Student

Intro What Is Microfluidics?

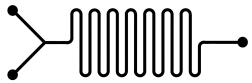
Microfluidic platforms, sometimes called "***lab on a chip***", are small devices used to control small amounts of fluids (usually liquid) using tiny channels and chambers. You can think of a big chemical factory full of pipes and tanks; now make it smaller and smaller until everything shrinks and can now fit in the palm of your hand. Some microfluidic chips can fit in the tip of your finger! You have heard of *microprocessors* inside of computers: microfluidic chips are very similar, but instead of electricity they transport liquids in channels that can be as thin as the leg of an ant. We measure these channels in ***micro****meters* (one millionth of a meter!). To give you an idea of how small this is, one inch is 25,400 micrometers long, and the average cell in your body is around 15 to 20 micrometers in diameter. But why does anyone want to put liquid in such tiny devices? There are several reasons, but we will explore two of them here:

1) To work with small volumes or small things: imagine you want to measure molecules like sugar or antibodies in a patient's blood. What if you can do many of these measurements in a small drop of blood instead of many tubes? Or imagine that you want to study how cells absorb nutrients or respond to vaccines. Would you rather work with them in big flasks or in small chambers that mimic the environment in which cells actually live?

2) Fluids and molecules do interesting things in small dimensions. Have you ever seen water defy gravity when it *climbs up* a piece of paper or a small tube (capillarity)? Could you pour lemonade and tea on a tall glass at the same time and keep them from mixing with each other? Inside of microfluidics chips, you can.

Scientists and engineers use the curious properties of the microfluidic world to analyze medical samples, synthesize chemical compounds, understand transport processes inside and outside of cells, test drugs in "***organs on a chip***" or to make nanoparticle vaccines, just to give a few examples.

Microfluidics is the manipulation of fluids in channels and chambers at the micrometer scale

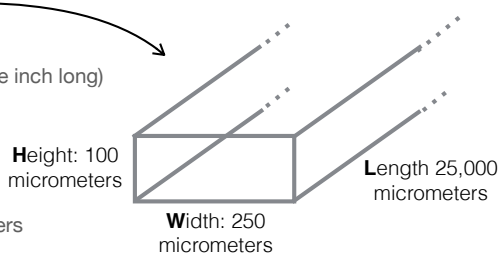


Microfluidics is the way of the future! Consider this:

A tube used to collect blood in a clinical laboratory can be filled with 10 milliliters of blood (=10,000 microliters). A channel in a microfluidic chip used to analyze blood has the following dimensions

Volume = **H** x **W** x **L**
Volume = 100 x 250 x 25,000 micrometers (one inch long)
Volume = 750,000,000 micrometers^3

Our channel is 750,000,000 micrometers^3
How many microliters of blood fit in it?



Each 1,000,000 micrometers^3 = 0.001 microliters

$$\frac{750{,}000{,}000 \text{ micrometers}^3}{1{,}000{,}000 \text{ micrometers}^3} = 750$$

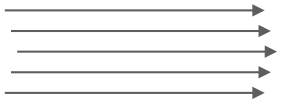
750 x 0.001 microliters = **0.75 microliters ! That is a drop about this big**

This means that instead of collecting 10,000 microliters of blood, the nurse can collect a tiny (really tiny) drop of blood from a finger to run the analysis. Scientists can take advantage of this kind of difference in volumes (e.g. going from 10,000 to less than 1) to conduct hundreds of experiments using *smaller samples and less reagents*, obtaining more information with less expense and often in less time. It is also easier for the patient to donate one drop of blood instead of several tubes.

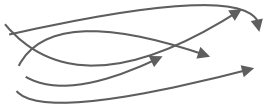
Cool physics in Microfluidics: **Laminar flow**

When you pour two liquids in a container they will mix (it is called convective mixing). However, in microfluidic channels you can have two or more liquids flow in the same channel, next to each other, without convective mixing! This kind of smooth or regular flow is called *laminar flow,* and it is opposed to *turbulent flow*. What is interesting and useful about laminar flow is that it can be used to carefully control the mixing of two liquids (to synthesize chemical compounds or separate molecules) or to generate layers of fluids with different concentrations (gradients).

