NICOLAS: Progress Report

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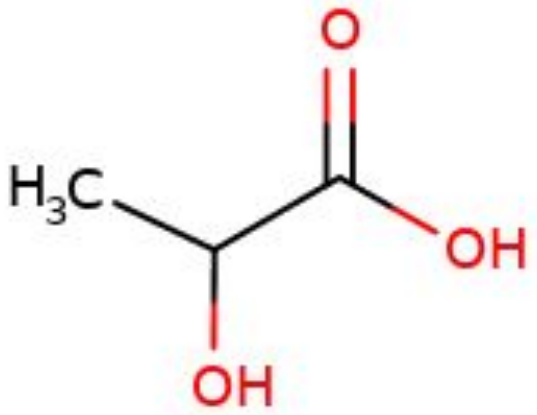
NI	Non-invasive
C	Continuous
O	Optical
LA	Lactic Acid
S	Sensor

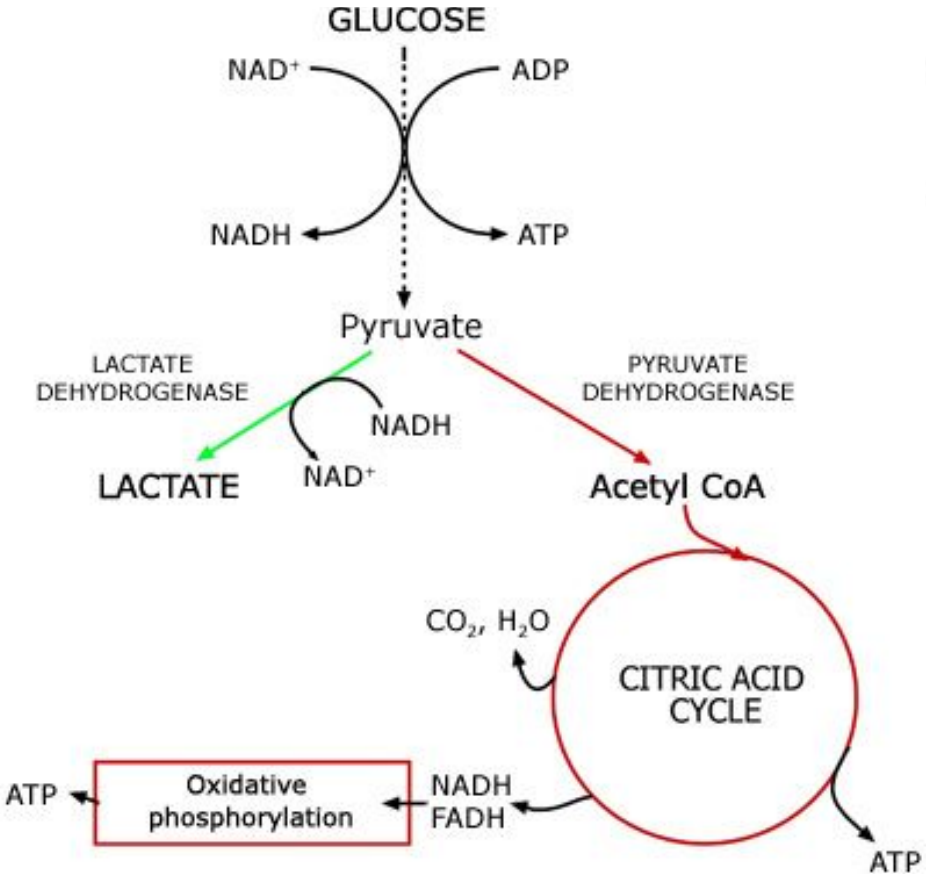
Contents

Background

- Septic shock
  - sepsis, which is organ injury or damage in response to infection
  - Causes death in 24% to 41% of cases
- Sepsis causes an increases in lactic acid
- Incrementally measured but the lactic acid can change quickly
- Want to improve response times



