N.I.C.O.L.A.S.
Oral Exam

February 26, 2020

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Clinical Advisor: Dr. Susan Eagle

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Non-invasive
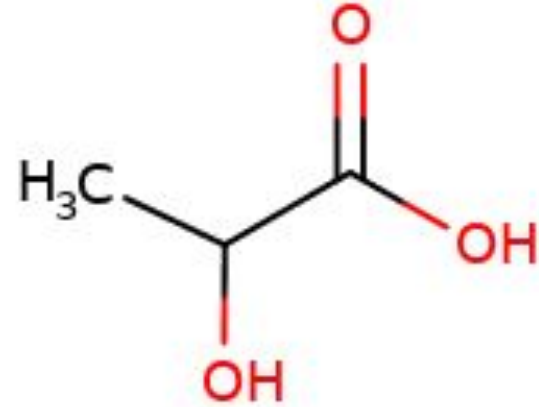
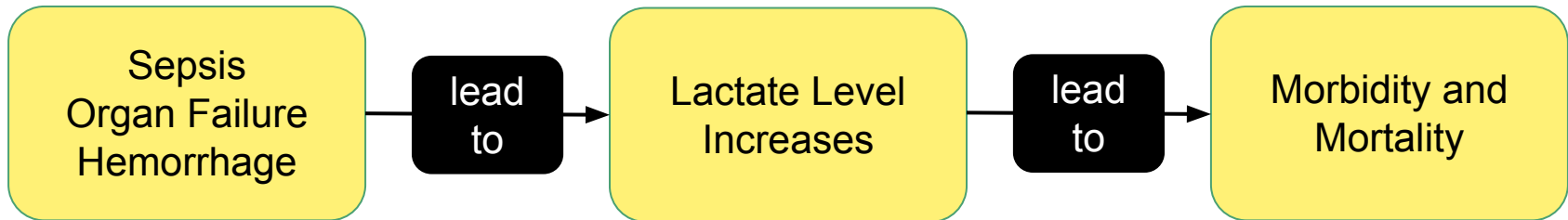**Continuous**

Optical

Lactic Acid

Sensor

Background

- Clinical biomarker used to measure tissue degradation

- Normal levels ~ 1 mM.

  - Relative > Absolute measurements

Lactic Acid
(2-hydroxypropanoic acid)

```
Sepsis                      Lactate Level          Morbidity and
Organ Failure   lead to     Increases     lead to  Mortality
Hemorrhage
```

Problem Statement

- Currently, blood lactate levels are undersampled in clinical settings, leading to undetected spikes in lactate concentration which indicate the onset of sepsis, organ failure, and hemorrhage

Needs Assessment

Patient

Insulated Device
Intermittent Pulses
Non-invasive

Practitioner

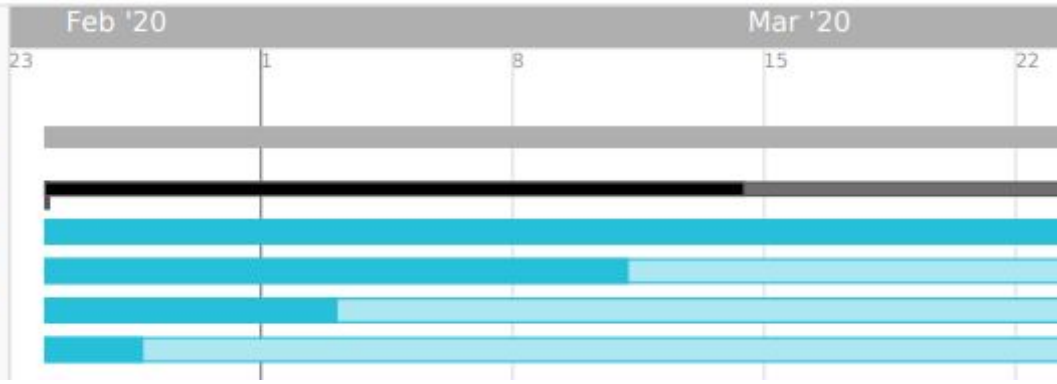Continuous Sampling
Ease of Use
Clinical Application

System

Simplest Modality
Cost Effective & Portable
Integrate with Hospital Systems

|			Feb '20			Mar '20	
			23	1	8	15	22
NICOLAS -- 2/12/20	**0h**	**36%**					
Current Tasks	**0h**	**36%**					
Circuit Development	0	95%					
Lactic Acid Absorbance	0	30%					
Research into Alternate Modalities	0	15%					
IRB Application / Process	0	5%					

This Week's Progress:

