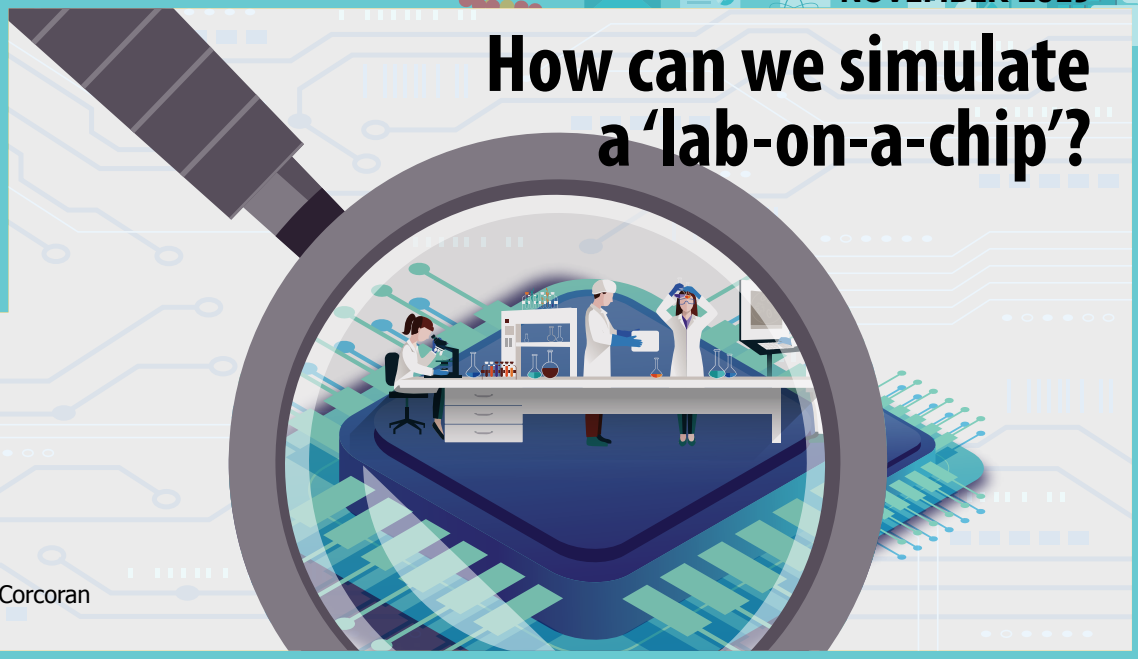
BIOMEDICAL SCIENCE JOURNAL FOR TEENS

NOVEMBER 2019

How can we simulate a 'lab-on-a-chip'?



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Abstract

Many chemical and *biomedical* experiments are conducted in labs that need a lot of space, expensive machinery and special substances. What if this process could fit onto a tiny chip? Wouldn't that save a lot of time, space and money!

So-called '*labs-on-a-chip*' (also called biochips) already exist but their design is tedious. Researchers still have to manually calculate a lot of the variables, which leads to the creation of lots of different possible chips, some of which won't prove useful. This 'trial-and-error' approach takes a lot of time and money. What if we could create a virtual biochip before we physically make one – so that we know we are always manufacturing the right one? Here we developed a computer simulation for a lab-on-a-chip and compared its predictions to existing biochips. We found out that our approach is great at its predictions, and chip designers could use it to create reliably useful biochips for lots of different experiments.

Introduction

Have you ever wondered how a laboratory tests your blood? To check for a disease, it not only takes a series of operations such as mixing, *incubation* and heating, but also a lot of expensive chemicals, machinery, and big spaces to do it all in. What if this entire process could fit onto a tiny chip? We could save tons of space, money and blood. So-called 'labs-on-a-chip' already exist, and they can indeed replace an entire lab. But how do they work?

The tiny chip looks like an electric circuit, but instead of electricity, fluid (such as an oil) flows in a network of channels (Fig. 1). To begin the experiment, researchers add another fluid (which will resist mixing with the first one) in the form of tiny droplets – for example, an infected blood sample. To test if a drug can cure the infection, the researchers then add drug droplets (which will also remain unmixed with the first fluid). Now the two types of droplets have to meet – they have to get trapped together for incubation. How does this happen?

Microfluidic resistance makes this happen. Much like in an electric circuit where the voltage depends on the current and the electric resistance, the *flow rate* in the chip's network depends on the pressure introduced by the pump and microfluidic resistance. The microfluidic resistance itself depends on the channel's length and diameter and on the presence of droplets: the tighter the channel, the higher the resistance. Droplets always prefer the channel with lowest resistance (Fig. 2).