Biochemical Mechanism

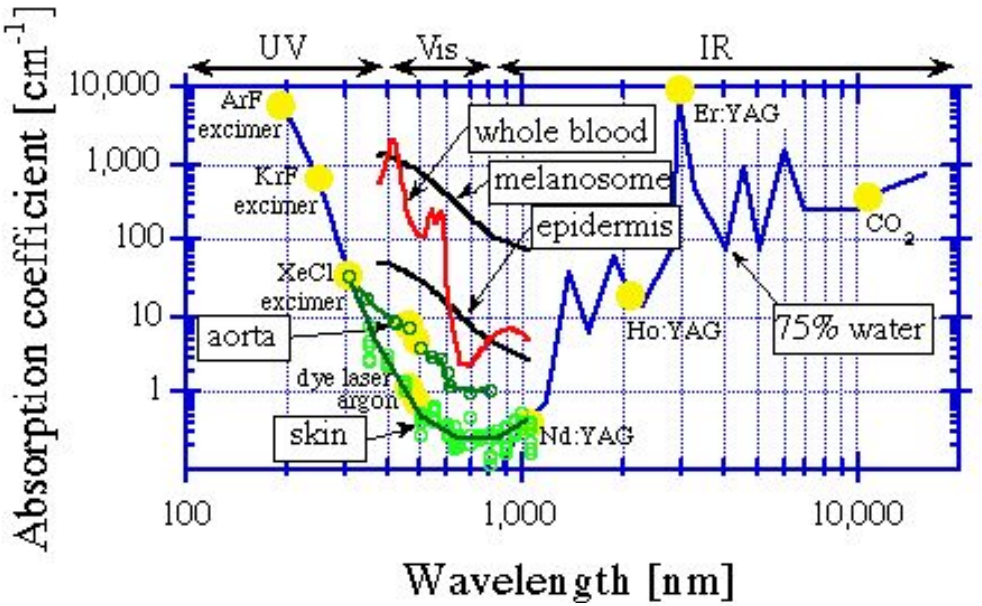


https://acutecaretesting.org/en/articles/lactate-and-lactic-acidosis

Problem Statement

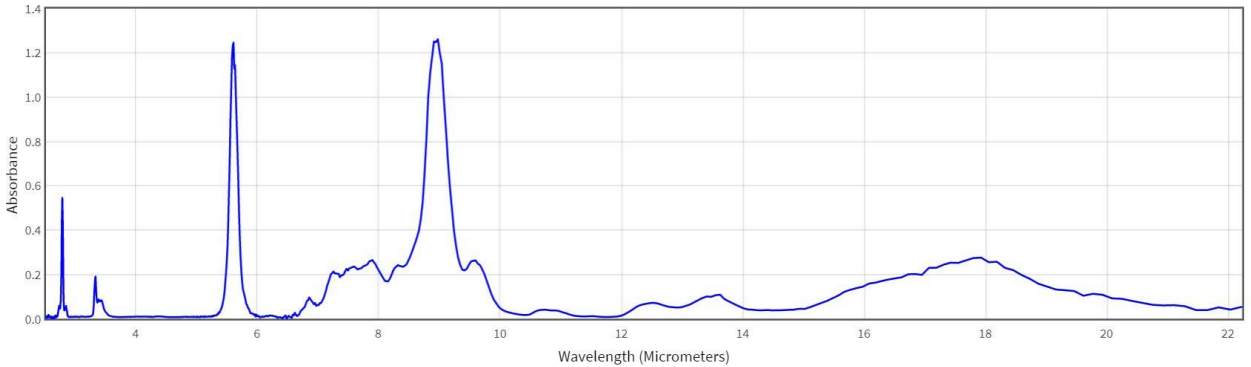
- Lactic acid is a clinical marker, measured for tissue degradation
- LA levels can predict tissue hypoperfusion, including:
  - Sepsis
  - Hemorrhage
  - Organ Failure
- Currently, LA levels monitored through intermittent blood draws; however, they do not occur at high enough frequency for real-time analysis
- Sepsis spikes can go unnoticed between draws, causing serious infection of death between typical testing intervals

