Cortical Spreading Depression Simulator

Final Report

cerebrosim

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Executive Summary

The goal of this project was to create a system that generates a simulated cortical spreading depression (CSD) that propagates through electrically modeled layers of head tissue. Completion of this project first involved research of the causes, prevalence, and characteristic features of CSDs. Next, with the help of our industry sponsor, Dr. Jones, we developed a list of performance requirements that the product needed to include to satisfy the needs of CerebroScope. Upon grasping the unmet need, the mechanical and electrical components of the device were designed and prototyped. After discussing the design with Dr. Jones and verifying the functionality of the initial prototype model, the design was scaled and the final prototype was fabricated. The deliverables of the project include a device that simulates and displays non-linear propagations of CSDs across a flat surface. Recommendations for future iterations of the device were also defined.

The product we were asked to deliver was a simulator to bench-test CerebroScope's prototype device that non-invasively detects CSDs in acute brain injury patients to support their pre-clinical prototyping process. Our interpretation of this need and iterative contact with Dr. Jones led us to design and produce a mechanical-electrical device that simulates the scalp surface voltage of a brain surface CSD. CSDs are slow-moving bioelectric phenomenon that present on the surface of the brain after an ABI. There are no current means of detecting a CSD non-invasively, which has motivated CerebroScope to develop a device that can track propagating CSDs.

CerebroSim's direct market is CerebroScope; the only company known to be creating a non-invasive CSD detection system that could benefit from a simulation device that generates said neural impulse. Indirectly, the market for CerebroSim includes the 3.2 million Americans who go to the hospital for a ABI-related injury each year, who could benefit from a non-invasive CSD detection device.

CerebroSim is a mechanical-electrical device that provides a means of verifying and validating CerebroScope's detection unit by generating CSD propagations that simulate real-time scalp potentials in human patients. The device is operated through GUI input, form which the user selects a desired CSD speed and pattern. This input is received by a raspberry pi that controls 20 custom PCB boards that control 800 pins to generate a propagating CSD of -20mV. The pins are surrounded by a grounding plate and directly contact layered resistive fabrics that have the lumped electrical properties of the cerebral spinal fluid, dura mater, skull and scalp. CerebroScope's detection device (once created) is intended to sit on the topmost material layer (representing the skin) in an attempt to detect and monitor the simulated CSD.

Future work would include finding materials that more closely fit the resistivity, thickness, and permittivity properties of the anatomical layers of the CSF, skull, dura mater, and scalp. Additionally, a functional CSD prototype with the dimensions and curvature comparable to the human skull should be created to more closely simulate CSD propagation. Furthermore, validation of the operating features of the device with the scalp-mounted, CSD-detection system produced by CerebroScope should be conducted to ensure the simulator provides the means to bench-test the company's High Density Electrode Array and satisfies the requirements to support future human subject testing. Lastly, it would be useful to implement a more developed interface that allowed the user to choose a CSD morphology (circle, expanding ring), dimension (2, 3, or 4 mm diameter), propagation speed (2, 3, 4, 5 mm/min), and propagation track (straight, wavy, irregular line). This interface would also allow the user to choose whether or not to provide a region of depressed voltage (15 mV) that would correspond to infarcted brain, on which a globular, circle-type CSD would travel along its edge.

Background

Project Origin

This project was initially introduced to Design Hub, a student run club that exists to provide undergraduate engineers exposure to industrial skills and projects to complement the ample research opportunities available at the University of Pittsburgh. Many students in the club join design project teams, in which they work with clinicians from UPMC and professors at the University of Pittsburgh to create medical devices. The project with CerebroScope was initially presented to Design Hub to initiate a movement of developing design teams to work with local startups to satisfy unmet needs. However, the development of an Intellectual Property (IP) agreement between the University of Pittsburgh and CerebroScope took longer than expected. As a result, three members of the CerebroSim team (all of which who were previously officers of Design Hub) pitched the project to Dr. Winter, with interest in taking on the project through the Product Realization course. This was proposed, since IP documentation had already been formalized for the course, the skillsets of the CerebroSim team fit the needs of the project, and collaboration between CerebroScope and Design Hub could still continue to develop. With Dr. Winter's permission, we were granted the right to take on the project with CerebroScope with the addition of a mechanical engineering student.

