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

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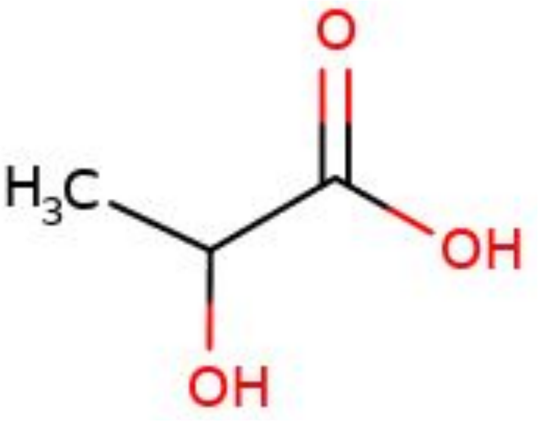
Faculty Advisor: Dr. Franz Baudenbacher
Clinical Advisor: Dr. Susan Eagle

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

Background

- Clinical biomarker used to measure tissue degradation
- Normal levels ~ 1 mM.
    - Relative > Absolute measurements



Lactic Acid
(2-hydroxypropanoic acid)

Problem Statement

- Currently, blood is drawn too infrequently to detect rapid spikes in lactate levels, which indicate the onset of life-threatening complications, such as:
    - Septic shock
    - Organ failure
    - Hemorrhage

