Reusable Microfluidic Device for HIV Detection

Zachary Niswonger, Sean Sullivan, Jessica Timog, Anjali Senthilkumar

Background

Human immunodeficiency virus (HIV) can have a devastating, often fatal impact on the immune system. HIV is most often transmitted through bodily fluids. Unprotected vaginal or anal sex, sharing of needles, and childbirth with an HIV-positive mother can all lead to new infections. This disease attacks human T-cells, inhibiting their adaptive immunity and capacity to respond to pathogens. The virus also infiltrates T-cells and hijacks their reproduction mechanisms, forcing them to manufacture new viral copies and enabling further spread of the virus [4].

If left undetected, patients with T-cell counts of <200 ppb have AIDS, a stage that leaves the immune system so depleted that even a minor cold can kill a patient [3]. The progression of this disease can be prevented by early testing if the patient suspects possible exposure. Our lab-on-a-chip utilizes existing technologies to provide the rapid testing necessary for the best patient outlook.

The T-cell response to infection is shown below in Figure 1.

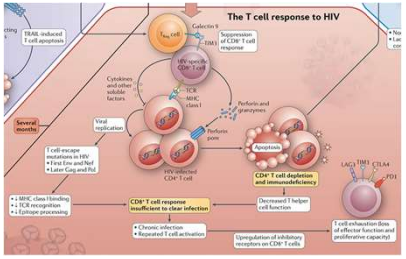

Figure 1: Image displaying immune system's reaction to HIV (STEMCELL Technologies)

Significance

The prevalence of HIV is alarmingly high in undeveloped countries, whereas developed countries with more access to testing have far fewer issues with HIV [7]. These developed countries make use of early detection and antiretroviral testing to reduce HIV to an almost undetectable level [4]. Regions such as Sub-Saharan Africa have yet to see such success [8], and an affordable, repeatable, rapid testing device could drastically improve their ability to treat HIV. The lack of established healthcare networks and transportation infrastructure make current methods such as antibody and antigen testing unfeasible as they require samples to be transported and undergo complex testing. Our device will allow for rapid, reliable HIV testing in doctors' offices around the world.

Design Components

- **Detection Method:** Our device detects the p24 protein, an HIV specific protein, using Plasmonic ELISA, which was chosen for its simplicity and ease of use, as it results in a color change visible to the naked eye [2]. Other methods such as standard ELISA needlessly complicated the design. Plasmonic ELISA functions due to the redox reaction that occurs between the reagents, as illustrated below in Figure 2, resulting in a blue color in p24 positive samples and a red color in p24 negative samples [2].

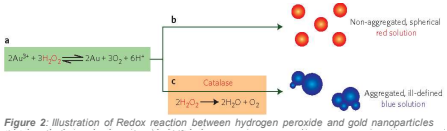

Figure 2: Illustration of Redox reaction between hydrogen peroxide and gold nanoparticles that results in a pronounced color shift

- **Filtration Method:** Plasma was required to more easily detect color changes, but traditional methods like centrifugation as it was not feasible at such a small scale and chose bifurcation as our method of filtration. This works by creating channels with a lower flow rate that branch off of the main channel, which leads to red blood cells staying in the main channel while plasma enters the side channels [6]. This is due to the law of bifurcation [6]. An illustration of this can be seen below in Figure 3.

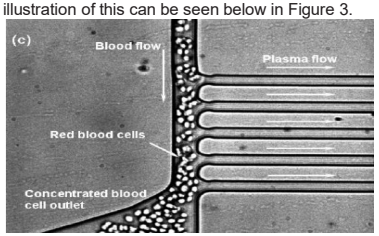

Figure 3: Image displaying filtration via bifurcation that will occur

- **Fluid Movement:** First, a peristaltic micropump is used to move fluid through the plasma filtration region. This was chosen over methods like piezoelectric pumps as it was completely external and provided great flow control which was desired [1]. This pump works by sending periodic negative pressure waveforms through PDMS layers, generating periodic flow[1].After filtration, the plasma is moved to the detection chamber using a finger pump, which was chosen for its high ease of use and construction. This finger pump works simply by having the user press on the PDMS surface, increasing pressure which forces the plasma to flow [7]. Once in the detection chamber, texturing will be used to mix components, which was chosen for its lack of mechanical components required and simplicity in comparison to other methods [5].

Final Design

The chip will be made of PMMA, with the channels being cut using UV microchanneling. The finger pump will be made of PDMS and will be attached separately. The final design can be seen below in Figures 4 and 5, with Figure 4 being the chip bottom and Figure 5 being the chip top.

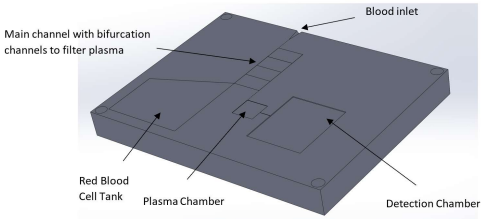

Figure 4: Labeled Solidworoks model of the chip bottom, illustrating all important features

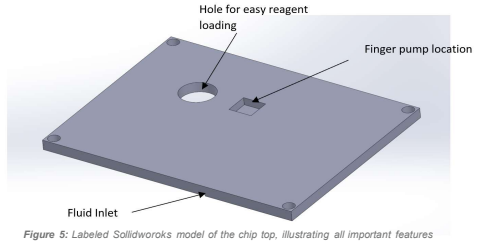

Figure 5: Labeled Solidworoks model of the chip top, illustrating all important features

