Point of Care Anemia Device

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Client: Dr. Philip Bain
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Motivation

- Anemia is a deficiency of the hemoglobin in the blood[1]
  - Characterized by abnormal size, shape, and reduced number of RBCs[1]
  - Quantified by measuring hemoglobin and mean corpuscular volume[1]
- Prevalent in underdeveloped countries, due most commonly to malnutrition[2]
- Anemia affects roughly twenty-five percent of the global population[2]
- Highest prevalence is in Africa, making up about sixty percent of those globally affected by anemia[2]
- Most types are not only treatable but can be prevented[2]
- Lack of funding and resources for complete blood tests in these developing countries block the ability for clinicians to properly diagnose anemia and suggest treatment[2]

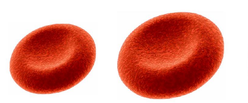
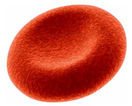


Figure 1:
Microcytic: MCV < 80 fL

Normocytic: MCV = 80-96 fL



Macrocytic: MCV > 100 fL

Figure 2: Client's organization: brings medicine to underdeveloped countries

Problem Statement

- A portable, easy to use, and cost-effective device is needed to diagnose at the point of care
- Fabricate a microfluidic device that effectively measures the MCV of red blood cells to determine if a patient has normocytic, macrocytic, or microcytic anemia

Past Work

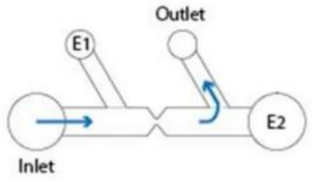


Figure 3 (Above): Channel design. The inlet and outlet represent the flow of the microparticles through the channel, and E1 and E2 represent the electrodes[3]

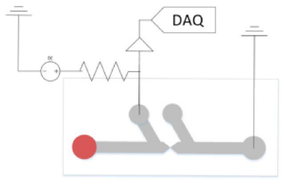


Figure 4 (Above): Circuit schematic of the electrodes that measure the resistance change across the microchannel[3]

- Continuation of a previous BME group's work
- The previous group focused on proving that particles could be recognized as they passed through a microchannel using a relatively simple circuit that functioned as a voltage divider
- Microparticles were passively pumped down a microchannel and as they crossed a small aperture, channel resistance increased therefore increasing voltage
- These changes are measurable and using the resulting peaks, particle size and number could be calculated using simple programming
- This group used microparticles as a proof of concept but believed that cells would act similarly

Design Criteria

- Device should provide an accurate diagnosis of anemia and differentiate between microcytic, normocytic, and macrocytic anemia
- Device should be low-cost and adaptable to resource-limited environments
- A clinician should be able to use the device easily and reliably after proper training with an intuitive user interface
- The device should be able to diagnose anemia at the point of care

Testing and Results

Filtering

- Created filtration device using circular polyester filter paper with 10 um pore size to separate WBCs from RBCs in diluted porcine blood
- Statistical analysis revealed filter was reducing cell count more than expected ($p < 0.0001$)
- Filtering approach was abandoned based on statistical evidence and since white blood cells only make up a small component (1%) of blood volume[4]

Table 1: Data and analysis from the filtering tests

Blood Sample (1:5000 dilution in PBS)		Cell Concentration in Square (cells/ mm²)		Cell Concentration (cells/mL)	P value
		Average per square	Avg. (n=12) +/- St. Dev.		
Unfiltered	Drop 1	64	74 +/- 14	$1.5*10^6$	<0.0001
	Drop 2	87			
	Drop 3	72			
Filtered	Drop 1	29	25 +/- 7	$5.0*10^5$	
	Drop 2	21			
	Drop 3	25			

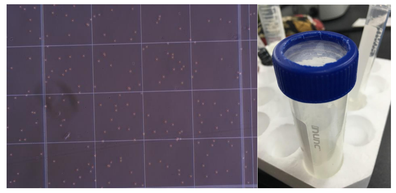


Figure 5 (Left): Cell counting using hemocytometer.
Figure 6 (Right): Filter design