Needs Assessment

Patient

Insulated Device
Intermittent Pulses
Non-invasive

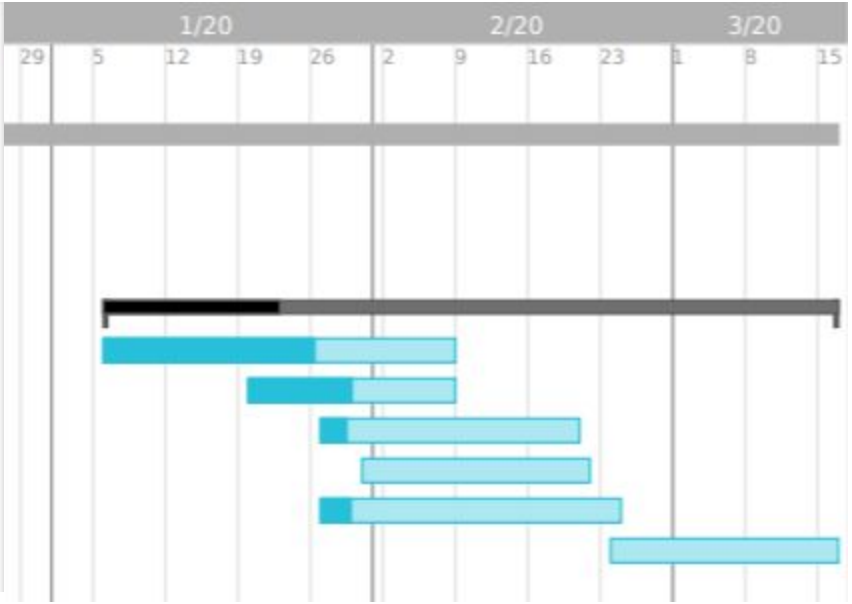
Practitioner

Continuous Sampling
Ease of Use
Clinical Application

System

Simplest Modality
Cost Effective & Portable
Integrate with Hospital Systems

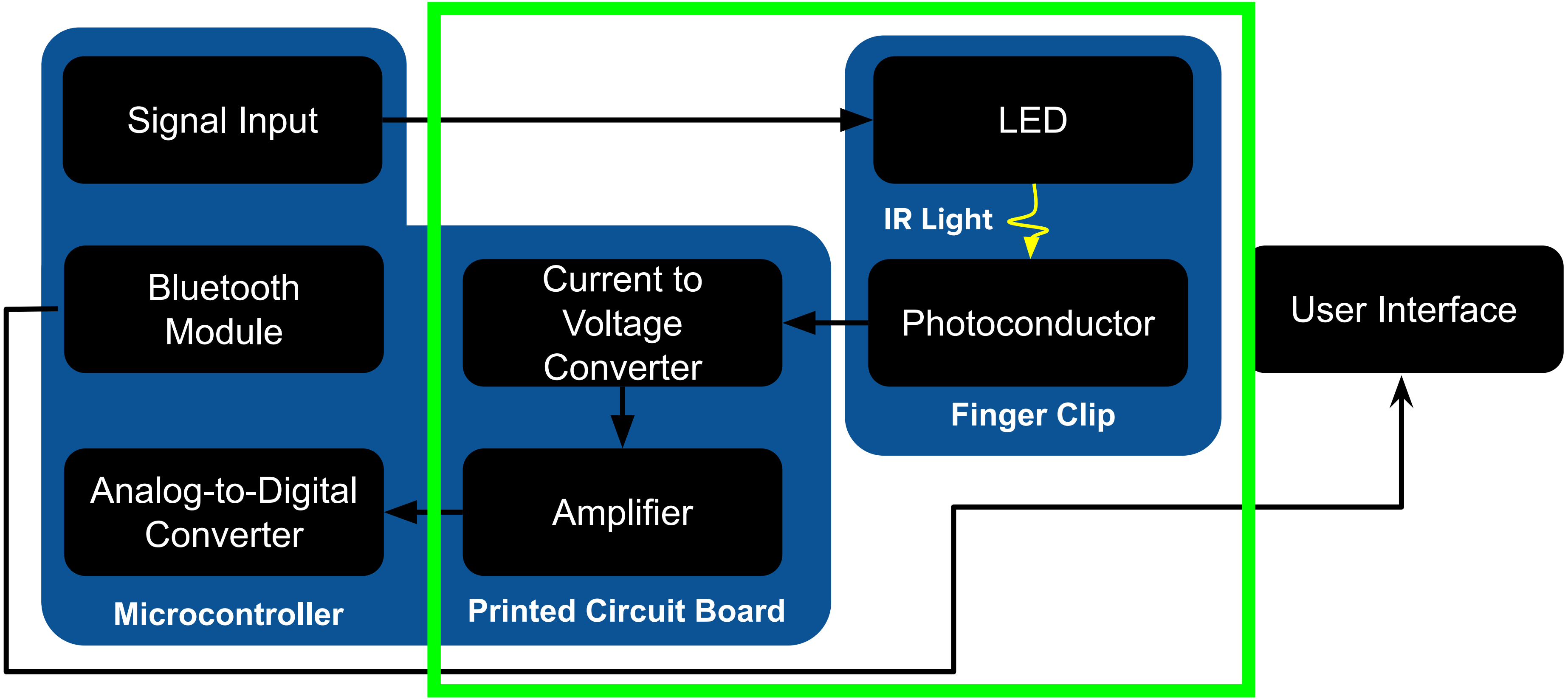
NICOLAS: Gantt Chart	**0h**	**39%**
First Steps	**0h**	**100%**
Ongoing Meetings and Updates	**0h**	**100%**
Prototyping, Design Validation	**0h**	**24%**
Circuit Optimization	0	60%
Design of Finger Clip	0	50%
Phantom Development	0	10%
Lactate Sensing	0	0%
IRB Application	0	10%
Clinical Validation	0	0%