Laminar flow



Turbulent flow

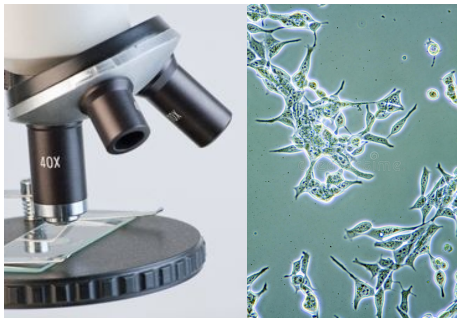


What are actual applications of Microfluidics in our world today? Turn the page!

Student _____

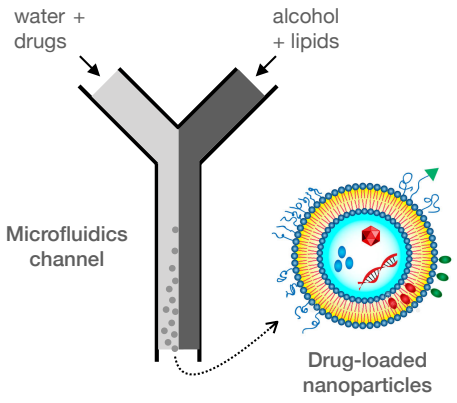
Applications of Microfluidics

We have learned that microfluidic technologies allow us, for instance, to reduce the volume of biological samples that are required to conduct clinical analyses. A great example is the personal device used by diabetic patients to measure glucose in blood. A thin cartridge featuring microfluidic channels directs the patient's blood from their finger to the reader inside the device. Here are other applications:



Did you know that some people apply engineering principles to biological systems? They are called Bioengineers. They can use microfluidic devices to measure how cells respond to stretching, or compression. They also use them to understand how cells communicate with each other and how they can self-assemble into tissues and organs. Controlling fluids and other materials at the micro scale allows them to study biology in a whole different way!

Because of laminar flow in microfluidic devices scientists can make tiny particles that are the size of a virus. These particles are easily absorbed by the body and can carry drugs to attack tumors, vaccine components to help the body fight infectious diseases, or even new genes for cells so they can fabricate new proteins. This is possible because inside microfluidic channels mixing occurs by *diffusion*, meaning that single molecules move randomly from one type of fluid to the other. When lipid (fat) molecules move into water, they all get together forming tiny particles and capturing a little bit of water (and whatever is in it) inside of them.



Quiz

1. Microfluidic devices are similar to _____ inside computers but instead of electricity they usually carry liquids.

2. There are one million micrometers in a meter. If you are 1.7 meters tall (about 5' 8"), how many micrometers tall are you? _____

3. _____ and _____ are two advantages of conducting experiments in microfluidic devices instead of using standard methods.

4. Turbulent flow leads to _____ mixing. In contrast, laminar flow allows for gradual or controlled mixing by _____.

5. _____ and _____ are examples of processes or applications made possible by laminar flow in microfluidic devices.

6. Imagine a channel with the height of a human hair (100 micrometers), triple the width, and 1.5 inches in length. How many microliters are needed to fill that channel?

Volume = **H** x **W** x **L** | 1 inch is ~25,000 micrometers | 1,000,000 micrometers^3 = 0.001 microliters

Bonus question: Bioengineers use physics and mathematics to understand and also to mimic and even improve biological systems. Can you think of a health or environmental problem that could be solved using bioengineering? How? Discuss with your instructor and classmates.

Student + Instructor

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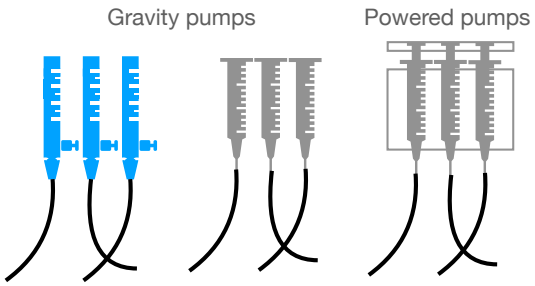
How do I run my **Microfluidic** devices?