Motivation

Approximately 3.2 million Americans visit the emergency department each year for acute brain injuries [1]. Common types of ABIs include severe-TBI (2.5million/year), stroke (691,000/year), and hemorrhage (30,000/year). An acute brain injury (ABI) occurs when the normal function of the brain is disrupted due to an external force or internal occlusion. This disruption is one of few known causes that lead to the development of a cortical spreading depression (CSD), a slow-moving, self-propagating wave of cellular depolarization that presents on the brain surface. CSDs are also known to be characteristic of other brain conditions, including cerebral hypoxia (a reduced supply of oxygen to the brain) and migrane auras (perceptual disturbances that occur prior to developing a headache) [2,3]

Depending on the type of ABI, common causes of the condition can include falls, sports-related blows, blood clots, or blood vessel bursts. ABIs are classified by their severity and presented symptoms as mild (i.e., a brief change in mental status or consciousness), moderate, or severe (i.e., an extended period of unconsciousness or memory loss after the injury). Most ABIs fall under the mild classification and are commonly known as concussions [3].

It is common for a ABI to go untreated or misdiagnosed, as it can be hard to pinpoint symptoms after the injury has occurred and there are no current means of non-invasive detection. This is especially true for mild ABIs, as the symptoms of this condition are hard to detect and are often diagnosed as a less severe condition. However, impact of this injury is dependent on response time; the longer it takes for the patient to receive treatment, the more susceptible the patient is to developing short-term or long-term issues affecting cognition, motor function, sensation, and/or emotion [4]

Currently, the only reliable method available to detect CSDs in humans is electrocorticography (ECoG), an invasive procedure that involves the direct placement of electrode strips onto the brain surface (Figure 1). Recent efforts have been explored to detect CSD propagation via the scalp, however, none have been successful without the guidance of concurrent ECoG measurements [2].

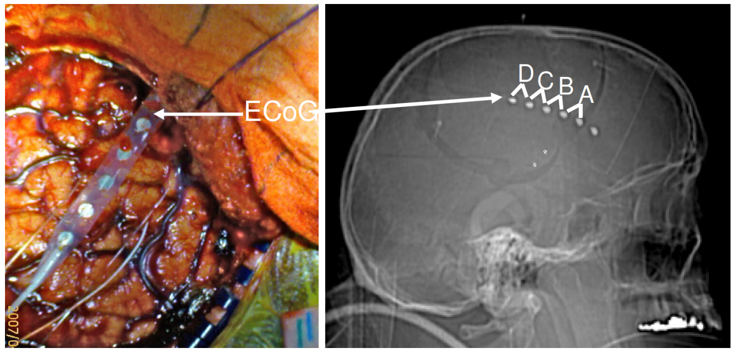


Figure 1. Representation of electrode placement in an Electrocorticography (ECoG) patient

This clinical diagnosis gap has motivated CerebroScope to work toward the creation of a non-invasive tracking device that uses DC-EEG to detect real-time scalp potentials in human patients, especially those with mild ABIs. Due to the stringent requirements and guidelines of the Food and Drug Administration (FDA), human subject testing of the diagnostic device cannot be conducted until their prototype meets certain verification and validation measures. As a result, our team created a device that would give CerebroScope the ability to test their prototype on a non-human model that simulates real-time CSDs. We predict that the data obtained from the simulation tests can be used to verify/validate the CSD detection system to support future human clinical trials.

Project Objectives

After developing a full understanding of the unmet need through extensive research and discussions with Dr. Jones, we defined essential short-term and long-term project objectives. These objectives were developed to serve as milestones that our project would aim to complete by the end of the semester. (Note: objectives listed in italicized font were added features the team felt would enhance device function, but were not required by CerebrScope for completion).

Short Term Goals:

- Understand the unmet need
- Create “plan of attack” (with task schedule and project milestones)
- Design electrical signal hardware / software mechanism for linear CSD generation
- Decide upon fabrication methods
- Find materials that satisfy the required resistive properties of the anatomical layers of the skin, skull, dura mater, and cerebral spinal fluid
- Create and implement test bench for electrical hardware/software verification

Long Term Goals:

- Purchase/create/modify a containment unit that houses all device components
- Scale device hardware / software
- Verify scaled design
    - Material properties comparable to anatomical specifications
    - Repeatable generation of various CSD patterns
- *Generate CSD patterns of varying complexity that represent multiple known forms of CSD propagation*
- *Establish and refine a graphical user interface*

Market Opportunity

Exploitation of an Uncharted Field

Currently, there are no FDA approved devices in existence whose indication(s) includes the non-invasive detection of a CSD. The exploration of CSDs is an up-and-coming field, presently led by the German company COSBID (a research interest group focused on the causes and consequences of spreading depolarizations as a pathologic mechanism in neurologic diseases). While this company aims to promote research, education, and innovation in the neural depolarization field, there is minimal understanding of the exact characteristics, causes, and diagnostic methods of CSDs. Our product supports the future development of such an understanding and aims to assist in the future approval of the first CSD detection device.