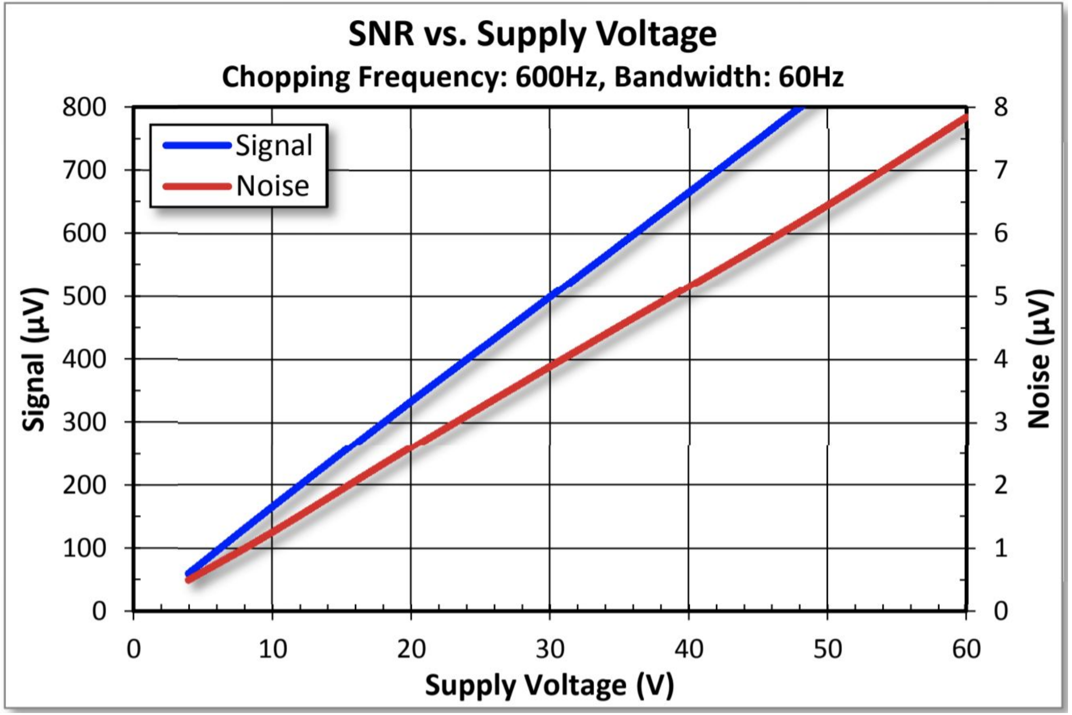
This Week's Progress:

- Secured new meeting time with Dr. Baudenbacher
- Parts Received
- Located IR Spectrophotometer
    - iLab and VINSE Access/Training
- Circuit Troubleshooting
    - Two Pronged Approach
- Laser-Tissue Interactions: IR on the Finger
- Phantom Research and Plan
- Transmission to NIRS

