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N.I.C.O.L.A.S (Non-Invasive Continuous Optical Lactic Acid Sensor)
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Progress Report 1

1. **Background on the project itself**

   The Non-Invasive Continuous Optical Lactic Acid Sensor (N.I.C.O.L.A.S.) is a SMART lactate sensing modality developed for continuous, noninvasive blood lactate level monitoring in clinical settings. It will be a vast improvement on the intermittent blood draws currently employed for blood lactate monitoring due to its ability to sample lactate levels continuously and noninvasively in a small package that will be less resource-intensive on hospitals. Our sensor will utilize near IR spectroscopy (NIRS) and ratiometric analyses to detect fluctuations and alert healthcare professionals of any rapid spikes in lactate levels. This will help healthcare providers better utilize lactate as an early indicator of sepsis, organ failure, and hemorrhage, allowing for earlier preventative intervention in these cases leading to improved patient outcomes. At last reporting, we gave updates on the following fronts:

   - Locating specialized IR Spectrophotometer
   - Circuit Troubleshooting (Supply Voltage and LED Pulse Frequency Optimization)
   - Light-Tissue Interactions
   - Phantom Design Requirements
   - Blood Analog Models
   - Lactate Absorbance Curve
   - Transition from Transmission to Near Infrared Spectroscopy (NIRS)

2. **Achievements since last reporting**

   Since the last reporting, we have made significant progress. With respect to circuit troubleshooting, we were able to identify the switching issue of our bipolar junction transistor (BJT) and rectify it by replacing the BJT with an N-doped MOSFET. This allows us to only activate the IR diode when there is enough voltage applied to the gate of the MOSFET to toggle switching. We've also made strides in determining why we were unable to read a signal from our photoconductor. We've begun a more systematic troubleshooting approach by starting with a very simple LED and photodiode circuit. Using this circuit, we first verified that our specialized components (the IR LED and the photoconductor) were operating as expected. With these components known good, we then used this simpler circuit design to verify our system is working. Now we are working towards figuring out why our filtering and amplification circuitry failed to provide the expected result. We located the Varian Cary UV-Vis-NIR Spectrophotometer in the Vanderbilt Institute for Nanoscale Science and Engineering (VINSE). Two of us have undergone analytical lab safety orientation and training and will be trained on the spectrophotometer itself on Wednesday, February 12. We have received both the fetal bovine serum and the defibrinated sheep blood for our blood analogs and found BSL-2 storage in Dr. Susan Guttentag's laboratory in the Vanderbilt University Medical Center (VUMC) department of neonatology. Additionally, we have been exploring alternative biomimetic materials to use for our phantom models as our planned process for constructing the finger phantom will not give us our desired vascular access. Lastly, we have done more research into NIRS to preemptively avoid potential pitfalls.

3. **Problems that have arisen**

With respect to the lactate absorbance curves, the main issues have been logistical in establishing iLabs accounts, being signed up for orientation, and training on the instrument to be able to begin constructing the curves. For the blood analog, there were significant issues about where the BSL-2 specimens would be stored, considering that our faculty advisor does not have BSL-2 lab space and the VINSE space is only BSL-1. Although this storage issue was solved, this presents another issue of how to analyze BSL-2 specimens in a BSL-1 lab, which will require creative solutions around lab restrictions, which we have been brainstorming. Finally, and most notably, for circuit troubleshooting, we are having a lot of difficulty getting our circuit to work as expected. Working with Dr. Baudenbacher, we are on the verge of a breakthrough as we verify that more and more of the elements in our circuit design work correctly. Our final hurdle in the circuit design, is receiving, filtering, and amplifying the voltage readings from our photoconductor. Currently our photoconductor signal is nearly impossible to distinguish from noise because it's so small. We found that with the digital filtering capabilities of the oscilloscopes at our disposal are limited and that analog filtering techniques have proven to be insufficient.

4. **Work that lies ahead**

Our expected objectives for this next week are simple. Since we will be trained at the VINSE, we will finally have access to the IR spectrophotometer. This means we will be able to test the lactate wavelengths to create an absorbance curve for proof of concept. This should result in a graph for presentation. Using this, we should be able to confirm as a viable option or not for our design. In addition, our calculations should be able to decide what biomimetic material should be used to create a finger phantom and how exactly that phantom will be constructed for testing prior to our IRB clearance.

5. **Assessment of objectives relative to proposed schedule and budget**

We should be on schedule for our objective. NICOLAS is supposed to be a non-invasive method to detect lactate. We theorize that we can use NIRS to modify the circuit and meet the proposed schedule and budget. There would be no required change in the materials, but the diode and the photoconductor would be re-arranged, and the microcontroller reprogrammed to analyze the modified Beer-Lambert's Law. Other changes would require a varied voltage source and adjustments in our finger clamp schematics to reflect the change in our circuit. We are still under budget with no foreseen purchases at the moment.