Project Plan (Version 2)
EE491 - Senior Design

Studying cell behaviors in 3D microtissues using a LabChip

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Project Statement

This project is to use a LabChip suitable for studying the cell behaviors in 3D microtissues, mimicking the tissue in human body. We will perform systematic studies of the migration of one or multiple cells in arrayed 3D microtissues formed by a polymer microfluidic chip developed in the lab.

We will make videos of the experiments, and then analyze the videos to study the migration trajectory of the cells in the microtissue in the microfluidic chambers. The analysis will be done using a Matlab program.

System Requirements

- ## Project Requirements

We must design experiments to study cell migration in microtissues and make videos of the cell migration using the optical microscope and provided software.

We must develop a Matlab program to identify and track the location of one or multiple cells in the droplets stored in the device chambers. The program must identify the number of cells in the chamber, collect location data and produce plots of the migration trajectory of the cells, as well as calculate velocity, distance traveled, and displacement of the cells.

We must then use the Matlab program we developed to analyze the data collected from the experiments we designed.

- ## Microtissue vs. Macrotissue

Traditional cell studies are done using large amounts of cells, in the range of hundreds to thousands of cells in a container. This is useful for studying cell behavior on a large scale, but doesn't provide much information on single-cell behavior.

The device we will be working with addresses this issue, allowing the storage of a single cell per chamber. Isolating single cells or just a few cells per chamber allows for the study of single cell movement.

- ## Validation Test

  There are other analysis methods for these kinds of experiments. One goal of our project is to improve on these other methods. We can verify the functionality and performance of both the design of our experiments and the design of our Matlab program by comparing our results to the other analysis methods. Our results should at least meet, but preferably exceed, the accuracy of the other methods.

System Description

- ## Design specification

  Each chamber of the microfluidic device contains one droplet with one or a few cells in microtissue. The cells are identifiable visually in the images, but are not different enough in color from the rest of the image to easily isolate the cells in Matlab. We must either manually mark the cells in red using ImageJ and send edited images to Matlab or design a method to identify the cells automatically in Matlab, without using ImageJ.

  The image of the chambers will be recorded every 1 or 2 minutes, creating videos over a long duration with a low frame rate. The frames of these videos will be the input to our Matlab program.

  The Matlab program will find the chambers by identifying the dark circle at the edge of the droplets, then split the image stacks into aligned image stacks for each chamber. The program will then identify which stacks actually have cell movement by checking for significant differences between the frames.

  The program will only identify cell locations in chambers that have significant movement between the frames of its image stack.

  The Matlab program will identify the location of the cells, either by identifying artificially colored parts of the images from ImageJ or some completely Matlab method not yet developed, and will store the coordinate data for the cells in each frame. The program will then use the coordinate data to plot the migration of the cells, convert the coordinate data to distance units suitable for analysis, and convert the frame rate and frame index data to time units suitable for analysis.

- ## Technical approach

  The more videos we can collect of the experiments, the more data we have to work with, and the more data our Matlab program is capable of handling, the better our results will be.

- ## Process details

1. Image the migration of cells in microtissues using optical microscope.

2. Plot the migration trajectory of the cells using our Matlab program.

3. Analyze the effect of density and composition of microtissues on the cell migration.

Work Breakdown

- ## Project Schedule

September:
- Understand the goal of the project
- Read papers on the LabChip functionality and design
- Read papers on analysis of cell migration to understand basic analysis functions our program must meet.

October:
- Understand the lab equipment and policy
- Understand the file types and basics of the data we will work with (optical microscope, tiff and avi files, etc.)
- Start getting preliminary data to test our code with

November:
- Work on getting the basics of the code working
- Focus on cell location in 2 dimensions (x-y plane of the images)
- Develop alternate methods using ImageJ if getting Matlab to do all the work is taking too much time at the moment.

Decemeber (End of 1st Semester):
- Have Matlab program able to identify cell location and trajectory in 2 dimensions
- Have program dynamically display the images as they're being processed
- Have a plan in place to extend Matlab program into 3-dimensional analysis
- Have a rudimentary GUI for the Matlab program

2nd Semester:
- Improve 2D program
- Shift focus to adding in 3D analysis
- Optimize/Finalize Matlab program
- Collect data and use program to analyze as much data as possible

- ## Risks

Accuracy:

There are concerns that the final product might not be as accurate as what our client wants. Our method and program must improve on the other methods, or it will not be accurate enough for our client.

Software feasibility:

The software that we are using might not be capable of actually tracking the target cell.

Licensing:

Might need access to additional software, and access to resources in ECpE teaching and research labs.

Data and Results:

We might have problems in analyzing data and the amount of data being processed is unexpected. The test code we come up with might not be able to actually track cell migration. We must be able to improve our program and method to handle the amount of data we collect.

- ## Cost

We may need to purchase items to perform the experiments, such as collagen, cells, syringes, etc. We have not yet had a reason to purchase anything and have therefore had no reason to create a cost breakdown yet. Our work has mostly been working on writing Matlab code and doing so with data provided to us by our client.

- ## Market

This research is important for understanding cell behavior. Understanding cell response to the Extracellular Matrix and how cells communicate is critical to gaining insight for human diseases.

Conclusion

By monitoring the movement of cells in microtissues in the microfluidic device, we get some basic understanding of the cells' responses to the extracellular matrix and how cells communicate.