The goal is to run liquid through those channels! The liquid in your experiments is usually water plus food coloring so you can observe what the fluid does. Infusing, introducing, pumping (all the same thing) liquid into the devices and then observing what happens might be all you need to do. But first you have to have your pump and your devices ready to go:



Tubing

The tubing should be firmly attached to the pump (burette or syringe). If you are using a gravity pump, attach tubing before filling the pump with liquid and either close the valve (burette) or clamp the tubing (open syringe). There are instructions for the **manual pump on a page below.**

Set up your "pump"

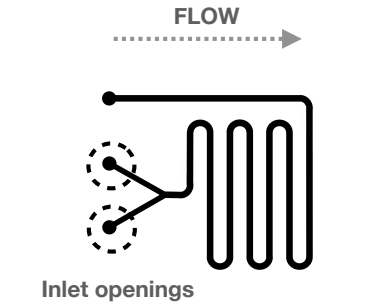
Whether you use gravity (burettes or open syringes) or a powered (manual or motorized) syringe pump, prepare colored water (food dye is great) and fill up the pump. For gravity pumps the higher the volume the better the flow. Purge the air in the tubing by testing the flow before connecting to the device (have a container or paper towels at hand). Check the pump **set up** instructions.

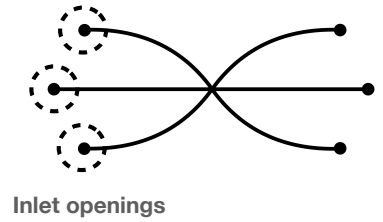
Attach the bumper inlets to your device

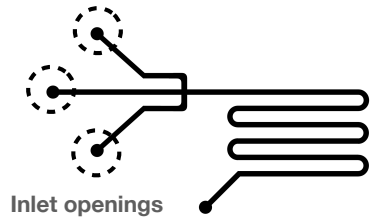
Take one of the bumpers and then feel with your finger the holes/openings of the device. That is the side (front) you want to apply the bumper on. We have a diagram that shows you how to do this! Press hard to attach the bumper firmly. This is the **number one mistake** we sometimes make, attaching the bumper to the wrong side of the device, where there is no opening!! If you fail to see flow when you start the pump, the bumper is probably placed in the wrong side of the device.

Let the pump work for you

Arrange everything so the device remains as flat as possible (you can use tape to secure the device down if needed). Set your device on top of a paper towel or sheet of paper and get the pump going! The white background will help you see the colored liquid run through the device. Observe the behavior of the liquid and **be ready with a paper towel to remove the liquid that comes out** from the outlet. You can observe the flow with the naked eye, but if your instructor allows it, you can use a phone with a camera to zoom in and take pictures or video of the channels. Check out laminar flow in action, it is really cool! Record what you see in the worksheet and explain your observations.







Student + Instructor

Set up: Pumps and Inlet Bumpers

Manual pump and bumpers video:
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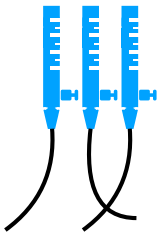
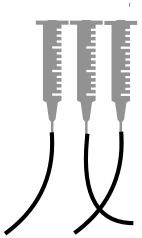
There are 3 kinds of pumps:

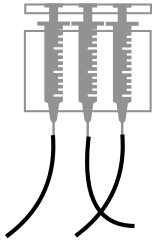
Gravity pump (burettes)



Gravity pump (open syringes)