Targeted Customers

In the short-term, the simulator device is targeted for use by CerebroScope employees to assist with verification/validation of their CSD detection device and support future human clinical trials. More significantly, our device supports the long-term goal of assisting CerebroScope in creating a non-invasive CSD detection device that can potentially help anyone with an ABI. Of the 3.2 million Americans who visit the hospital for and ABI each year, very few undergo ECoG to further diagnose their injury.

By backing the future approval of a CSD detection device, our project supports the future non-invasive diagnosis of ABI for the millions of patients who suffer from this condition. Those who survive an ABI can face effects lasting a few days to disabilities which may persist the rest of their lives. Effects of ABI can include impaired thinking or memory, movement, sensation (e.g., vision or hearing), or emotional functioning (e.g., personality changes, depression). By providing a means to diagnose this injury, we can potentially prevent some of the lasting effects that progress due to mis- or late-diagnosis of ABIs.

Project Success Criteria

Through extensive research and iterative discussions with Dr. Jones, the following specifications were defined as success criteria that the CSD simulator must meet to accurately replicate a real-time CSD and satisfy the needs of CerebroScope:

- Simulated CSD region on the brain surface is ~3 mm
- Simulated CSD potential difference is -20mV
- Simulated CSD region moves at ~3 mm/min
- Simulated CSD must propagate a total displacement of 8cm
- Simulated scalp size is 12cm x 12cm (at minimum)
- Simulated scalp is a flat surface (curved scalp not required)
- Simulated CSD measurement is comparable to CerebroScope data
- Simulated CSD accounts for the lumped electrical properties of the layers from the brain surface to the scalp (either through simulation or material design)
- Simulated CSD can propagate in a linear motion (at minimum)

Project Description

Functional Specifications

- Mechanically the simulator needed to incorporate:
  - Material(s) that have the resistive properties of the anatomical layers of the CSF, dura mater, skull and scalp
  - Containment unit to house all simulator components
- Electrically, the simulator needed to:
  - Create complex CSD patterns of varying complexity
  - Generate -20mV signals at pinpoint locations
  - Transmit -20mV signals to an electrode array that represents brain surface

For each of the functional specifications, initial design concepts were brainstormed and implementation methods were developed to plan how to create the hardware and software needed to satisfy the product requirements.

Material Design and Development

Upon starting the project, we spoke with Dr. Uber of Bayer HealthCare for material advice on methods to represent the anatomical layers of the brain. He advised the team use foams of varying densities and thicknesses submerged in saline solution to simulate the anatomical layers (Note: each foam would need to be the same thickness as the actual anatomical layer).

To test this notion, we ordered a foams of various types from McMaster Carr and submerged them in saline solution. However, we were unable to get consistent resistance readings for each of the tested foams using a multimeter. We also concluded that submerging materials in a liquid solution would be difficult to contain and maintain (the fluid would evaporate over time) and that the foams would have to be custom ordered to the correct thickness, which would be expensive. As a result, foams were eliminated from the design.

Next, materials with resistive properties were outsourced from various companies. Initially, we obtained donated material samples from Eeonyx Corporation. Once received, the ability for the materials to be laser cut was tested to ensure the materials could be fabricated to fit within a containment assembly designed using SolidWorks (Figure 2). The assembly was intended to consist of two acrylic pieces that "sandwich" layers of resistive fabrics to maximize contact between the layers. Screws were to be used to hold the fabrics taut and the acrylic pieces together to prevent expansion.