- Circuit Optimization and Data Processing

- Lactic Acid Absorbance

- Alternative Methodologies
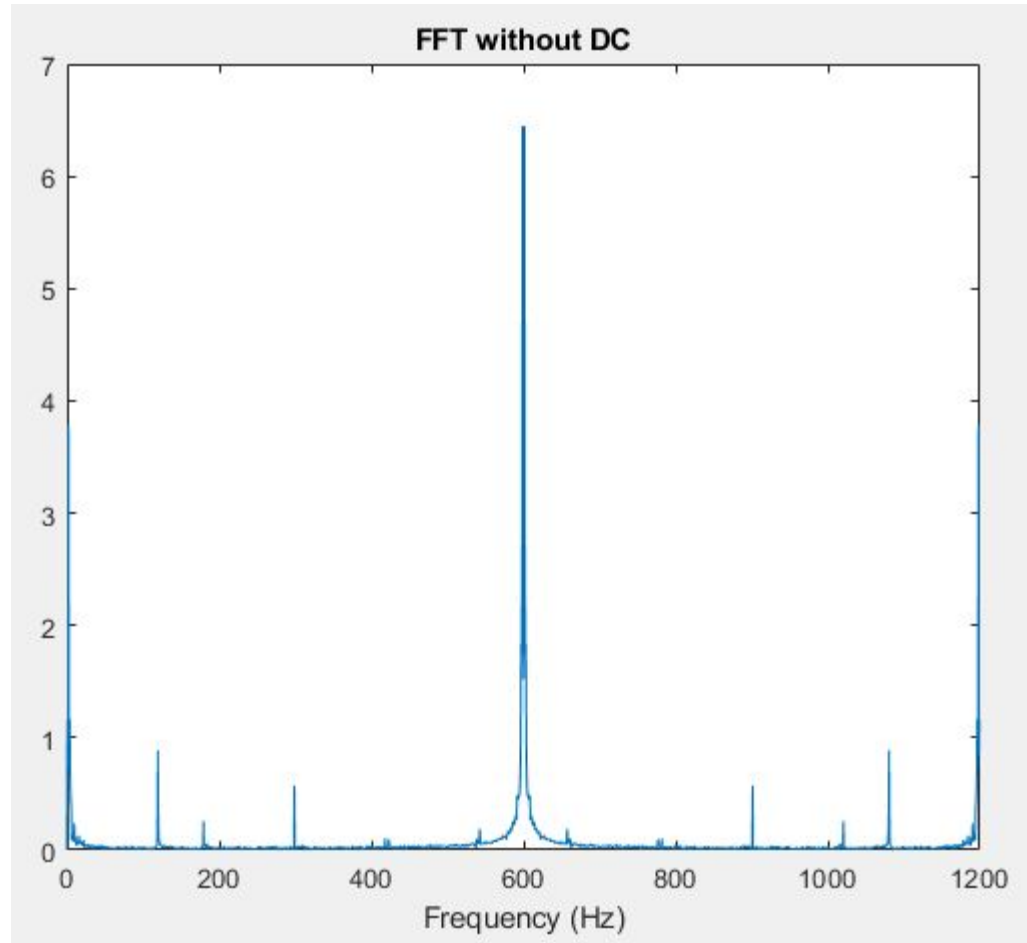
- Proposed New Strategy

