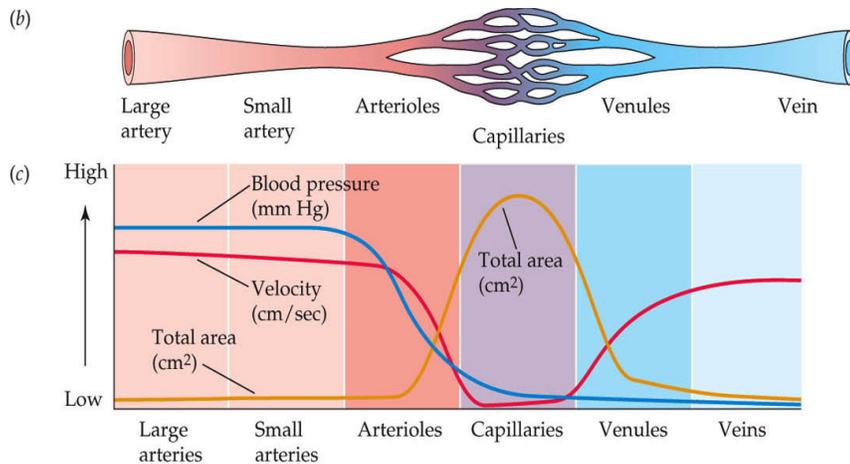**Modeling a Microvascular Network on a Chip**

Introduction

The microvasculature system (the portion of the circulatory system composed of the smallest vessels, such as the capillaries, arterioles, and venules) is comprised a series of vessels and networks with extensive redundant connections.

Figure 1: Branching of a typical microvasculature showing change of blood pressure, total area, and velocity.

These extensive connections are necessary to provide a high surface area for blood flow to the various organs in the body. In addition if there is an occlusion in any of these vessels e.g. a blood clot, the redundant nature of the network allows blood flow to be rerouted with minimal damage to the organ.

As a result of a blockage in the microvasculature one would expect a redistribution of flow in the neighboring vessels, a change in velocity and a change in pressure across the network.

The objective of this experiment is to characterize a simple model of the microvascular system using a PDMS (polydimethylsiloxane) microchip. This chip was made using photolithography and simple microfabrication techniques. You will measure flow velocities within the model network before and after a blockage and track the redistribution of flow when a channel is occluded. Figure 2 shows a schematic of the microchip. This lab will be followed by a session where you will theoretically calculate the pressure and velocity in each channel before and after blockage using Matlab. You will then compare your calculated pressure and velocities with your measured velocities.
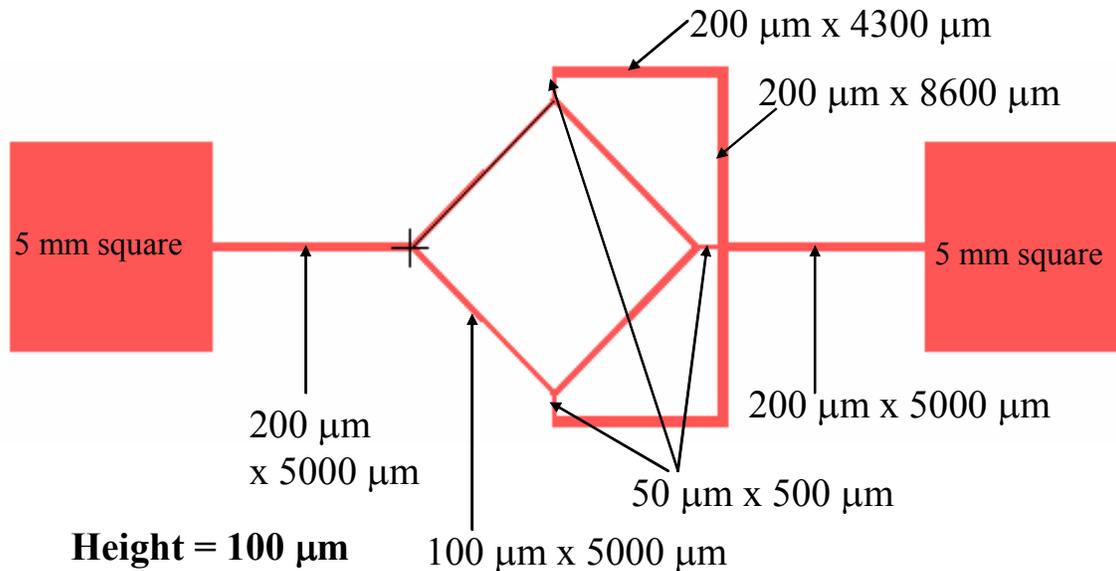
1

