

Microfluidics Design Project

Human-body-on-a-chip architecture for testing and fabrication of biological agents

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1 Introduction and Intended Purpose of the System [10 marks]

This human-on-a-chip design is intended to act as an experimental test bed to test out new medication and the effects of other foreign substances on the physiological function. The device shown in this report can act as a base for the research and development of even more advanced versions of the human-on-a-chip design as the device describes here is a basic three organ layout connecting the heart, lung, and the liver creating a pseudo human being for testing.

The driving force for envisioning a device like this was to eliminate the need for testing medication/drugs and foreign agents on non-human test subjects like mice. As it is clear with common sense that mice are not an accurate representation of the human physique. Also testing out experimental treatments on real humans is also not ethical as this can lead to severe damage or even death if the substance tested is not complete. So, in order to tweak the chemical composition, a more real-life alternative was to design a device which can sustain living cells and they will not lose their function as the objective is to mimic conditions in the living body in real time.

This approach will work as a cost-effective solution and has the potential to rule out human trials altogether as making a microfluidic chip as close to the human body with cells extracted from a human will give immense opportunity.

Also, in cases where mainstream medication doesn't work for a certain individual, the specific chemical composition of a medication can be altered and tested on the human-on-a-chip designed with the person's stem cells so that effects of the foreign substance can be observed on the specific individual.

In real life, some people may have allergies to certain medication so this device can open a whole new avenue of personalized medicine.

2 Technical Specification: Channel Design [10 marks]

2.1 Problem Definition

A microfluidic channel should be adequate to let the specific fluid flow through. Therefore, the channel should be designed with the working fluids property in mind like density, bouncy and viscosity.

If the channel is designed to ferry lymphatic fluid for example, the channel needs to be properly permeable so white blood cells can travel freely in the channel-microchip interface.

Moreover, the channel might have to be flexible to a certain degree as in some applications, the channel might be mimicking the natural expansion/contraction of a blood vessel or lymph node.

2.2 Design Requirements

2.2.1 Functions

Now since the specific channel for the project at hand is an extension of the organ on a chip concept, different types of channels for different types of microfluids are needed

The principal functions of the circulation channels are transporting physiological agents like enzymes, blood cells and proteins.

Permeability is the other primary objective as the channel is adequately designed to let osmosis and diffusion occur.

2.2.2 Objectives

The entry points for the microfluidic device are going to be mostly made to be a valve as to not allow two directional flows.

The wall of each channel will be free to move laterally to a certain degree of freedom.

The double exit valves are designed to be a redundant system in case of overload for any component.

Each valve will be designed to have a certain maximum pressure threshold as to mimic the aortic valves.

The convoluted duct inside some channels is used to increase the surface area for better absorption.

2.2.3 Constraints

One of the most important factors is that the channel can handle adequate flow rate of the designated fluids. This must be done with selecting materials which are selectively permeable. In the materials section, the use of selectively permeable and wettable materials is discussed, and this satisfies the constraint of flow rate control.

In terms of letting fluids with different permeability and properties flow, specialized surface modifications like coatings were added and this satisfies the constraint of having control over what flows through the channels.

For example, on the lung-on-a-chip, a special polydopamine coating was added to give proper conditions to the epithelial cells of the bronchial tissue [1] and act as an adhesive agent.

3 Technical Specification: Material Selection [10 marks]

3.1 Problem Definition

When it comes to choosing a base for the material, it is always preferable to use a polymer which has characteristics like ductility and flexibility.

3.2 Design Requirements

3.2.1 Functions

The chosen material is a PDMS based material which is used as the base because whatever material is included, must follow certain characteristics which should be chosen for with the channel design in mind

3.2.2 Objectives

The PDMS material will be established as the base for the integration of all the chip components

The material will be providing structural support for the organs. The interface between two plates in the lung and liver structure has variable thickness for the permeability of the material.

Moreover, the modularity of different chips is intended to create a seamless transition of fluid between organ for example excess liquid can be drained or it can be passed on to the kidney.