Circuit Output
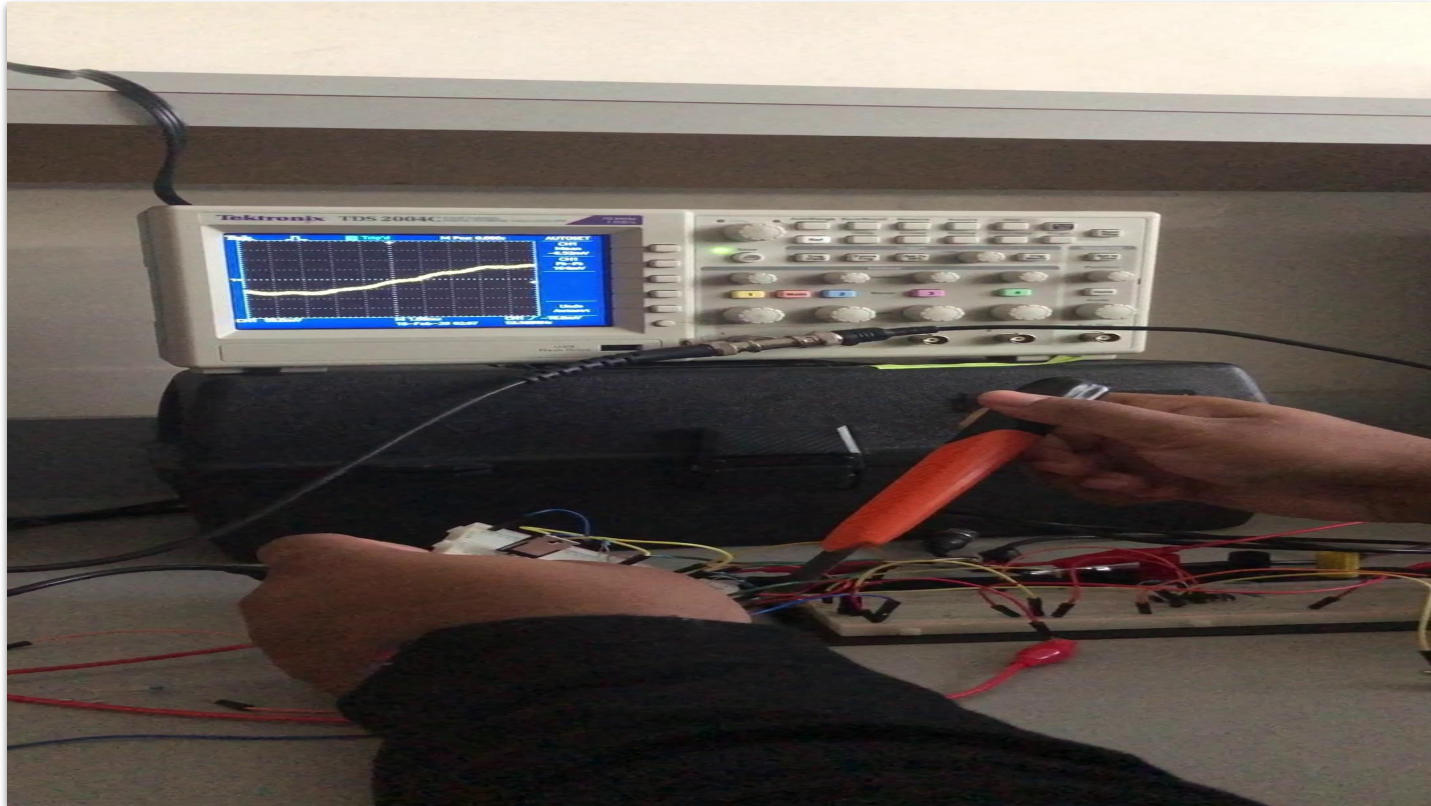
Circuit Output

- High Pass Filter-100Hz
- Notch Filter-55-65Hz
  - In LabVIEW
- Moving Average Filter
  - Window = 0.0066 s
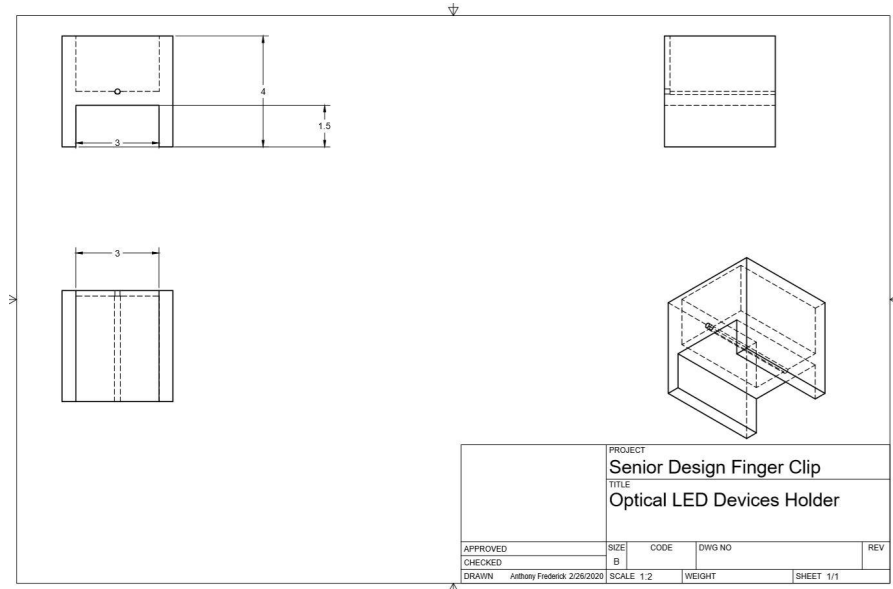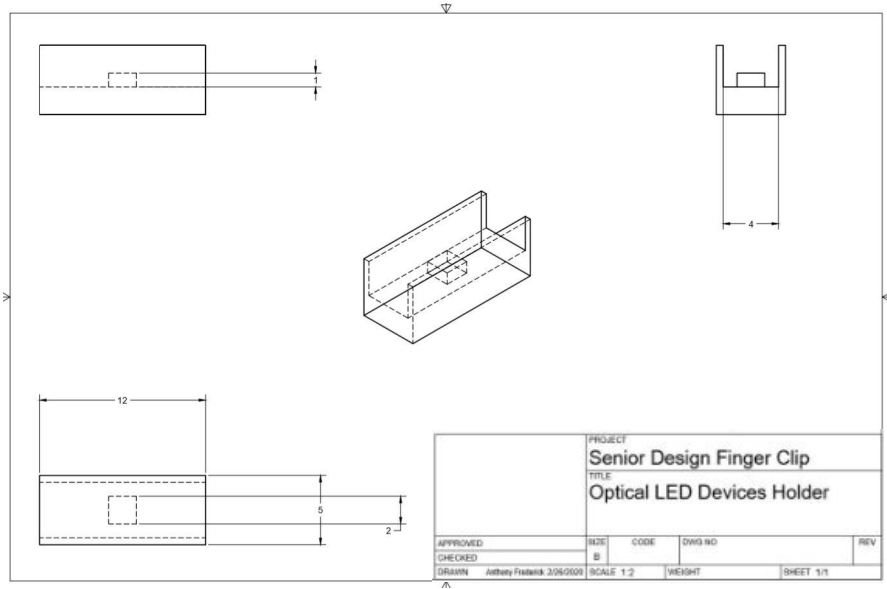 - Matlab
- No Amplification
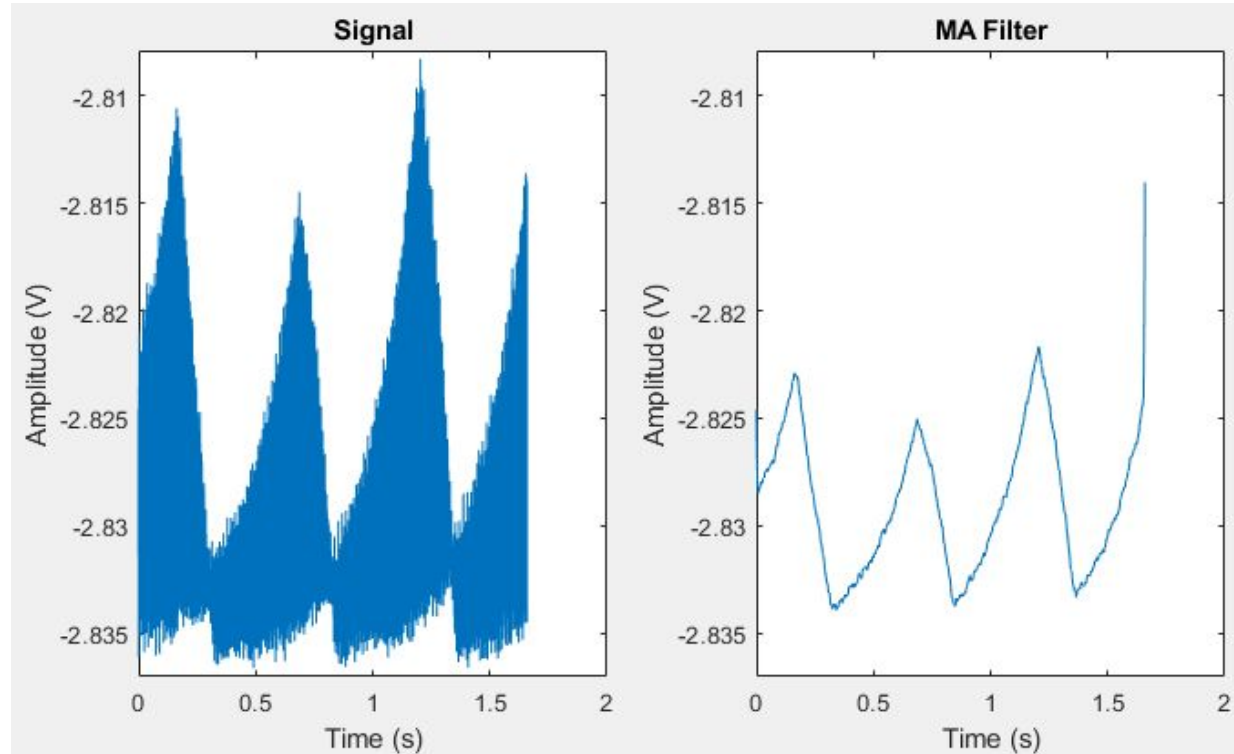
FFT of Circuit Output

```
time = table2array(data(:,1));
amplitude = table2array(data(:,2));