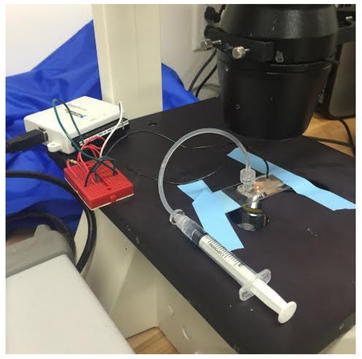


Figure 7: Testing of microchannel and syringe pump using video analysis under the microscope in the Tissue Engineering Laboratory

Pumping

- Trials were performed with diluted whole blood testing both active and passive pumping techniques
- Channel acts as a resistor, as particle passes through the channel aperture resistance increases and can be recorded
- Active syringe pumping showed large fluctuations in voltage making peaks undetectable
- Few peaks were detected with passive pumping

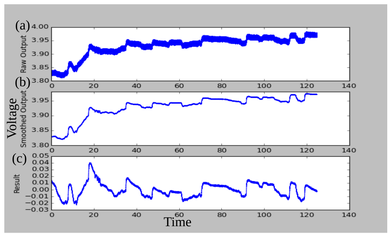


Figure 8: Voltage over time as blood cells were actively pumped through micro-channel. (a) The raw output data (b) Filtered data (c) Curve fit data to level voltage

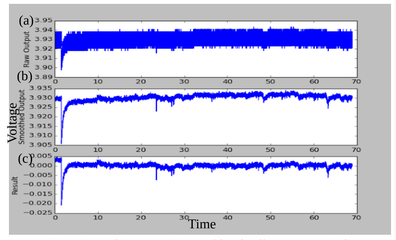


Figure 9: Voltage over time as blood cells were passively pumped through micro-channel (a) The raw output data (b) Filtered data (c) Curve fit data to level voltage

Final Design

Figure 10: The box connects from the NI-DAQ to a computer which reads data through a custom LabView script

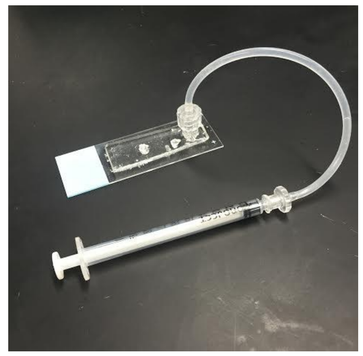


Figure 11: Channel is connected to the syringe through tubing and a series of Luer lock attachments

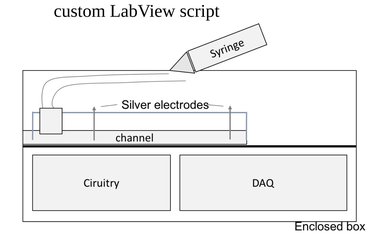


Figure 12 (Left): All of the components of the final design enclosed in an electrical box. Syringe attaches at an inlet port at the top. Tubing attaches syringe to channel. NI-DAQ and circuitry located at the bottom

Future Work

- Short term goals:
  - Redesign the device's channel
  - Create an automated active pumping mechanism
  - Find relationship between voltage and cell volume
  - Test unit as a whole
  - Receive IRB approval to test device with human blood
- Long term goals:
  - Replace current circuitry with microcontroller
  - Attach screen to box that displays MCV
  - Test device with clinicians in low-resource settings

Figure 13: Potential future channel design

Acknowledgements

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Advisor, Dr. Thomas Yen
Department of Biomedical Engineering

References

1. Mayoclinic.org, 'Anemia Symptoms - Mayo Clinic', 2015. [Online]. Available: http://www.mayoclinic.org/diseasesconditions/anemia/basics/symptoms/con-20026209.
2. Who.int, 'WHO | Worldwide prevalence on anaemia 1993-2005', 2015. [Online]. Available: http://www.who.int/vmnis/anaemia/prevalence/summary/anaemia_status_summary/en/. [Accessed: 04- Oct- 2015].
3. Chiang, M., Choi, U., Enge, J., Little, R. (2015). BME 402. Development of Anemia Detection Device for Low-Resource Setting
4. Blood Basics. American Society of Hematology. http://www.hematology.org/Patients/Basics/