200 μm x 4300 μm

200 μm x 8600 μm

5 mm square

5 mm square

200 μm x 5000 μm

200 μm x 5000 μm

50 μm x 500 μm

Height = 100 μm

100 μm x 5000 μm

Figure 2. Schematic of PDMS microchip with dimensions

Materials
1 microfluidic device
3ml syringe with 23G needle
empty syringe with 23G needle
Syringe pump
6 ml of 10μm bead solution
6 ml of DI water
blocking tool (hole puncher –purple needle and yellow needle)
Hole filling tool –blunt yellow needle
silicone sealant
microvascular chip
stereo microscope with camera
computer with StreamPix software and Image analysis program
Image Analysis instructions
60C oven

Methods

1. Your device should be filled with liquid

2. Fill the 3ml syringe with bead solution, invert the syringe, tap on the sides, then gently squirt out any air bubbles that rose to the top.

3. Connect the 23G needle to the syringe, invert the syringe and push on the plunger so that liquid is coming out of the needle.

4. Place your syringe in the syringe pump (operating instructions given by instructional staff). Start pumping at a flow rate of 50 μl/min, until liquid is dripping out of the tubing.

5. Connect to your microdevice. You want to make sure your connection does not introduce air the microdevice. Keep pumping at 50 µl/min until all the channels are free of air bubbles. Increase the flowrate as necessary to remove air bubbles. When your device is air free set your desired flowrate for measurements. Your volumetric flowrate should be in the 1-5 µl/min range. Anything faster may be difficult for the camera to capture.

6. While waiting for the system to come to steady state become familiar with the capture software (TA/Instructor). **PLEASE BRING a USB Memory Flash drive** to store your images you will have a lot of data with large file sizes. Instructions for the image capture software will be available in the lab

7. You are expected to measure the velocity of the particles in each channel, some channels would have similar velocities (6 separate channels). Instructions for velocity measurements are on the Image Analysis sheet.

8. Take your appropriate images and store on your USB memory device.

9. These images can be analyzed in Image J (free software available online) or any other image analysis program. Using the coordinates of the particles you are tracking and their position from image to image, as well as the known capture rate, you should be able to estimate a velocity. You will be expected to track more than 10 particles per channel type in order to get statistically relevant data.

10. When you have taken images of each channel before a blockage. You will use the blocking tool to block a channel. The purpose of blocking is to see a redirection of flow e.g. flow backwards and a change in velocity.

11. Blocking your channel

    a. Disconnect your device from the syringe.

    b. With an empty syringe flush air through the channels ensuring that your device is somewhat dry

    c. Take the purple hole puncher and make a hole in the channel you would like to block. Turn the needle as you punch.

    d. Make sure the plug is removed from the hole with the yellow needle or by providing suction on the purple needle with a syringe. The TAs will check that the plug has been removed.

    e. The TA will give you a syringe filled with a sealant. Slowly inject the sealant into the hole whilst looking at the channel under the microscope. Stop when you see that the sealant has gotten in the channel. It is important that you are as neat as possible and just fill the hole and not cover the surrounding channels which will become hard to see if obscured by sealant.

    f. Place device in the 60°C oven for 10 minutes to harden the sealant.

    g. Connect the sealed device to the syringe as before (step 5), remove air bubbles.

      h. While your device is in the oven, draw a schematic of the device and show if you expect the velocity to increase or decrease after blockage.

12. Take images of the unblocked channels, and measure the velocity in each channel (9 channels) as well as note if there is redirection of flow.

* All needles and syringes must be disposed in the Sharps Container*

Results and Data Analysis Expected.

- Average velocity for each channel before blockage (weighted average)

- Average velocity for each channel after blockage (weighted average)
- Prediction of flow pattern after channel blockage. Include the schematic from 11(h) of the protocol. If you expect a reversal of flow support with an image of flow reversal.

Useful Equations:

$$Q = \text{Volumetric Flowrate} = \underset{(v)}{\text{velocity}} \times \underset{\substack{(A) \\ \text{cross-sectional} \\ \text{Area}}}{\text{cross-sectional Area}}$$

$$Q = v \times A \implies v = Q/A$$

$\Delta P = $ pressure drop along a channel, $\Delta P = Q \ast R$

$$\Delta P = \frac{12 \mu Q L}{w h^3} \text{ for a single rectangular closed syste}$$

$\mu = $ viscosity

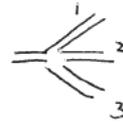$L = $ length of channel

$h = $ height of channel

$w = $ width

$$R = \frac{12 \mu L}{w h^3}$$

Resistance add in Series

$$R_{TOT} = R_1 + R_2 + R_3$$

Resistance split in Parallel

$$\frac{1}{R_{TOT}} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3}$$

* make sure all units are consistent