It sounds easy enough, but to design such a chip is very hard! Currently, researchers design biochips using a huge number of calculations, they then make it and see if it works. If it doesn't – they start over. This is expensive and inefficient. Which is why we wanted to try a different approach – what if we could simulate the biochip before we make it?

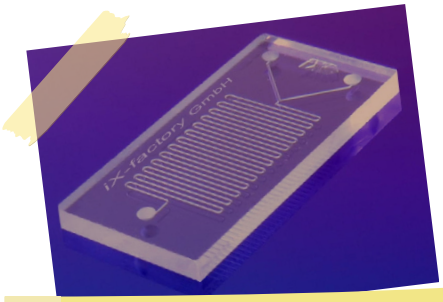

Figure 1:
A biochip. Fluids run in the tiny channels which are 50µm (micrometer - equivalent to one-millionth of a meter) deep and 150µm wide. That's very narrow! The width of a human hair ranges from 10µm – 200 µm, for example.

Please see Figure 2 Page 2

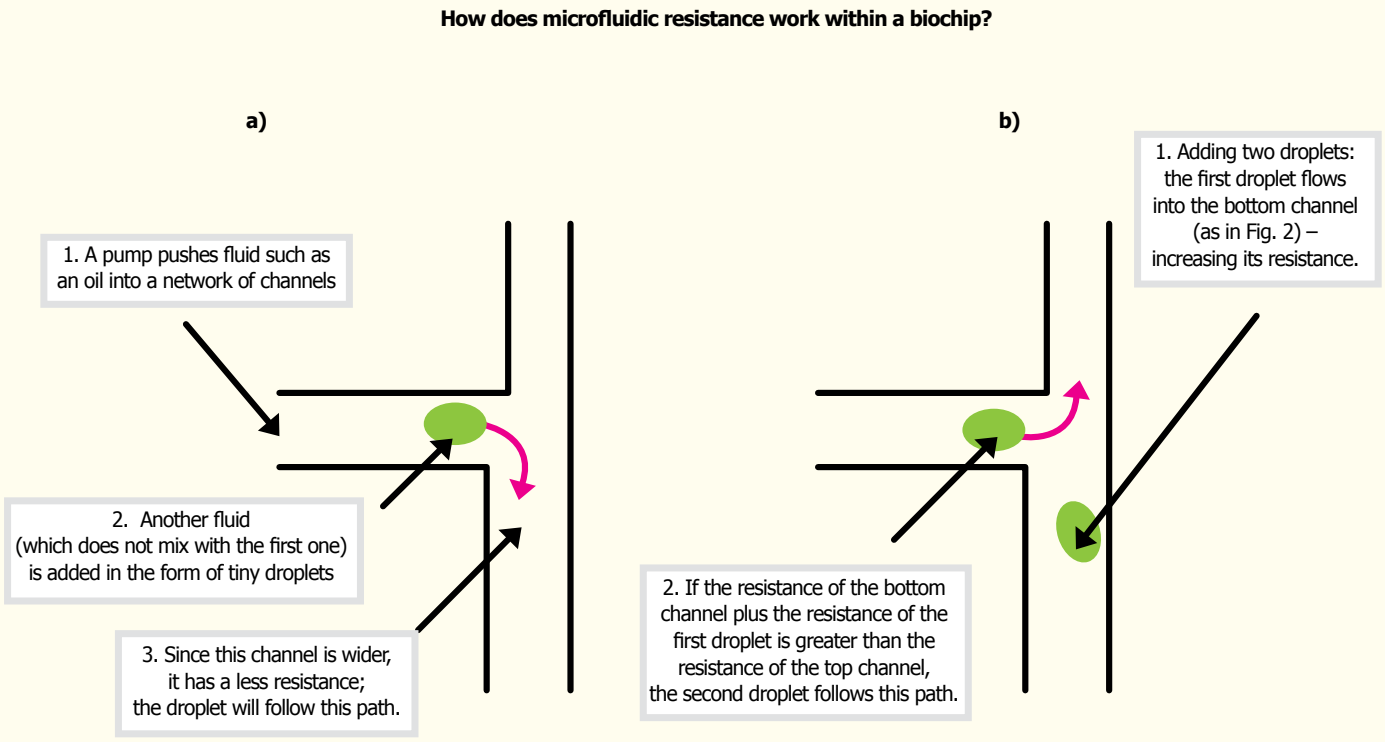

Figure 2:
a) The single droplet will move into the bottom channel (since the bottom channel is wider and, hence, has less resistance)
b) However, the presence of a droplet increases the resistance as well. The first droplet, which is already present in the bottom channel, increases the resistance of the bottom channel. This allows us to make a second droplet move upwards, into the narrower channel.