amp_fft = fft2(amplitude);

N = length(amplitude);
fs = 1200;
f = 0:fs/N:((N-1)*fs)/N;

figure;
subplot(121)
plot(f,abs(amp_fft))
title('FFT with DC'); xlabel('Frequency (Hz)')

% Remove the DC and represent the DFT again
amp = amplitude - mean(amplitude);
y = fft(amp,N);
subplot(122)
plot(f,abs(y))
title('FFT without DC'); xlabel('Frequency (Hz)')
```
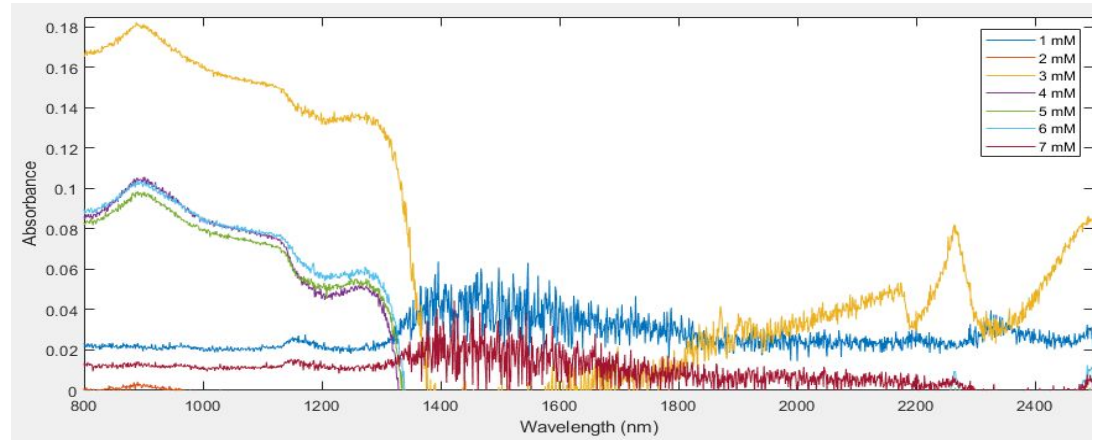