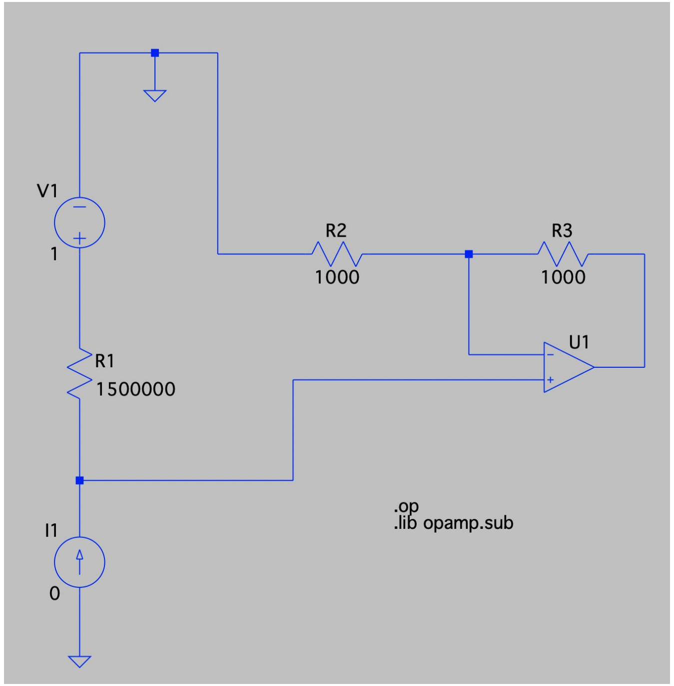
Block Diagram



Circuit Troubleshooting – Supply Voltage Optimization

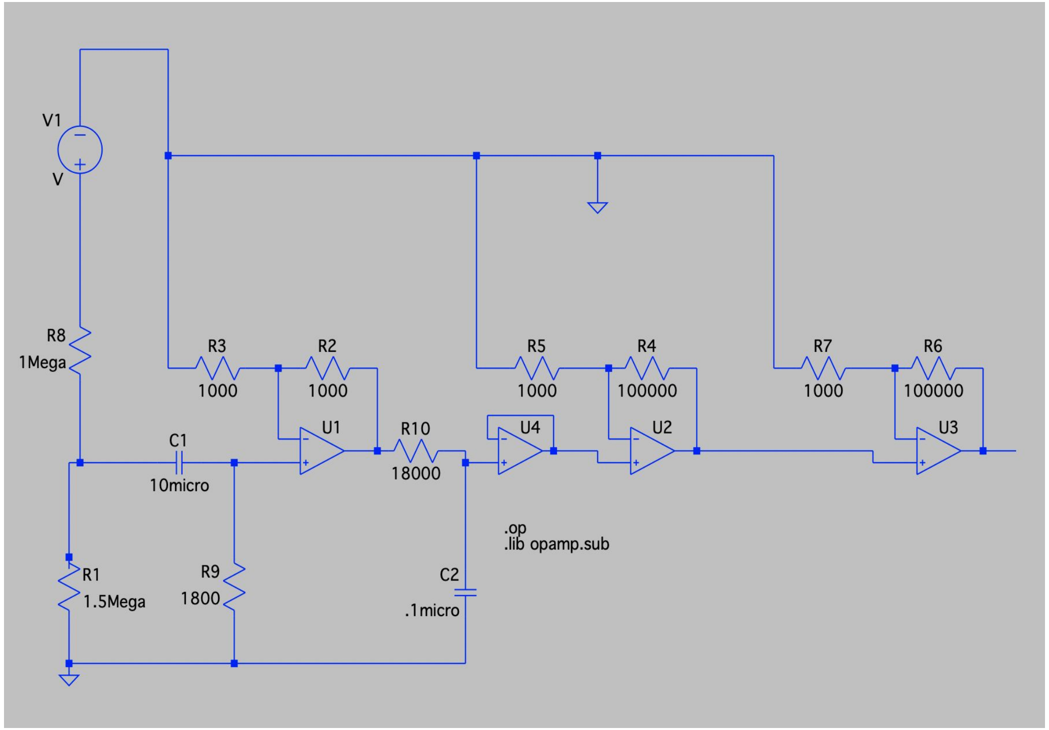


Current to Voltage Converter v1.0

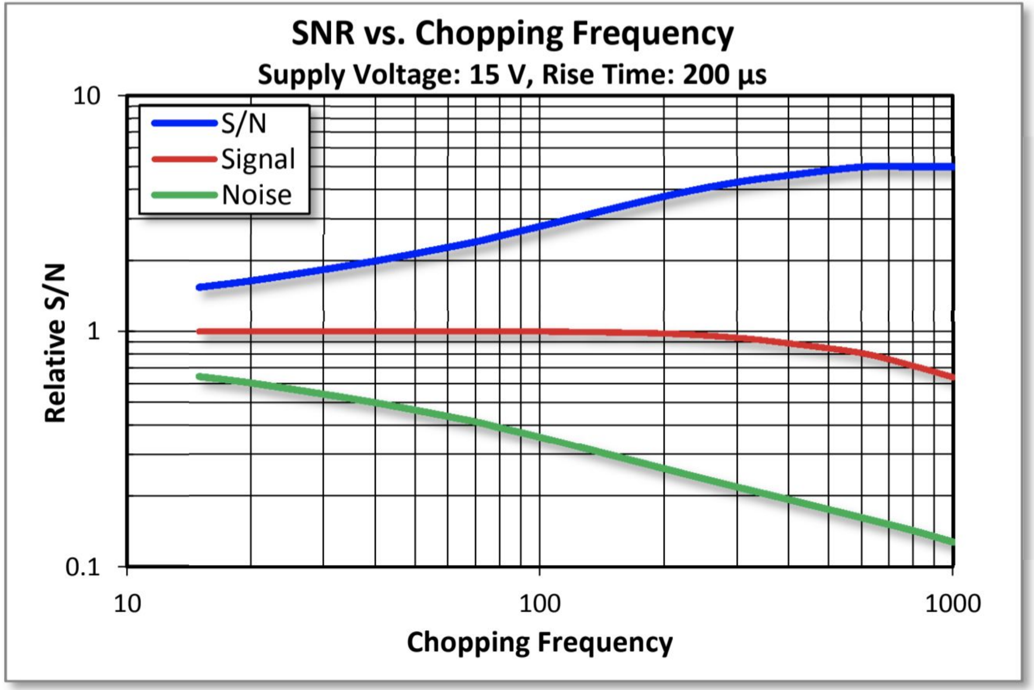


Circuit Troubleshooting – Supply Voltage Optimization

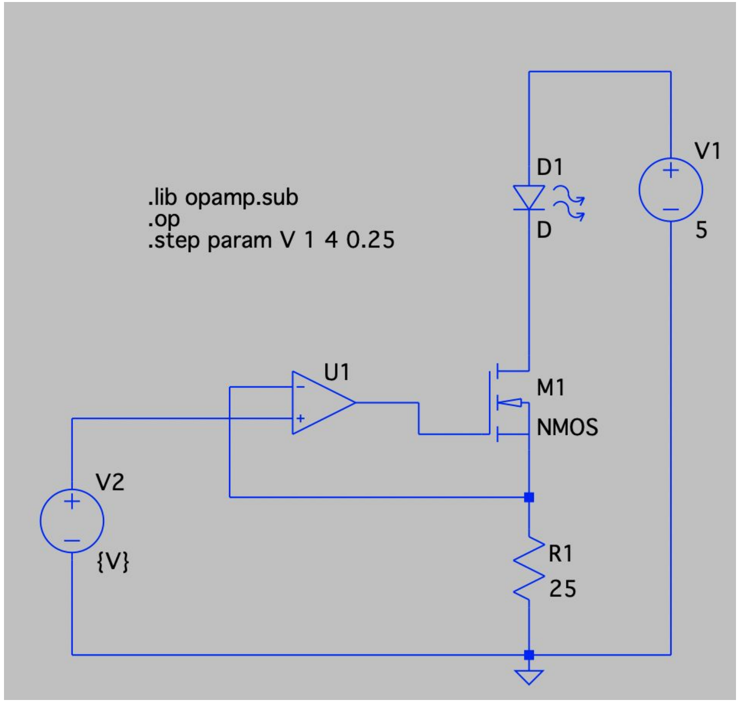
Current to Voltage Converter v1.1



Circuit Troubleshooting – LED Pulse Frequency Optimization

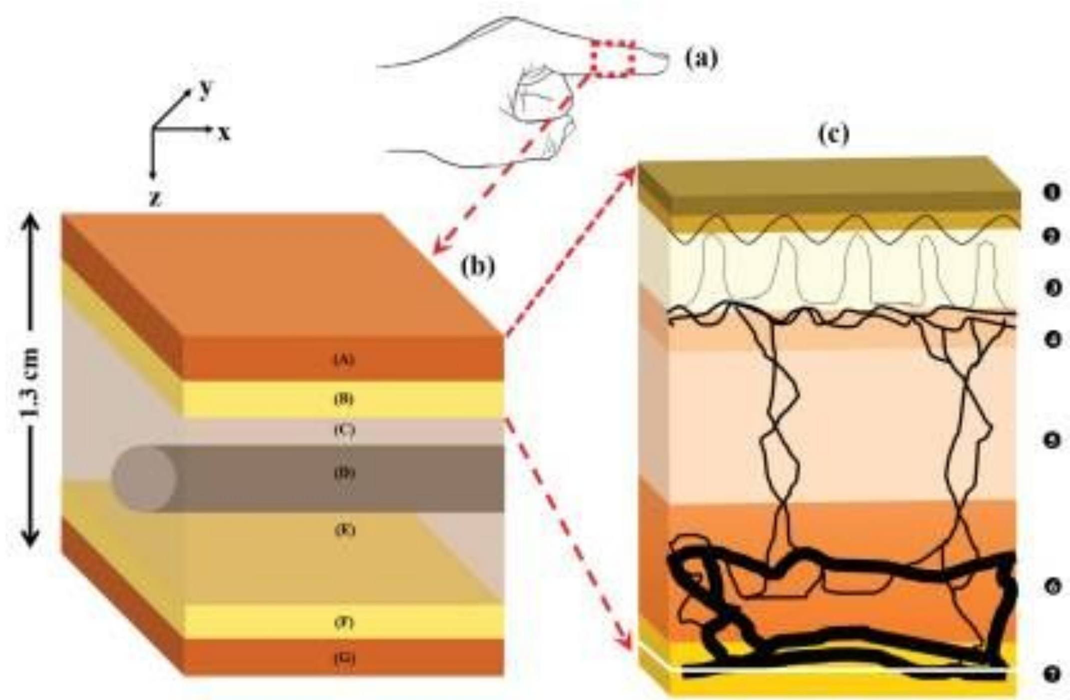


Pulsed Current Source v1.0



Light and Tissue Interaction

- Light interacts with skin tissue in two ways
  - Scattering, u_s