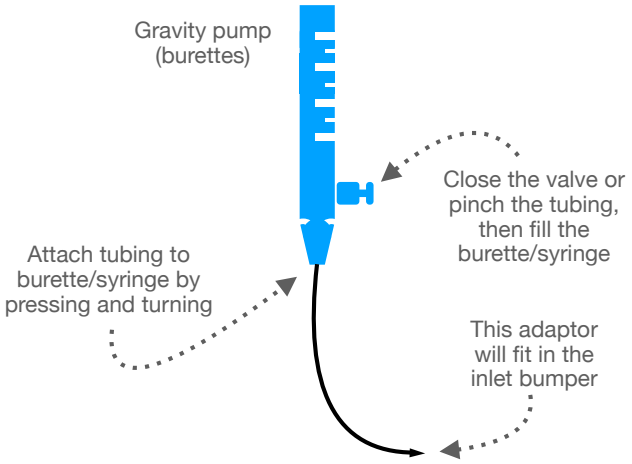


Powered pumps ▶ See instructions in the next page



Fill the pump with colored solution

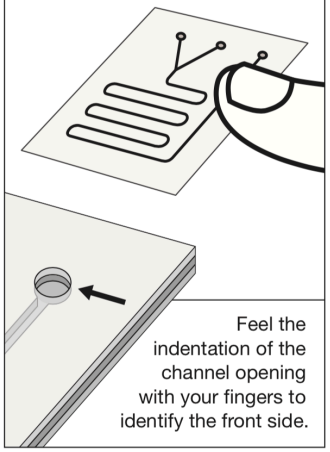
For gravity pumps the more solution the better the flow. **Concentrate** the color; small amount of liquid in channels can be hard to see unless color is concentrated. For powered pumps, (manual or motorized) the flow should be really slow. Do not attempt squeezing syringes individually by hand; the pressure is too high (it can delaminate devices) and it is hard to make flow even in every channel.



1

Identify the front side of the PETL device.

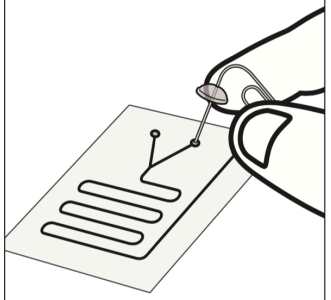
The front side has open access to the channels.



Feel the indentation of the channel opening with your fingers to identify the front side.

2

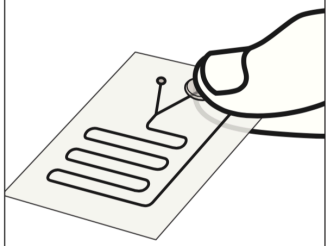
Use a paper clip to guide the bumper onto the channel opening.



Slide the bumper down a bent paper clip onto the device. The perforation in the bumper should be centered directly over the channel opening.

3

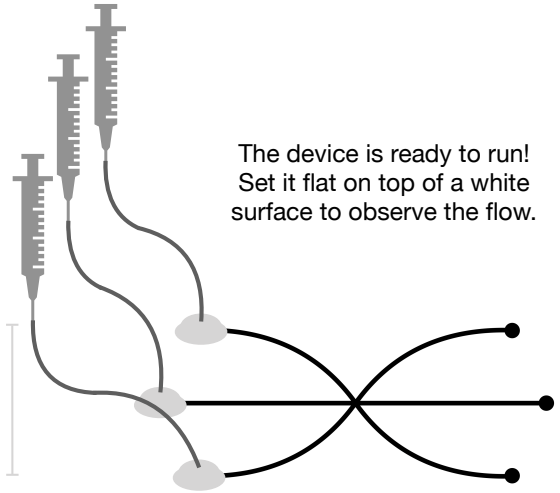
Press firmly to attach and seal the bumper to the device.



Continue applying bumpers to channel openings (*inlets*). Bumpers may also be attached to *outlet* openings if sample recovery is desired.

Add bumper inlets and insert tubing

Follow the 3 steps above to add the bumper inlets to your device. When using a gravity pump make sure the device is below the tip of the burette or syringe. Insert the tubing adaptor into the inlets; move the pump so the device lays flat over a white surface. You may want to use some tape, but do not block the view of the channels. Have some paper towels at hand, use them to remove liquid from the outlet. Run one device at a time.



The device is ready to run! Set it flat on top of a white surface to observe the flow.

