Studying cell behaviors in 3D microtissues using a LabChip

Advisor: Long Que
Client: Long Que

The team — May1634

Role	Team Member
Team Leader	Jonathan Yatckoske
Team Webmaster	Yaxiong Zhang
	Chun-Hao Lo
Team Communication Leader	Yuqian Hu
Team Key Concept Holder	Kaiyu Xu

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.

Contents

Design specification

Each chamber of the microfluidic device contains one droplet with one or a few cells in microtissue. In the images, the cells appear a different color than the microtissue around them. If the cells don't stand out enough, we can use a fluorescent dye to make them appear red or green, making them easier to identify.

The image of the chamber 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 identify the location of the cells by looking for the expected color of the cells, 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.

System Requirements

Experiments on cell migration in microtissues is needed. Also, using the optical microscope to get videos of the cell migration is expected.

A Matlab program is needed 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.

Functional Decomposition

1. Using different colors to dye the cells. (Red or Green)

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

3. Track these dyed cells and take pictures of them every two minutes.

4. Load photos into Matlab.

5. Find locations of cells using a Matlab program.

6. Save the location data in files. (Likely .csv files.)

7. Plot the migration trajectory of the cells using a Matlab program.

8. Analyze the effect of density and composition of microtissues on the cell migration.
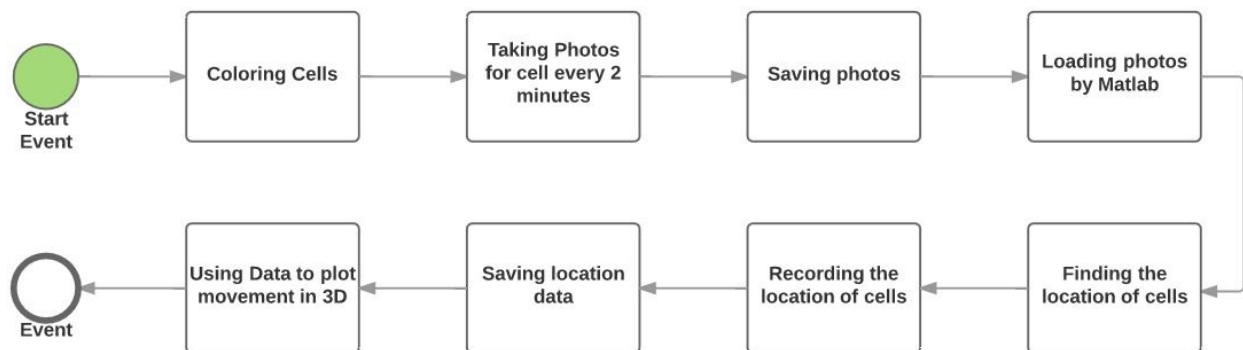
Figure 1

Detail Description

Droplets & Chips

The input for our collection data will be the cells within the droplets that will be collected in the storage chambers. As Figure 1 shows, after the droplets with the cells are formed, individual droplets are stored in the chambers.

After the droplets have been stored, the microscope is used to analyze the behavior of the cells in the microtissue. The output of this experiment will be videos that record the behavior of the cells.
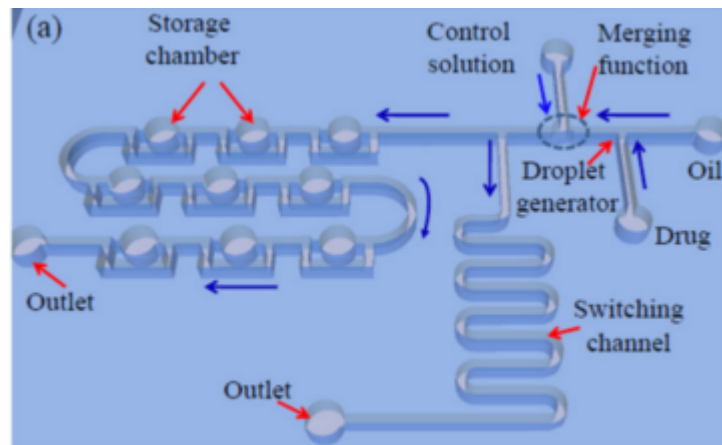

Figure 2

Matlab Program

The input for the Matlab Program will be the output from the data collection, which are the videos of the chambers on the chip. The program will analyze the behavior and the migration of the cells in the microtissue by determining the location of the cells in the chamber, specifically the x and y position. Some method will be developed for tracking z position as well.

The output of the final Matlab program in the system will be the plots of the graphs, and the calculation results.

The trajectories will be plotted with a set of plots for trajectory relative to the chambers and a set of origin-centered plots to show trajectory relative to the other cell trajectories.

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.

One such test will be to compare the plots from our Matlab program to the plots from the program used by the other researchers.

Issues & Challenges

The main issue we have right now is to detect and plot the cells in 3D movement. By collecting the data from the microscope, it is hard to analyze cell movement in z position. Additionally, we cannot plot the graphs in Matlab program as easily as the sample code at the end of this document because we don't have the data for the z position. For this reason, figuring out how to collect the movement of cells in 3D position will be the main issue for our group.

Additional Documents

Images of the chip's output/microscope

Matlab Code

The following Matlab code represents a sample program of plotting cell migration trajectory. This code makes a useful starting point for our Matlab program, but has a few aspects we will likely have to alter. Our equipment only has 2-dimensional imaging capability and can only track x and y location in real time easily. The sample code assumes 3-dimensional location data. We will develop a method for determining the z location and/or trajectory from the 2-dimensional images available.

```matlab
1    import traj = csvread('Data/NK data.csv');
2    % Input data in .csv format [data_id;Time;X,Y,Z,(Z/2)]
3    traj num = length(traj matrix);
4    % Get the length of matrix
5    global black blue green red gray
6    black = [0 0 0]; blue = [0 0 1]; green = [0 1 0]; red = [1 0 0]; gray =
7        [0.8 0.8 0.8];% Set for the color
8    % Declare colors as global variables
9    % Interpolate missing data
10   numintp = 0; % Number of interpolated data points
11   for i=1:traj_num %scan the data by i,j,k axis
12       for j=1:size(traj_matrix{i},2)
13           for k=1:size(traj_matrix{i},1)
14               if traj_matrix{i}(k,j) == 0
15                   traj_matrix{i}(k,j) = (traj_matrix{i}(k-1,j)
16                       +traj_matrix{i}(k+1,j))/2;
17                   numintp = numintp + 1;
18               end
19           end
20       end
21   end
```

The researchers that developed the sample trajectory code did not develop their own method for determining the location data from the images. We will develop a Matlab program to do exactly this, and format the output of that program to work with our version of the trajectory plot.

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. 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.