Methods

We used the similarity between biochips and electric circuits to develop a simulator. The pressure of the pump equals the voltage, the flow rate equals the current, and the microfluidic resistance equals the electric resistance. With this in mind, we calculated how a biochip would behave.

We used chips we had developed previously as a control case. The previous chips were designed to discover a drug to treat *Alzheimer's disease*.

1. In our previous experiment, we had to manually do all the calculations to design the chip. We calculated all the channels' dimensions, the applied pressure and the flow rate. This process yielded a total of six possible chips.

2. Then we made these six chips and tested them to see whether they behaved in the way we expected and selected the best version for the job.

To test our simulator we compared its results to the outcomes from the six existing chips described above.

Results

Using the simulator we tested the six chips from our previous experiment. We were able to confirm before making any chips what we had found out after making the six original ones: one of the designed biochips was working as desired. We found that our simulation perfectly predicted how droplets would behave in the real biochip (Fig. 3).

Please see Figure 3 Page 3

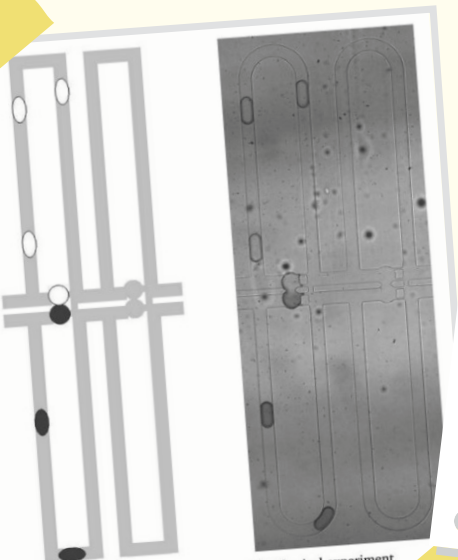

Figure 3: In these screenshots from our video (see https://youtu.be/f5v9KlGIQB4) you can see that the physical chip performed in exactly the way that the simulator predicted. The droplets moved at the same rate and occupied the same positions.

Discussion

We strongly believe our simulator could greatly help in the design process of biochips. What took a month and $1200 to achieve before, took us one day and $200 with our simulator. With our approach we were able to accurately pick the working chip before making any of them, proving that our simulator works.

Moreover, designers could use our simulation to explore many possible chips. They could easily test multiple variations of a biochip before physically making it. Rather than using a 'trial and error' approach, the simulator proposes which chip design will be the right one for the job. Less information needs to be entered by the designer, and fewer actual chips need to be made.

Perhaps in the first study there might be a seventh chip – even better and more efficient than the working one. It would have been very expensive to try and test for it without a simulator. The simulation allows researchers to test out possible chips and find the right one in a matter of hours.

Conclusion

Simulations are often very helpful as they allow us to predict some events with a great amount of certainty. They also allow us to control factors which we can barely control in real life.

Sounds fun? Anyone can try our simulator for biochip behavior here:
http://iic.jku.at/eda/research/microfluidics_simulation/

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https://pubs.rsc.org/en/content/articlelanding/2018/ra/c8ra05531a

What is Lab-on-a-Chip?
https://www.news-medical.net/life-sciences/What-is-Lab-on-a-Chip.aspx

Microfluidic droplet production method
https://www.fluigent.com/microfluidic_droplet_production_method/

Glossary of Key Terms

Alzheimer's disease – a chronic disease which leads to (a slow) degeneration of nerve cells (neurons).

Biomedical – application of natural sciences, i.e. the biological and physiological sciences, to clinical medicine.

Flow rate – the volume of fluid which passes per unit of time (for example liters per second).

Incubation – keeping substances at the right temperature and other conditions for a certain period of time in order to observe a possible reaction.

Lab-on-a-chip – a device which can automate several laboratory techniques in a single tiny chip. A biochip is a type of 'lab-on-a-chip' and is capable of performing thousands of simultaneous chemical/biochemical/biomedical reactions.

Microfluidics – science which studies the behavior of fluids in tiny channels.

Resistance – in electricity - the opposition to the flow of electric current; in fluid dynamics (and microfluidics) the resistance is a force which acts opposite to the flow rate.

Check your understanding

1 What are some advantages of using biochips?

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2 What is the current design process for biochips (before our approach)?

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3 How does our simulation make this process easier and better?

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4 How do scientists direct the droplets' movements?