Absorbance Curves

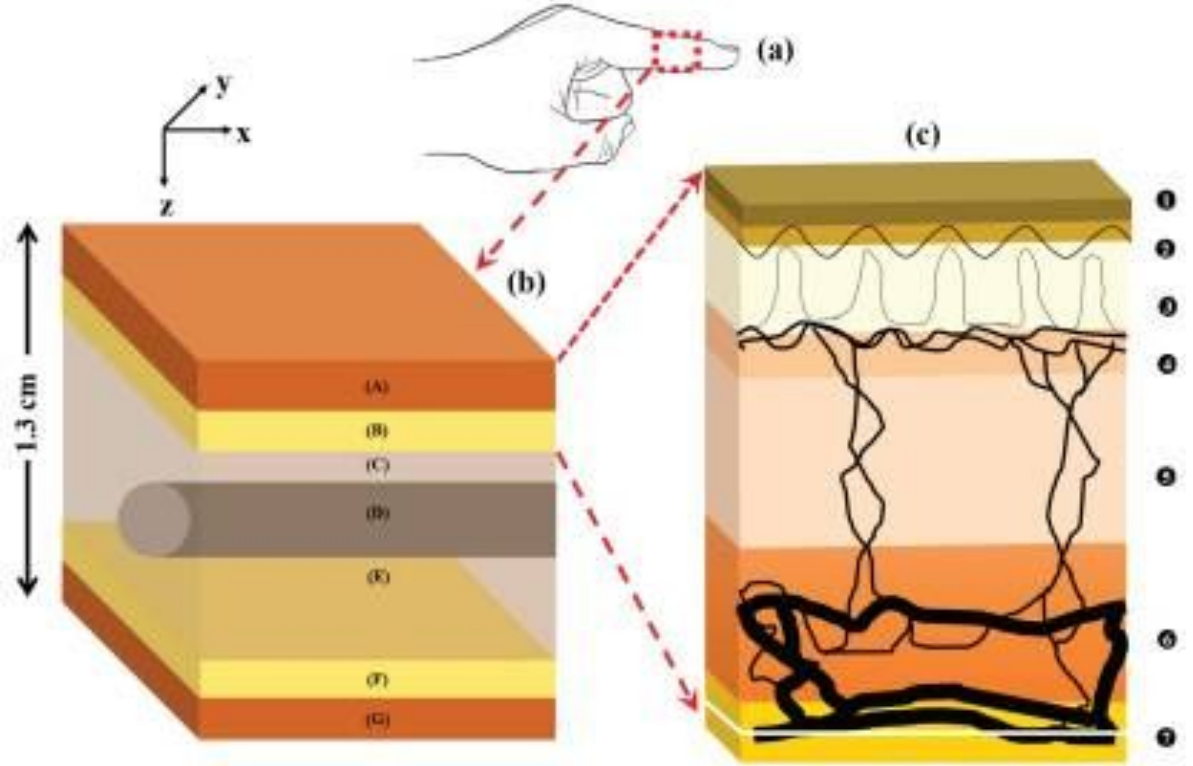


Propanoic acid, 2-hydroxy-

Infrared Spectrum

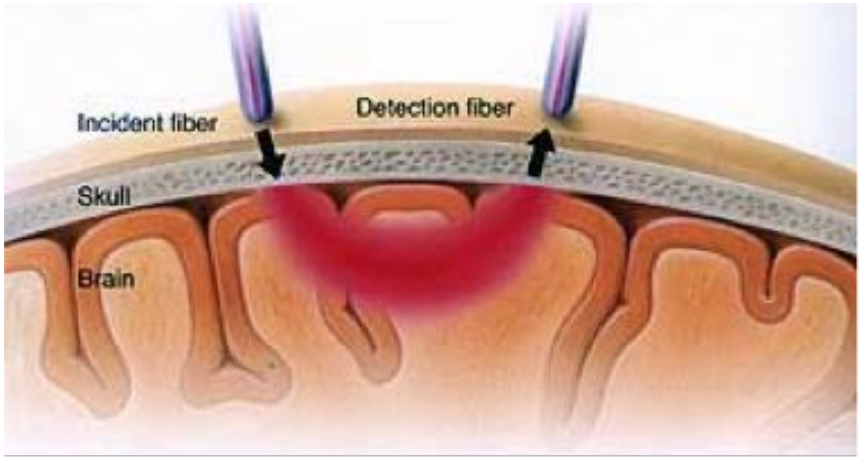


Optical Research Problems

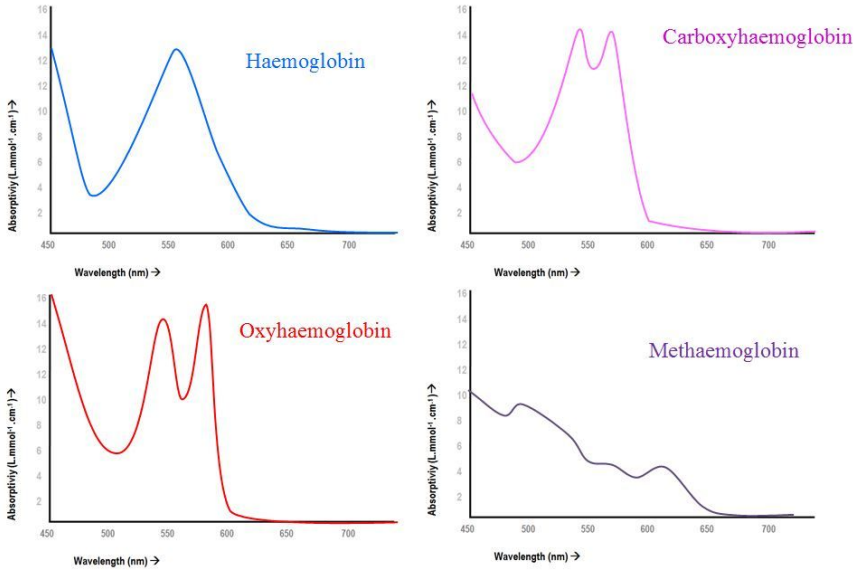


Optical Research Methods

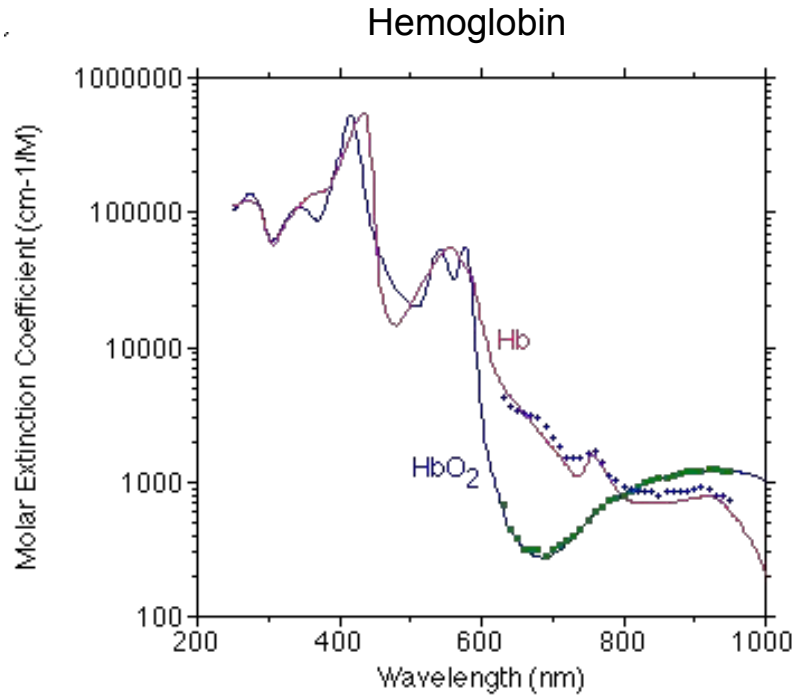
- Raman
  - Firing full spectrum at small object to determine composition
- Visible spectrum
  - Doesn’t absorb for Lactic acid
- IR Spectroscopy -- transmittance, reflectance, absorbance
- Near Infrared Spectroscopy



Peak Absorbance Wavelengths:



derangedphysiology.com



omlc.org/spectra/hemoglobin/

Needs Assessment - Patient

- The device should be noninvasive in order to test the device in the clinic.
- The device should not exacerbate hypoperfusion.
- The wavelength of infrared used should be safe for intermittent, pulsed exposure.
- The circuit components should be insulated as to protect the patient from electrical shock.

Needs Assessment - Practitioner

- The protocol should sample more continuously than the current intermittent blood draw method.
- The device should be easy to use.
- The data should be easy to analyze and interpret.
- The device should have an algorithm to detect proximity to sepsis given lactate levels and other physiological signals.
- The device should be able to be tested and iterated in clinical settings.

Needs Assessment - Device

- The device's diode should emit light near the IR range to excite lactate.
- The light should be able to be transmitted through various thicknesses of epidermis and blood vessel thickness.
  - If not, the reflectance should be able to be measured and analyzed mathematically.
- The device should be specific and sensitive to biologically sensitive markers:
  - Have the ability to distinguish between the noise in the signal
  - Have the ability to measure the signal ratiometrically relative to biological markers
- The device should be a finger clip and operate similarly to a pulse oximeter.
- The device should insulate the patient and user from heat injury.