  - Absorption, u_a
- Each layer of the tissue is examined in differential process for u_s and u_a
  - Mie scattering - light goes forward



Light and Tissue Interaction

- Absorption coefficient of skin layers(epidermis and dermis)
  - u_s= 8.31 cm^{-1}
  - u_a = 5.75 cm^{-1}
  - u_t= 7.412 cm^{-1}
- Subcutaneous Fat Layers and Blood
  - Strongest absorbance is water
  - u_a = 1 cm^{-1}
- Important for light to transmit through finger with least amount of attenuation

Light Tissue Interaction

Scatter

Rayleigh Scatter

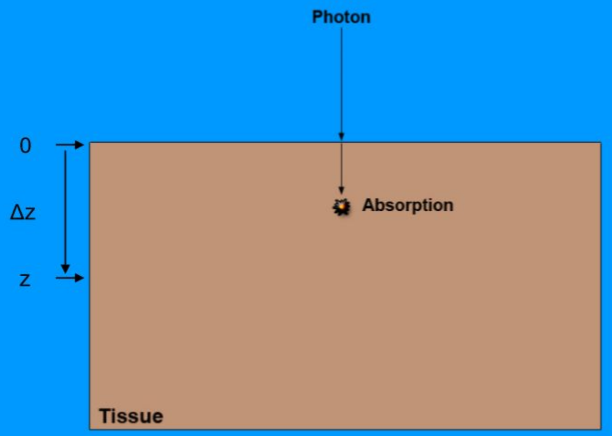
- Wavelength much larger than particle size
- Scatter is isotropic
- Scattering is proportional to $1/(\lambda^4)$, where λ is the wavelength of light being scattered
- Rayleigh scatter is the reason that the sky is blue

Mie Scatter

- Wavelength is approximately equal to the particle size
- Scatter is highly forward
- Scattering is proportional to $1/(\lambda^{0.4})$, where λ is the wavelength of light being scattered
- Mie scatter is what makes clouds appear white

Light Tissue Interaction

Absorption



E_0 = initial irradiance (W/mm^2)

E = irradiance after Δz

c = chromophore concentration (moles)