Blood Processing Algorithm

1. Collect 1-2 mL of blood using a new syringe, ensuring the environment is sanitary.
2. Insert sample from syringe into tubing of peristaltic pump.
3. Pump sample into inlet through secondary syringe that connects pump and chip inlet.
4. Blood flows through the 5 bifurcation channels in order to filter blood and obtain plasma
5. Due to bifurcation, red blood cells continue to flow down main channel into separate chamber
6. Plasma enters side channels due to bifurcation and flows off to separate chamber
7. Plasma all gathered in one chamber for testing
8. Plasma pumped into detection chamber manually using a finger pump.
9. The presence or lack of p24 protein in plasma causes a color shift in detection reagent
10. Color shift is observed by human eye and compared to key
11. Test is determined to be positive or negative based on color change, color change will be easily seen by human eye

Future Work

- Construct prototype chip
- Test accuracy of chip design in a clinical trial or similar experiment
- Determine relative amount of false positives and negatives and work to reduce them
- Optimize reagent mixture for detection to minimize cost by testing lower concentrations of reagents and testing effectiveness compared to the initial

Conclusion

With recent advancements in HIV treatments, patients that have been diagnosed early can still have a great outlook. This makes this lab-on-a-chip design even more important, as it allows whole communities to have access to easy, inexpensive, rapid HIV testing. Especially in less wealthy communities, this lab-on-a-chip can give patients a much better outlook and the chance to seek treatment much earlier.

References

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ACKNOWLEDGEMENTS

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What To Expect:

- **Background, Significance:** Jess Timog
- **Design Components:** Zach Niswonger
- **Final Design, Blood Processing Algorithm:**

  AJ Senthilkumar
- **Future Works, Conclusion:** Sean Sullivan

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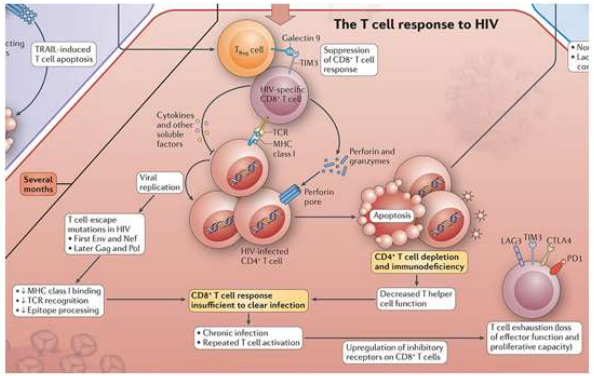

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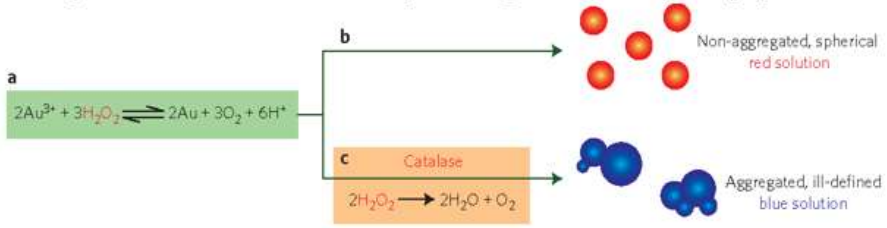

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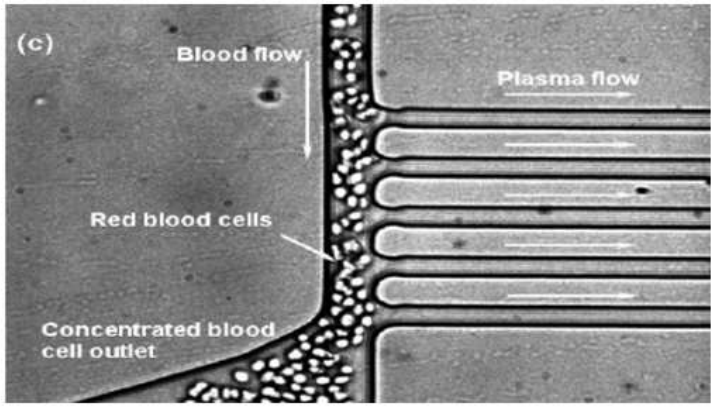

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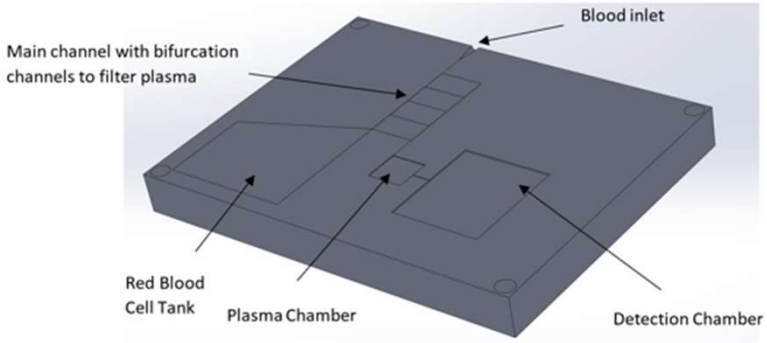

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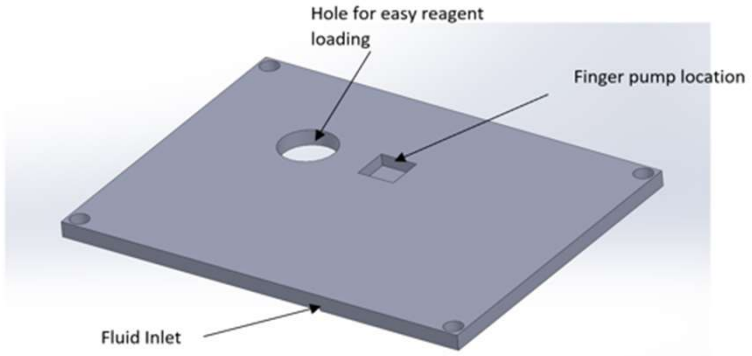

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