Needs Assessment - System

- The system needs to easily integrate into current hospital infrastructure.
- The system needs to be cost-effective.
- The system needs to work in the event of power loss.
- The system should be portable and handheld.

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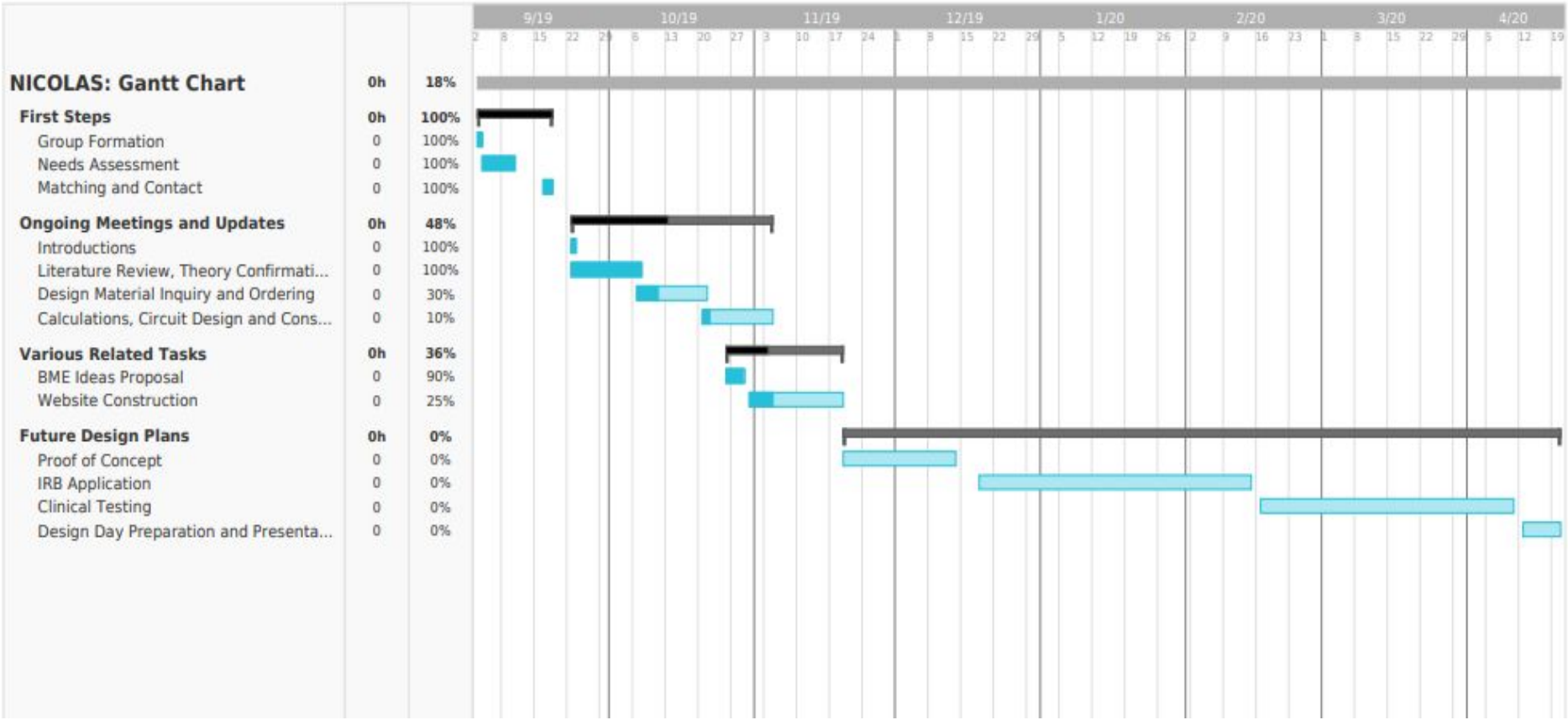

Proposed Solutions

- Three Approaches
  - Indirect electrochemical measurements using sweat or saliva as lactic acid
  - Direct electrochemical measurement using a microdialysis system
  - Direct optical measurement of blood lactate concentration

