CREATING AN OSTEOCHONDRAL BIOREACTOR FOR THE SCREENING OF TREATMENTS FOR OSTEOARTHRITIS

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INTRODUCTION

A bioreactor is an apparatus in which tissues or cells are cultured, and it can be used to monitor the response to candidate drugs. In microfluidic systems, an exit for air bubbles is necessary as they tend to build up around the flow path; therefore, the flow path design must allow for the removal of bubbles without obstructing the transport of drugs and nutrients to the cells/tissues [1]. An example bioreactor and its negative (i.e., the flow path) are shown in Figures 1 and 2 below.

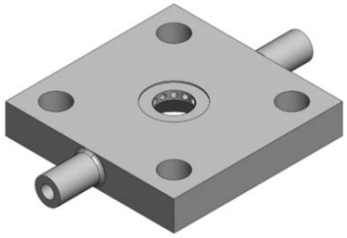

Figure 1: The physical bioreactor

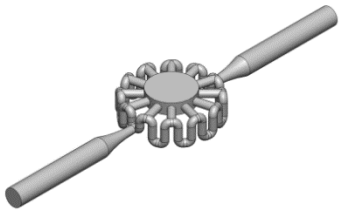

Figure 2: Flow path of an example bioreactor

Cells are hosted in the central chamber within a scaffold with low permeability, resulting in a relatively low amount of drug exposure since most of the fluid will travel through the surrounding channel [1]. The goal of this project was to develop a bioreactor design that would maximize drug exposure, and this can be achieved by maximizing the velocity of the fluid through the central chamber.

METHODS

Models of the flow path were created using SolidWorks, a computer-aided design software, and tested using ANSYS Fluid Flow (CFX), a finite element analysis software. A volume flow rate of 1 mL/day was placed at the inlet, and the outlet was open to the environment. The central chamber was considered as filled with GelMA, a hydrogel with a permeability of $1*10^{-16}$ m^2 and a porosity of 0.8 [2].

Velocities through the central chamber were measured in CFX Post. The design was altered by changing the diameter and height of the channel. The central velocities were plotted against these dimensions to determine any relationships between design features and central velocity. Each model was assessed based on the velocity of the fluid through the middle of the central chamber as this is a fair representation of drug exposure.

RESULTS

The first feature to be altered was the height of the step function channel. This was increased from 0.50 mm to 2.50 mm in 0.25 mm increments. The velocity through the central chamber was measured and plotted against the step height shown in Figure 3.

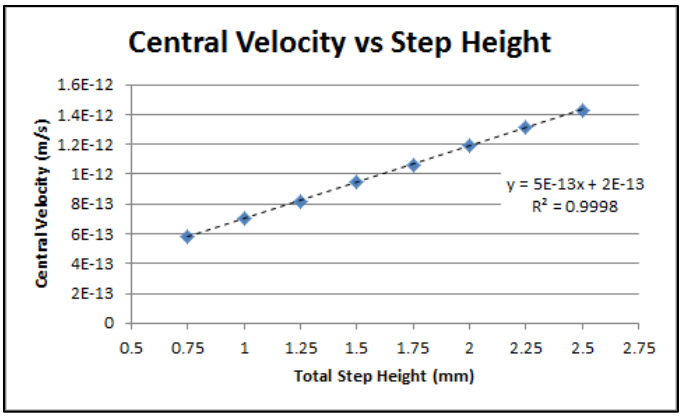

Figure 3: Positive relationship between central velocity and step height

This is a linear relationship with a coefficient of determination (R^2) of 0.9998. This means that the relationship can be expressed with an equation seen below where V is the central velocity in meters per second and H is the height of the step function channel in meters.

$$V = 4.8817 * 10^{-10} * H + 2.1137 * 10^{-13} \quad (1)$$

The next feature to be altered was the diameter of the channel and pores. The pores can only be as large as the channel, and from previous simulations, it is seen that the flow is maximized when the pores are the same size as the channel; therefore, the channel and pores will always remain equal in size and will increase/decrease as one. Dimensions ranged from 0.35 mm to 0.65 mm and increased in increments of 0.05 mm. Velocity versus channel diameter can be seen in Figure 4.