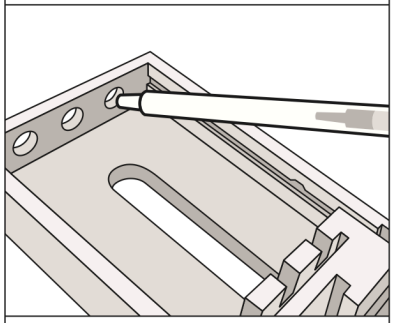
Manual Pump

Tips & Instructions

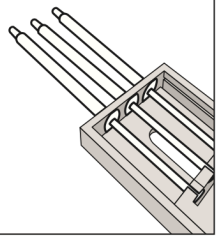
- We designed this pump to make it easy and affordable to access microfluidic channels.
- First, prepare 2 or 3 different color solutions. Water-dye solutions are best prepared by adding 1-2 drops of food coloring per milliter of water.
- Use 1 ml syringes. Wait to load the syringes with the dye solutions until *after* Step 3.
- Push the syringes all the way forward (emptying the air) using the rotating lever before loading.
- Load the solutions all at the same time by submerging the adaptors/tubing in the solution.
- It is not necessary to completely fill the syringe with solution, remember that the entire PETL chip can be filled with less than 20 microliters.
- Purging (Step 4) so the solution completely fills the tubing + adaptor helps to eliminate air bubbles in the chips.
- Secure the chip to a surface before connecting to pump.
- Infuse liquid by rotating the lever at about **one full revolution every 10 seconds**. Chip delamination (and leaking) may occur if too much liquid is infused too fast. Go slow!
- Enjoy the show! Flow within tiny channels is full of surprises.

1

Insert syringe into the opening.

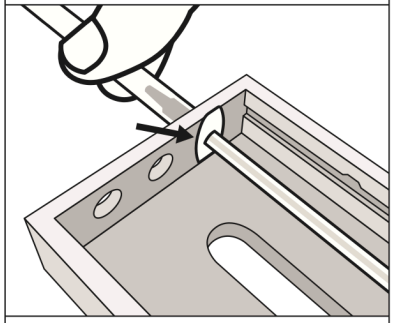


The entire length of the barrel exits through the opening.



2

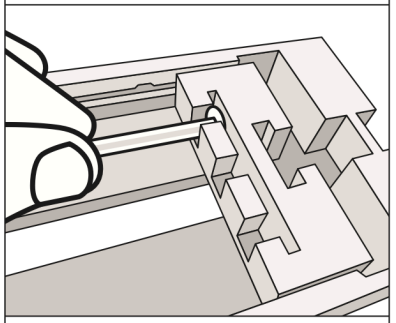
Rotate the barrel to secure flange in slit.



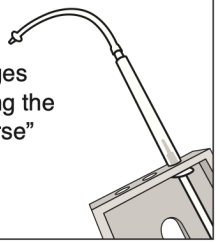
This keeps the syringe's barrel from moving while the cartridge pushes forward or withdraws the plunger.

3

Insert back of plunger into the cartridge.

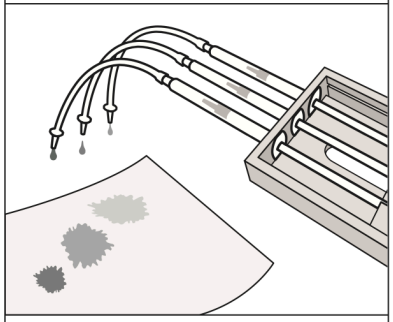


Attach tubing. You can now load the syringes with liquid using the pump "in reverse"



4

Clear air from the tubing.



Pump a couple of drops from each tube onto a paper towel to eliminate any air bubbles from the tubing.

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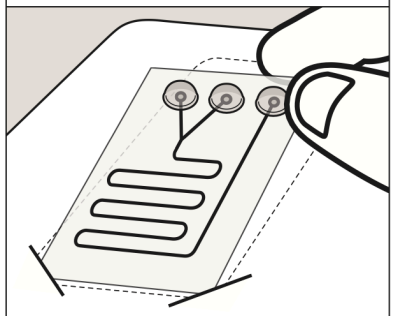
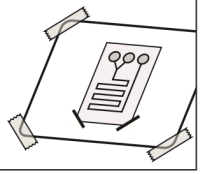
5

Insert the chip into the base.