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  - Very invasive
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  - Transmittance or NIRS
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  - Quick response to physiological changes
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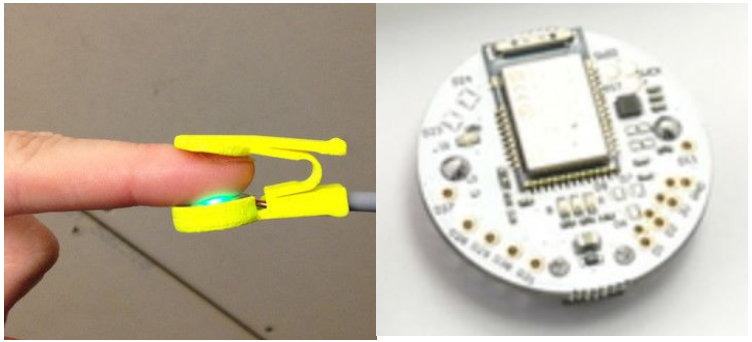
Design Components

- First Prototype
- 1 LED and 1 photodiode integrated into a 3D printed finger clip
- We will test 3 different wavelengths to determine the one that yields the strongest signal
- The analog front end will be integrated into a printed circuit board and routed to a bluetooth capable microcontroller to transmit data to a laptop

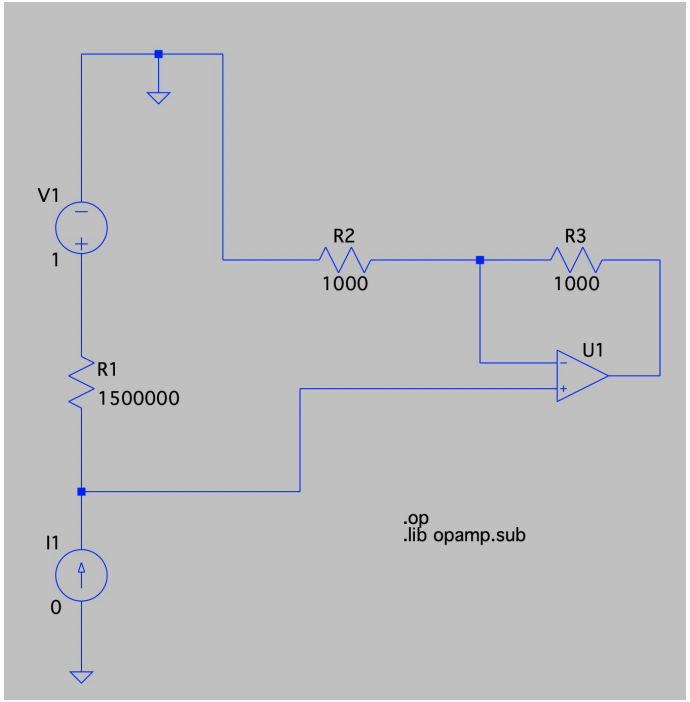
https://www.gophotonics.com/products/led-light-emitting-diodes/led-microsensor-nt/25-661-lms27led-cg
https://www.thorlabs.com/newgrouppage9.cfm?objectgroup_id=6479



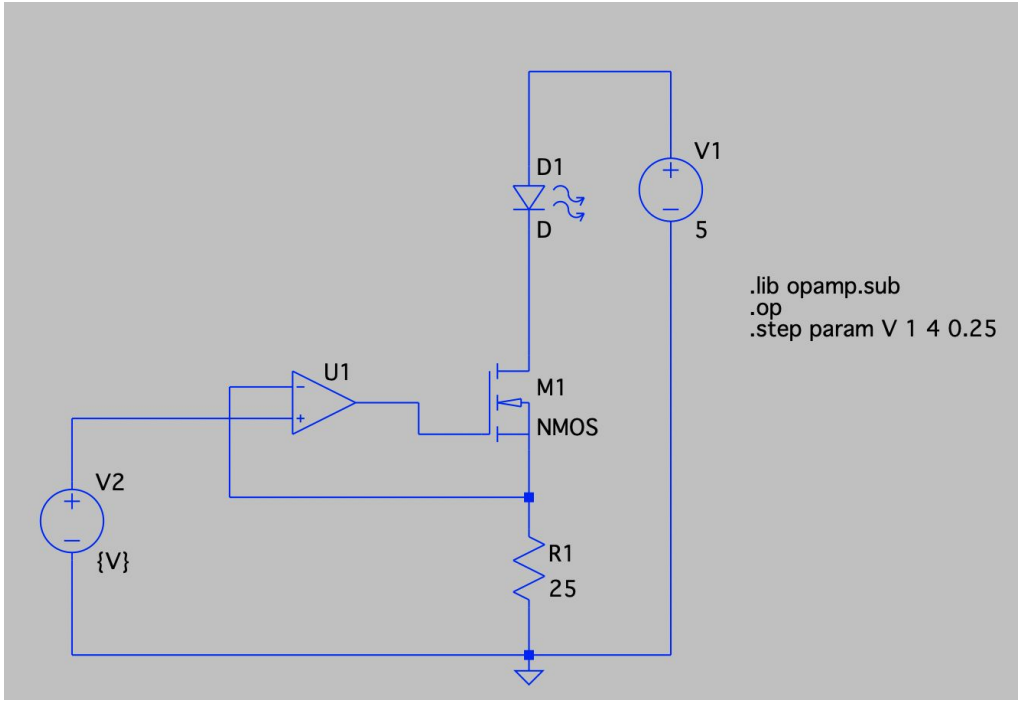
https://grabcad.com/library/finger-clip-for-pulse-sensor-arduino-1
http://www.espruino.com/Puck.js