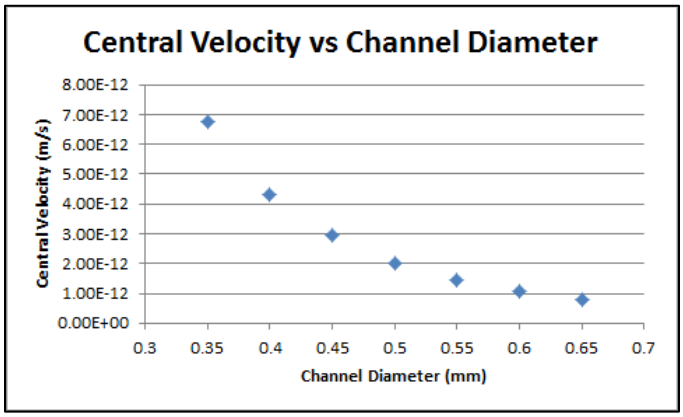

Figure 4: Negative non-linear relationship between central velocity and channel/pore diameter

The relationship is clearly nonlinear; however, there appears to be a consistent trend in the data. Taking the log (base 10) of both variables shown in Figure 5 presents a near perfectly linear trend in the data with a coefficient of determination of 0.9996.

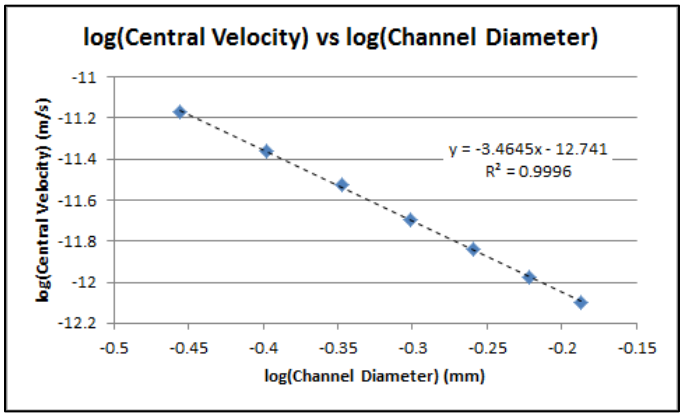

Figure 5: Negative linearized relationship between central velocity and channel/pore diameter

This linear data is much easier to visualize and represent with an equation. The relationship can be seen in Equation 2 below where V is the central velocity of the central chamber in meters per second and D is the diameter of the channels and pores in meters.

$$V = 7.328 * 10^{-24} * D^{-3.4645} \quad (2)$$

DISCUSSION

The relationships expressed with Equation 1 and 2 show that the velocity of the fluid through the central chamber can be controlled by simply altering the geometry. With these relationships, it is apparent that the velocity of the fluid, and therefore the total drug exposure, can be maximized by maximizing the step height and minimizing the channel diameter. These dimensions are limited by the resolution of the 3D printer and the overall design of the model. The smallest void able to be printed with the 3D Systems Vyper (Rock Hill, SC) is 0.60 mm meaning that this is the minimum size that can be used for the channels. The step height can be extended only a certain amount before it runs into other portions of the model; therefore, the maximum size for the step height is 1.75 mm.

This increase in central velocity is the result of an increase in the hydraulic resistance of the bioreactor. Hydraulic resistance is the resistance a volume experiences as it moves through the model. Hydraulic resistance and volume flow affect the pressure difference across the model as expressed by Equation 3.

$$\Delta p = Q * R_T \quad (3)$$

Where Δp is the pressure upstream minus the pressure downstream, Q is the volume flow rate, and R_T is the hydraulic resistance. As the hydraulic resistance increases, the pressure will also increase, and an increased pressure is able to more effectively force fluid through the central chamber. For future work, each portion of the bioreactor will be studied in order to understand how each segment contributes to its own flux through the central chamber. An array of bioreactors is also currently being studied in order to see how the pressure changes as fluid runs through multiple bioreactors.

REFERENCES

1. Lozito et al. *Stem Cell Research & Therapy 2013*, 4(Suppl 1):S6
2. Iannetti et al. *PlosOne, submitted*.

ACKNOWLEDGEMENTS

Simulations were run in the lab of Paolo Zunino, PhD. Funding was kindly provided by the Swanson School of Engineering and the Office of the Provost. I would also like to thank Dr. Riccardo Gottardi for his help and supervision.