FFT without DC

Calibration for Optical Setup (inches)

PROJECT
Senior Design Finger Clip
TITLE
Optical LED Devices Holder

DRAWN Anthony Frederick 2/26/2020   SCALE 1:2   SHEET 1/1

PROJECT
Senior Design Finger Clip
TITLE
Optical LED Devices Holder

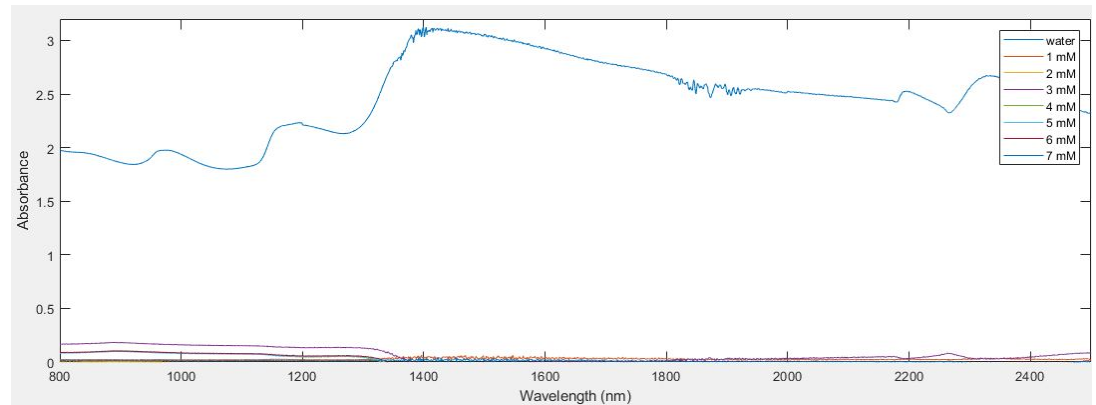DRAWN Anthony Frederick 2/26/2020   SCALE 1:2   SHEET 1/1