Analog Front End Design

Current to Voltage Converter

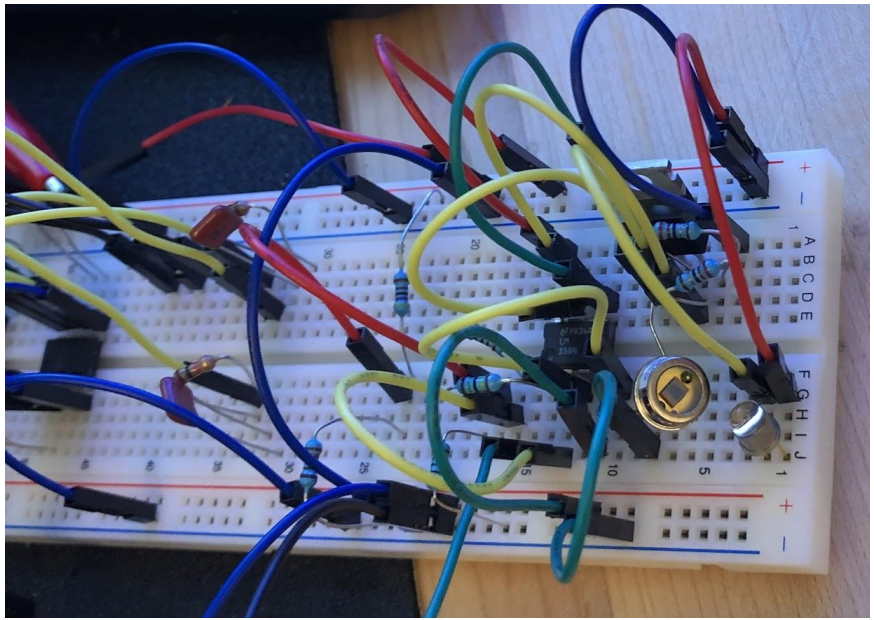


Pulsed Current Source



Preliminary Proof of Concept Testing

LED setup to excite photodiode



Waveform of the photodiode voltage output

Planned Proof of Concept Studies

- Determine appropriate analog filters amplifiers for analog front end
- Determine lactic acid sensing capability of photodiode
  - Test ability of photodiode to detect varying concentrations of lactic acid in cuvettes of water; adjust filters and amplifiers as needed
- Develop finger phantoms of increasing complexity
  - Test ability of photodiode to detect varying concentrations of lactic acid in phantoms accounting for
    - Hemoglobin, Tissue thickness, Blood heterogeneity
- Design finger clip for mounting the sensor to a finger
  - Mounting the photodiode to optimize the directionality of light through a finger

Future Design Path

- Test this initial concept
- Alternatives for this concept
  - Try reflectance
  - Non-invasive glucose sensor remodeling for lactate sensing
  - NIR spectroscopy
    - This might allow for us to better characterize things seen in a spectroscopy
    - In an IR, water and other components might be too noisy for us to analyse through

Other Details

- Patent search
  - No other similar designs: closest product is a glucose sensor, which is horribly inaccurate
- Anticipated regulatory
  - Class II
  - IRB Approval
    - Dr. Eagle wants us to pursue clinical trials by February
- Manufacturing costs
  - As of right now, $500 spent
    - The diodes cost ~$200; prices may increase if we use NIR instead
  - Could be looking at ~$700 per device assuming transmittance technology is feasible