Bioreactor Outputs	
Stepper Motor Speed	Tube Outer Diameter	Tube Inner Diameter	Flow Rate	Flow Speed
1	4 mm	2 mm	4.67 mL/h	0.37 mm/h
2	4 mm	2 mm	9.33 mL/h	0.74 mm/h
3	4 mm	2 mm	15.1 mL/h	1.19 mm/h

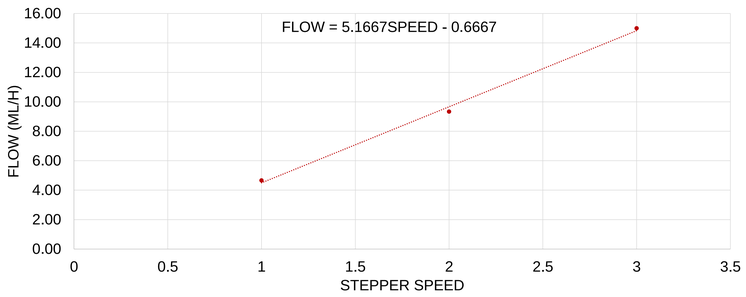

Table 1 and Figure 4. The parameter input values and the relative output values, showing an increase in flow as the stepper speed increases.

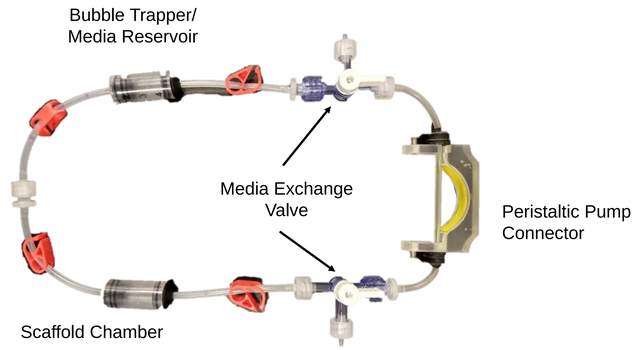

Figure 4. Final perfusion bioreactor system fully assembled. The rightmost part attaches to the peristaltic pump and motor.

Conclusions

- The diameter of the cylinder is the most important factor in ensuring that media flows through the scaffold instead of around it.
- As a result, the scaffold must be very close inside to the diameter of the tube.
- Due to the natural occurrence of shrinkage in the PPF scaffold, this must be taken into account. The PPF prints were made larger so that the diameter after shrinkage would fit the tubes snugly.
- The final bioreactor system includes a bubble trapper to prevent CO2 from entering the scaffold system and depriving cells of media and flow, this killing the cells.
- The next steps would include testing the static and dynamic flow of the bioreactor and comparing them.
  - Static scaffold analysis would include the set-up but would not use the use of the peristaltic pump to induce velocity flow.
  - Dynamic scaffolding would include the whole set up and running of the peristaltic pump for long periods of time.

References Cited

[1] Sladkova, Martina, and Giuseppe De Peppo. “Bioreactor Systems for Human Bone Tissue Engineering.” *Processes*, vol. 2, no. 2, 2014, pp. 494–525., doi:10.3390/pr2020494.

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