LA Absorbance: Recap
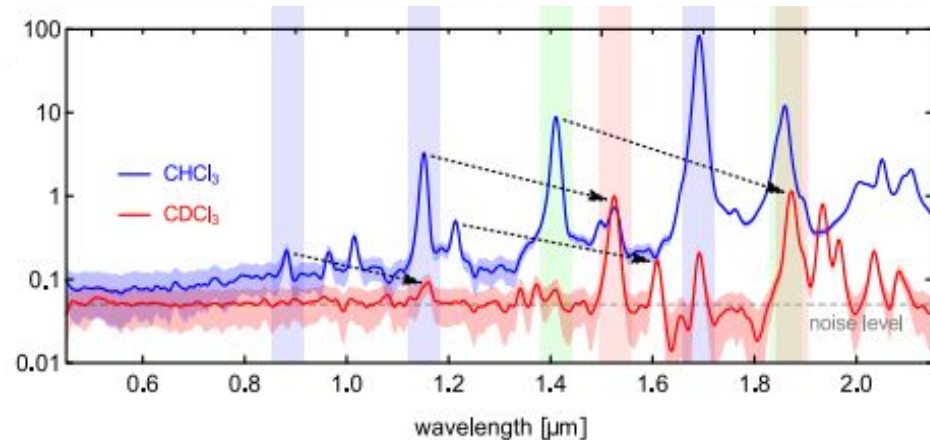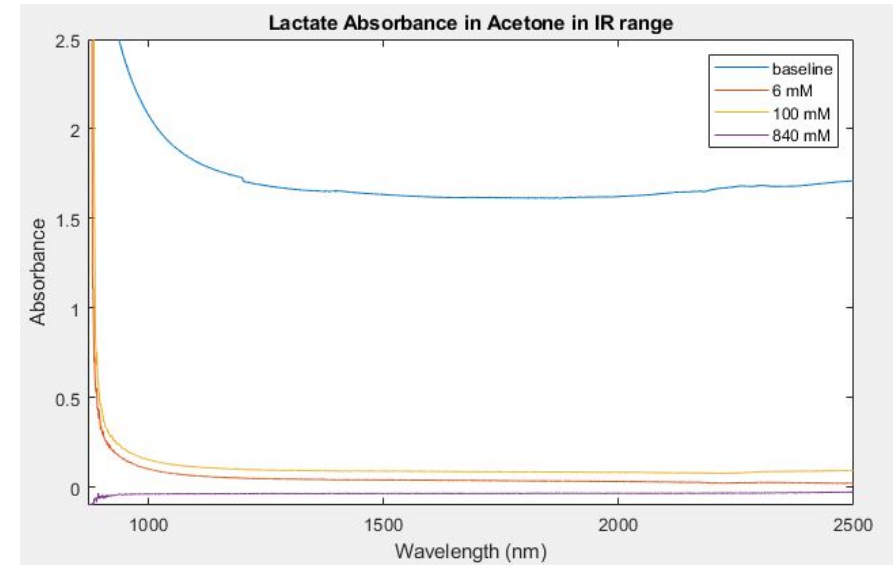
Low absorbance,

in general

Low absorbance,

relative to water

LA Absorbance: New Trials

1. Aqueous lactate in UV

2. Lactate in acetone, full spectrum

3. Lactate in 'deuterated' organic solvents

   a. Solvents show decreased absorbance with new structure

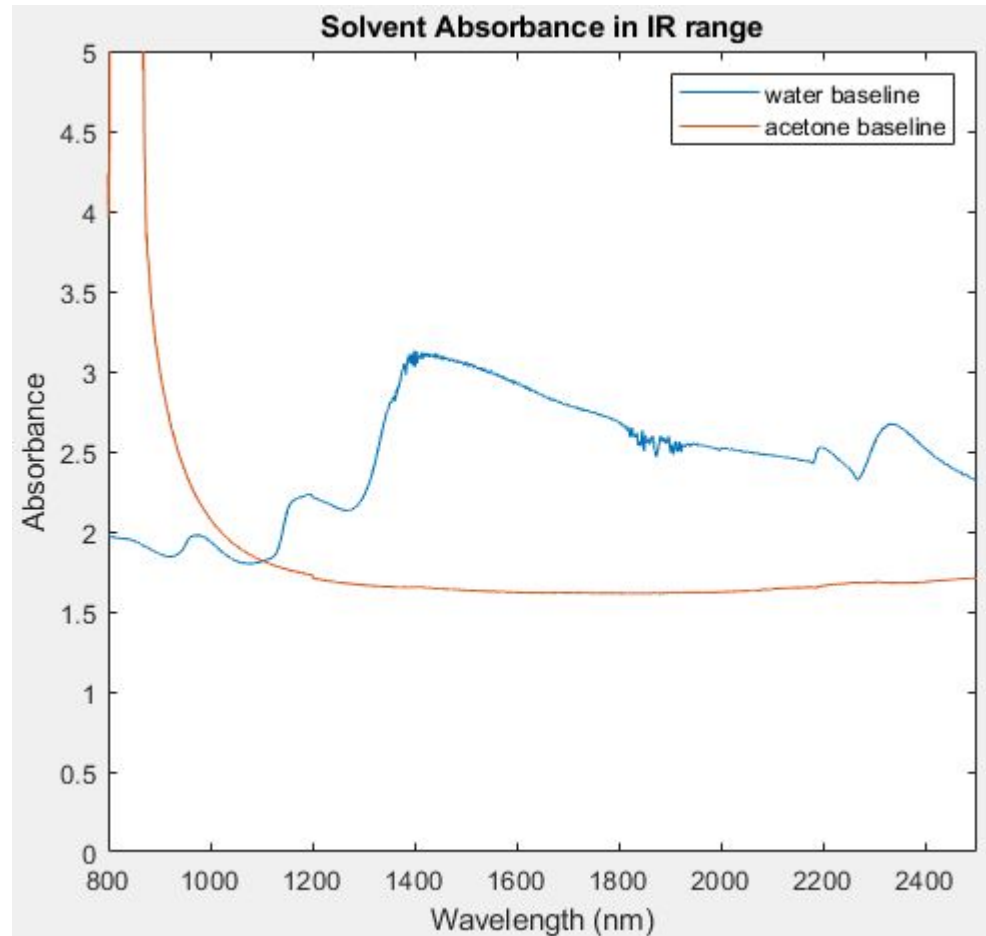   b. Allow lactate in solution to contribute more system absorbance