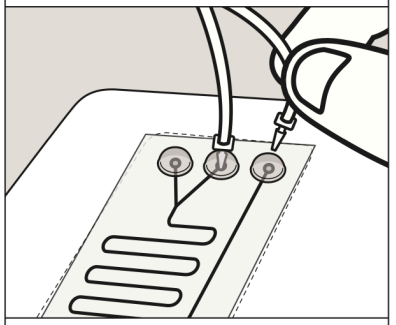
Place the bottom corners in the slits cut into the base.

Use tape to secure the base to the surface of the table.



6

Connect the tubing to the chip.



Push each adapter into a bumper. Apply pressure to ensure a firm connection. You can now infuse liquid into the chip. Go slow! Those channels are tiny! :)

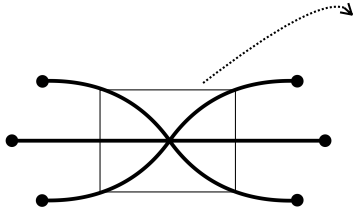
Student **Worksheet**

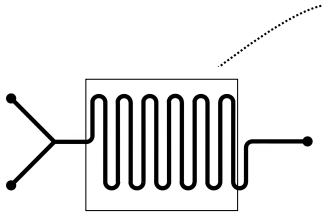
Student: _____

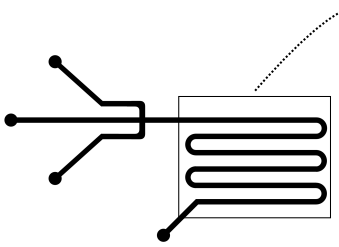
Predictions (do this first!)

What do you think will happen when you pump liquid through these channels?

NOW RUN YOUR EXPERIMENT!







Make a drawing or diagram of the actual flow

Briefly explain your observations and compare with your predictions

Instructor

Intro What Is Microfluidics?

Learning outcomes:

a) Students are able to describe microfluidic devices and name some of their properties and applications.

b) Students can calculate dimensions at the microscale and make approximations for comparison to familiar objects.

c) Students can predict patterns of flow based on their knowledge of laminar flow.

d) Students are able to explain how controlled diffusion in microfluidic devices leads to molecular mixing and/or separation.

e) Students can formulate potential solutions to scientific problems by applying their knowledge of microfluidics.

Laboratory Session Work Flow (1.5 - 2.5 hrs)

1. Students are separated into groups of 2 or 3 students.

2. Each student or each group is given an Intro-sheet and a Worksheet. The instructor can decide whether students will complete the sheets individually or as a group. Instructor may use *PETL Fluidics* slides to give an introduction.

3. Students are given time to read and work through the Intro-sheet (approx. 30 minutes). Alternatively, they work on this sheet prior to attending the laboratory session.

4. The instructor and students discuss the reading and the answers to the Quiz.

5. Each team receives 3 devices, one of each pattern. Students add inlet bumpers to their devices (approx. 15 minutes), observe the different channel designs and then complete the first part of the worksheet (predictions).

6. The teams run their devices one at a time and make observations (approx. 30 minutes).

7. Students complete the worksheet and draw conclusions based on their observations.

Quiz **KEY**

1. Microfluidic devices are similar to ___microprocessors___ inside computers but instead of electricity they usually carry liquids.

2. There are one million micrometers in a meter. If you are 1.7 meters tall (about 5' 8"), how many micrometers tall are you? 1.7 million micrometers

3. Smaller volumes of samples & reagents | Use of laminar flow | Many experimental steps in one chip are 2 advantages of conducting experiments in microfluidic devices instead of using standard methods.

4. Turbulent flow leads to __convective__ mixing. In contrast, laminar flow allows for gradual or controlled mixing by ___diffusion____.

5. Chemical synthesis, molecule separation, glucose measuring, etc. are examples of processes or applications made possible by laminar flow in microfluidic devices.

6. Imagine a channel with the height of a human hair (100 micrometers), triple the width, and 1.5 inches in length. How many microliters are needed to fill that channel?

