Facilitation of Microfluidic Channeling to Generate Concentration Gradients for Cellular Culture

Ryan Hatch, Tanner Hunt, Steven Rupp, Hyrum Wendel
Utah State University, Logan UT, 84322

Introduction
This project aims to utilize the advantages of a microfluidic system to generate a testing apparatus that can be used in drug trials to observe the effects of different concentrations of nutrients or drugs on cell growth. With this proposed device, drug research companies can save time, materials and money during the research and development phase. Critical aspects of the project include three areas: simulation, fabrication, and validation. This project is supported by GE Healthcare and is a continuation of a senior design project completed in 2015 by utilizing the COMSOL modeling software to simulate the microfluidic flow, accurate alterations can be made to the previous design to enhance the accuracy of the concentration gradient generator (CGG). The CGG will then be combined with a cell culturing well array to test and analyze cell growth in various concentrations.

Objectives

Simulation
Develop complete, multi-physics models in COMSOL to predict channel mixing and appropriate channel length.

Fabrication
Following the procedures outlined and dimensions within COMSOL and CAD, create a working system.

Validation
Ensure the concentration levels are within a range of 5% and repeat until it fits the criteria. Ensure that cell array is capable of viable cell growth.

Criteria
Simulation
Using COMSOL, achieve a theoretical concentrations of 0%, 25%, 50%, 75%, and 100% in channel outputs.

Fabrication
Replicate the models using photolithography and 3D printing without leaks and complete glass adhesion.

Validation
Use a spectrophotometer to verify less than 5% error in the CGG.
Have cell count within 10% of the control flasks.

Background/Literature Review
It was determined that microfluidic devices will be made using both photolithography and 3D printing.

Photolithography
- Widely used in microfluidics
- Highly accurate
- Reusable

3D Printing
- Widely available
- Inexpensive
- Rapid prototyping
- Reusable
- Varying depths of channels and cell wells are easily made

Design Process

Simulation
AutoCAD was used to design the devices and was exported to COMSOL Multiphysics. Laminar flow and diluted species physics were used to calculate the concentration gradient across the device.

Fabrication
Microfluidic chip are made by producing a PDMS imprint of the master to form the channels. A master, and making a photomask for photolithography methods and extruded to be 3D printed.

Validation CGG
Upon the completion of the microfluidic devices, dye and distilled water were ran through the device and the output concentrations were collected and tested for accuracy using spectroscopy.

Validation Cell Culture
Cells were grown in stock solutions of 0%, 25%, 50%, 75%, and 100% (right) as a control, and compared to final results.

Final Design
The concentration was within 5% of the theoretical values in channels 1, 3, and 5. Most cells died after 2 days and were not comparable to control stock.

Conclusions
The outputs from the final device were 0.1%, 17.3%, 51.9%, 80.7%, and 97.6%. Though these were close to the desired values, they did not meet the evaluation criteria in channels 2 and 4. The CGG design did show improvements when compared to the design of the previous group.

The cell well array was a major source of error for this final design. The final confluent cells were not comparable to the control batches of cells created. It was determined that the error resulted from an insufficient cell concentration that was originally injected into the device.

One major accomplishment of this project was the proven validity of utilizing a 3D printer to create a model for a microfluidic device, providing that the 3D printer has adequate accuracy. This finding enables the creation of custom microfluidic devices for any company or institution with access to a 3D printer. More benefits from 3D printing includes rapid prototype and iterative testing, as well as drastically reduced costs.

Literature Cited


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