Solvent Absorbance

[Water] in water baseline = 55.5 M

[Water] in acetone baseline = 46.6 mM

Over 1000-fold decrease in water

Alternative Methodology

How can we detect lactate in the case that it cannot be seen in IR?

- Using Digital signal processing and analysing our data to remove baselines
  - By using Fourier transform, derivative filters of our signal, and various window widths
- Tracking LDH throughout the body because it should be alongside lactate
  - Enzymes look the same in IR
  - LDH is found in the cell
- Using biomarkers to tag lactate
 - Current modality would work but just needs a change in wavelength

Lactate Dehydrogenase
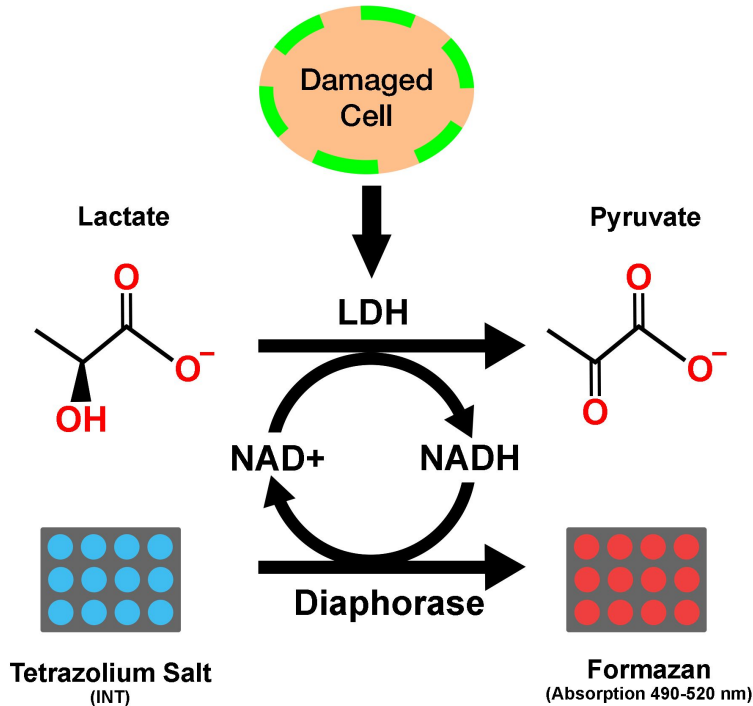
- LDH has multiple forms that can diagnose various ailments: (LDH-1, LDH-2, LDH-3, LDH-4, LDH-5)
- LDH is made from the same amino acids as everything else, cannot distinguish
- LDH is also in the cell so the assays for this all need some methodology to extract this from within the cell (lysing): takes time in modality
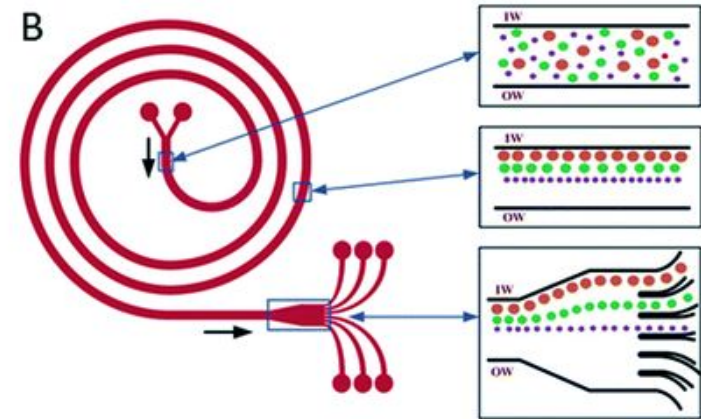
Biomarkers