Volume = **H** x **W** x **L**
Volume = 300 x 100 x 37,500 micrometers (one inch is ~25,000 micrometers)
Volume = 1,125,000,000 micrometers^3
Each 1,000,000 micrometers^3 = 0.001 microliters

$$\frac{1{,}125{,}000{,}000 \text{ micrometers}^3}{1{,}000{,}000 \text{ micrometers}^3} = 1{,}125$$

1,125 x 0.001 microliters = **1.125 microliters**

Bonus question: Bioengineers use physics and mathematics to understand and also to mimic and even improve biological systems. Can you think of a health or environmental problem that could be solved using bioengineering? How? Discuss with your instructor and classmates.

Instructor

Worksheet **KEY**

Predictions (examples)

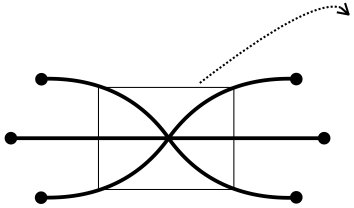
What do you think will happen when you pump liquid through these channels?

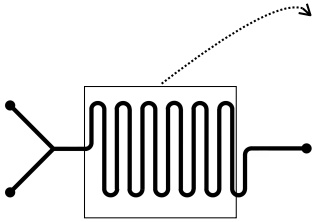
The dyes will mix at the crossing and a combination of the colors will be seen in all 3 channels

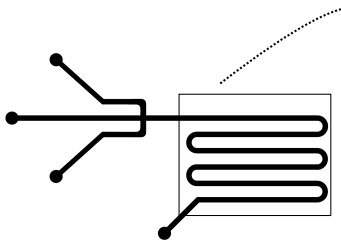
When the dyes reach the main channel they will remain separate and flow next to each other the whole way.

The dye will mix with the other solution at the crossing and there will be only 1 diluted color at the end of the channel

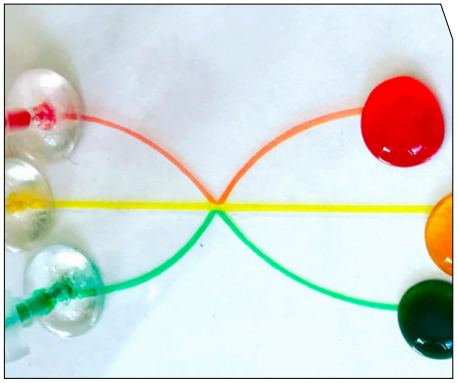
NOW RUN YOUR EXPERIMENT

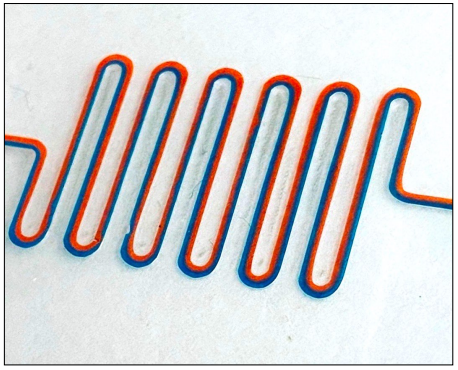


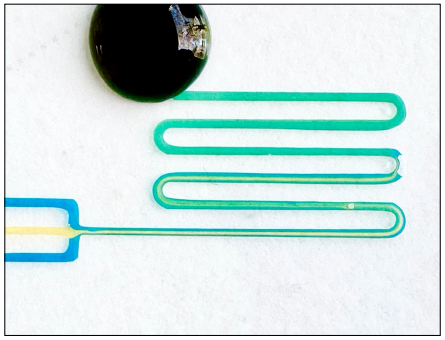




Make a drawing or diagram of the actual flow







Briefly explain your observations and compare with your predictions

Answer Key

The prediction was incorrect; there is little to no mixing at the crossing, the dye in the middle continues along the central path while the top and bottom dyes "bounce back" to the side channels. There is no convective mixing

My prediction was correct, the dyes join at the crossing but do not mix because of laminar flow. They run together without obvious mixing to the end of the channel.

My prediction was partially correct, the dye did not mix at the crossing but one can see diffusion at the interface of the liquids that eventually results in the dye changing color by the end of the channel.