ε= molar extinction coefficient ($1/(mm \cdot mol)$)

$$\frac{\Delta E}{\Delta z} = -c\varepsilon E$$

Beer's Law: $E(z) = E_0 e^{-c\varepsilon z}$

Light Tissue Interaction

Absorption

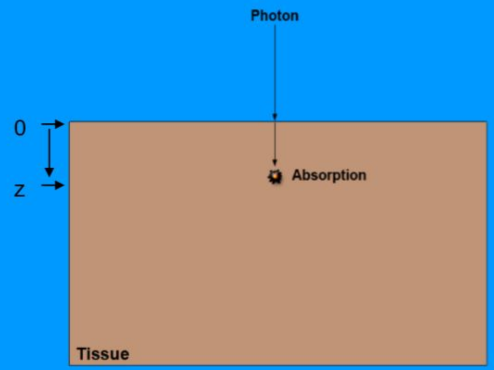
Beer's Law: $$E(z) = E_0 e^{-\mu_a z}$$

Penetration depth: Let $z = \frac{1}{\mu_a}$

$$E(z) = E_0 e^{-\mu_a \left(1/\mu_a \right)}$$

$$E(z) = E_0 e^{-1}$$

$$E(z) = 0.3679 E_0$$



Penetration depth is defined as the depth at which 63% of the light has been absorbed. However, 37% of the light still makes it beyond this depth!

Phantom Design

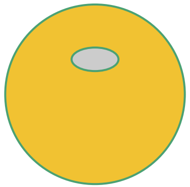
Tissue Requirements:

- Laser interaction with layers of tissue
    - Absorption and Scattering of IR
- PVA (polyvinyl alcohol)
- Agarose-albumin (egg whites)
- Acrylamide

Vessel Requirements:

- Path length to capillaries
- Shape of capillary bed beneath nail
- NMR Tube / Silicone Catheter

Side View



Front View

Blood Analog

- Model for Blood Plasma
  - Aqueous lactate solution
  - Charcoal-stripped Fetal Bovine Serum + Lactate
    - Plasma w/o clotting factors
  - Defibrinated Sheep Blood + Lactate

Lactate Absorbance Curve

- Standard curve
  - 0.25 - 7 mM
  - 15 point curve
- Equipment
  - Varian Cary UV-Vis-NIR Spectrophotometer (175 to 3300 nm)
- First trials
  - Waiting on access to VINSE

Transition to Near Infrared Spectroscopy (NIRS)

- What are our current challenges with IR spectroscopy and lactate sensing?
  - Various analytes absorb very similar wavelengths (we can confirm this in our situation).
  - Water absorbs most of the IR signal and emits heat
- What exactly is NIRS?
  - Near Infrared = different optical window
  - Focuses on refractance vs transmittance
  - More specific for each particulate
- How can we use this?
  - Using the modified Beer-Lambert's law
  - Can measure in relation to various wavelengths and absorptivities
  - Would use the same circuit as the IR (just optimized for the SNR).

$$r_{\mathrm{HbO_2}}^{\lambda_1,\lambda_2} = \frac{\alpha_{\mathrm{Hb}}^{\lambda_1}\frac{K^{\lambda_2}}{L^{\lambda_2}}\mu_{s,0}^{\prime\lambda_2} - \alpha_{\mathrm{Hb}}^{\lambda_2}\frac{K^{\lambda_1}}{L^{\lambda_1}}\mu_{s,0}^{\prime\lambda_1}}{\alpha_{\mathrm{Hb}}^{\lambda_1}\alpha_{\mathrm{HbO_2}}^{\lambda_2} - \alpha_{\mathrm{Hb}}^{\lambda_2}\alpha_{\mathrm{HbO_2}}^{\lambda_1}},$$

Next Steps:

- Lactate Standard Curve
- Tweaks to Circuit Design
- Proof of Concept -- lactate absorbance in cuvette
- Phantom Development -- lactate absorbance in phantom

Materials to be Purchased:

- Charcoal-stripped Fetal Bovine Serum ($118.00 for 50 mL)
- Defibrinated Sheep Blood ($104.27 for 25mL)
    - Need a BSL-2 lab space