- Need something that can bind with good affinity and quickly in blood
  - Are there antibodies that already do this for lactate or LDH?
- After meeting with VAPR
  - Said that a protein that binds to LDH (structure) and lactate does not exist
  - Could use an assay but would structurally alter lactate (need to be disposed)
- We need to use a current assay and search patents to use their reagents to bind to lactate.
  - WGT assays
  - Glo-Lactate assays
  - Ultra-Glo rLuciferase
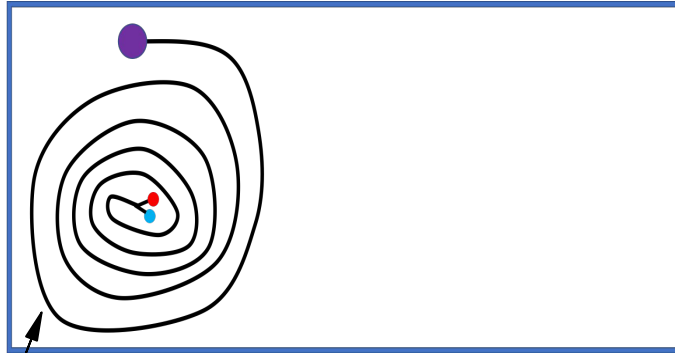 - FADH/NADH excitation
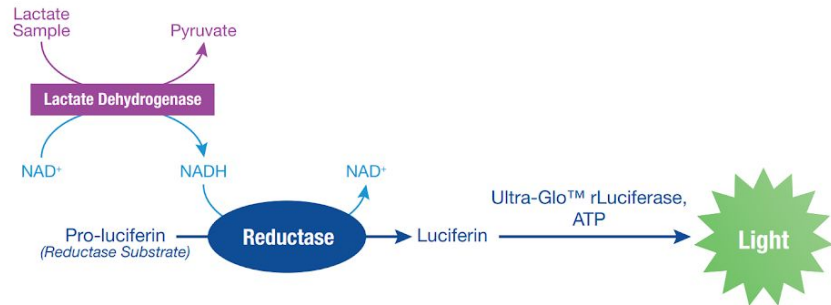
Microfluidic device

- Integrate well defined microfluidic principles into lab-on-chip system
    - Sorter, Mixer, Reaction Chamber
- Miller et al. patented whole blood filter
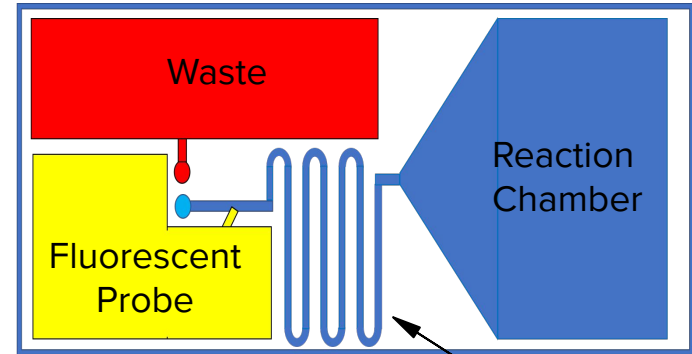- More controlled environment, better optical window, retains current hardware

https://pubs.rsc.org/en/content/articlelanding/2015/lc/c4lc01246a#!divAbstract

Microfluidic Device Concept

Top View - Layer 1

Top View - Layer 2

Sorter

Waste

Reaction Chamber

Fluorescent Probe

Mixer
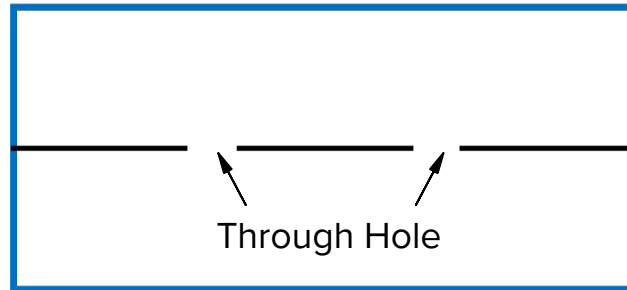
Through Hole

Front View

Outstanding Questions

- How does the pumping mechanism of the IV work?

    - Do we need to introduce our own pump?

- Patent search: how do we find the exact reagent protocols

- Reagent accessibility, how soon can we get these materials

- Our solid lactate order got sent in a week plus late. We need this soon!