3.2.3 Constraints

The modularity of the design will make the device difficult to manufacture and it has the potential to make the fabrication process more expensive.

In the fabrication process, there were limited success to make the cost go down but overall, this aspect was satisfied

Time consideration is also a big factor if the device needs to be fabricated in a short time. In preliminary fabrications, it can be said that the time constraints are not satisfied but it is projected that with a streamlined process, this can be eliminated, and the time constraint and cost can be satisfied.

4 Technical Specification: Surface Modifications, Biocompatibility and Sterilization [10 marks]

4.1 Problem Definition

Surface modifications must follow a pattern of accommodating different needs for different Organ-on-a-chip designs as not all organs function the same way and also operate in the same way.

So custom fabrication techniques and modification is needed for each one of them, for example the heart on a chip design is made to be run in extreme stress as a pumping mechanism is in place as opposed to the liver which does not have the same muscles so they need to be modified differently

4.2 Design Requirements

4.2.1 Functions

The decision to use PDMS was made because plasma treatment can make this material selectively hydrophobic in certain places.

Moreover, specialized coatings can be used in some parts of the microfluidic device.

A lipid-based coating is used to control the wettability of the microfluidic channel to properly calibrate the flow rate of different biological fluids.

4.2.2 Objectives

Selective wettability [1] was the precedent here. The coating for example is applied in varying thickness throughout the channels to keep the flow rate within bounds of the materials tolerance.

The surface valves in the entry and exit points of the channels maintains a steady flow rate and prevents backflow of fluids.

The polymer-based collars at the entrance re-enforces the fluid so it acts as a leak preventive measure.

The lipid-based coatings used also doubles as a protective coating in case of agitation by the elements as sometimes it is not possible to create the outside environment just like inside the body

4.2.3 Constraints

The constraints for a surface modification technique were the fact that as different organs have different flow rates going in and out, it was very integral to the function of the device to make sure it mimics the real flow rates and in cases where some

physiological functions are scaled down, it can properly calibrate the rate of fluid flow. In this case this specific constraint was properly satisfied.

In case of each distinct organs, different types of binding agents were used so as not to put the cells in a foreign environment where they are not used to be in.

This is also satisfied as one single binding agent cannot be used as the goal is to let the cells function in their natural habitat.

5 Analysis of Design and Conclusion [10 marks]

5.1 Summary of design

The achieved design features a three-organ layout to mimic a circulation flow of blood. This is primarily designed to act as a test bed for testing out new experimental medication of mainly the three organs used, the heart, lung, and the liver.

For clarity, a new blood pressure relaxing agent can be introduced in any one of the channels and the flow can be directed toward or away from the lung to see how the new drug affects the function of detoxification by the liver.

It has been seen in many cases that heart medication can affect organs like kidneys and livers as they have long convoluted flow paths, and the introduction of a heart rate medication can overly relax the blood vessels in the liver and kidney causing kidney failure in extreme cases. So, testing out new drugs on a test bed closely resembling the human body is a huge advantage.

One of the other most important property of this design is the harvest of important hormones as this can also be used as a platform to create synthetic materials like insulin in a cheap manner.

5.2 Limitations and Risk Analysis

As with most things which are designed for biomedical use, strict quality control and scrutiny is to be done on this device and one of the potential points for failure is the accidental backlog of blood. As mentioned earlier, multiple valves are placed along entry and exit points to ensure no backflow happens but still if by any chance the pumps exert excessive pressure, some ruptures or backflow might happen in the microfluidic chip causing the test bed organs to be damaged.

Moreover, since many channels in the device will be interconnected with other channels from a different organ, sometimes non-detoxified blood might flow out from the liver and go into the heart channels damaging the heart cells.

6 References [5 marks]

7 Bibliography

[1 [Online]. Available: https://link.springer.com/referenceworkentry/10.1007/978-0-387-48998-8_1503#:~:text=Surface%20modification%20techniques%20can%20be,and%20capillary%20effects%20%5B2%5D.. [Accessed 13 April 2023].

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9 Appendix