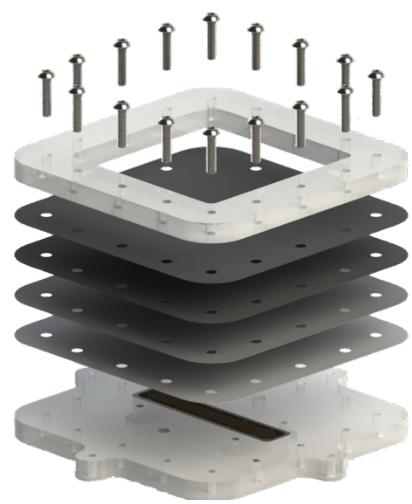


Figure 2. Material SolidWorks Assembly

After compatibility between the materials and the laser cutter was confirmed, we obtained a larger set of donated fabrics from Eeonyx to satisfy the resistance and thickness requirements for the skin and skull layers. Fabric for the dura layer was purchased from Metal Textiles and the CSF layer was donated from a company called LessEMF.

As we began verifying the obtained materials, we identified a misunderstanding between the resistive properties we wanted and the fabrics that were sent to us. Companies that sell resistive fabrics give their product dimensions in two forms, Ohm*cm and Ohm/sq. For several materials we purchased, we thought we were getting Ohm*m or Ohm*cm, but we were really getting

Ohm/sq. This resulted in some layers being less resistive than they should have been, beyond a margin of error.

Upon this discovery, we outsourced feedback from material companies that specialize in making resistive fabrics. We had a lengthy discussion with Art Henn from Marktek Inc., a materials company that specializes in making materials related to EMI shielding & suppression, static dissipation, microwave and radar absorbing, resistive heating, and more. Art provided a lot of great insight and advised us on future steps to obtain the materials CerebroScope needs. After describing our project to Art, he assured their company could make materials that meet the exact thickness and resistivity requirements defined by CerebroScope. Marktek has a minimum purchase cost of $1000, however, Art said he had negotiated lower costs for small companies before and would definitely consider doing so for CerebroScope.

When speaking with Art, we questioned the possibility of also getting donated samples from his company that meet the specifications we need. He said even if we had attempted to get the correct resistivity values to begin with, there is a good chance we would not have been able to get the materials for free or even at a somewhat reasonable cost, because the values we need are so specific that material companies (like Marktek) don't keep them in stock. Therefore, we likely would have paid >$1000 to get the materials, consuming all of our budget up front.

Moving forward, we notified Dr. Jones of the concern and determined whether or not the simulator would still be useful to CerebrScope in its current state. Fortunately, CerebroScope affirmed the simulator would satisfy their current needs. By having the ability to detect -20mV voltages through layers of lower resistance, our simulator can be used as a stepping stone for future bench-testing with greater resistivity values. Additionally, the fabrics are one of the most modular components of the design. Therefore, CerebroScope has the option to increase the simulator's precision by purchasing the correct materials from Marktek or another company. Upon purchase, we can laser cut the fabrics to the correct size to fit within the simulator as designed, as two CerebroSim members plan to stay in the Pittsburgh area over the next few years.

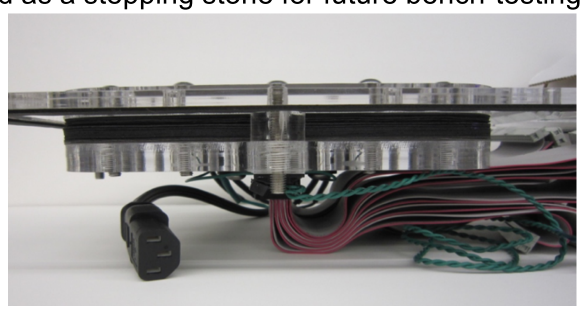


Figure 3. Final assembly of material containment

The lower resistance fabrics were laser cut, layered, and held taut in contact with one another in within the acrylic housing as designed (Figure 3). Table 1 presents the properties of the materials used in the current simulator model.

Table 1. Fabric Properties of Current Design

Anatomical Layer	Desired Anatomical Thickness (mm)	Desired Resistivity (ohm*m)	Desired Resistivity for a Single Sheet of Goal Thickness (ohm/sq)	Resultant Layered Material Thickness (mm)	Resultant Material Resistivity (ohm/sq)	Supplier Name
Skin	3.4	5000	1470588.2	3.4	66666.7	Eeonyx Corp.
Skull	5.7	26.3	4616.8	5.8	2000.0	Eeonyx Corp.
Dura Mater	0.4	2	5000.0	0.4	0.05	Metal Textiles
CSF	0.5	0.5	1000.0	0.4	<0.5	LessEMF

Also retrieved were donated samples from Marktek, two of which have the correct resistivities of the Dura Mater and CSF layers (Table 2). These samples were given to CerebroScope for future integration into the design.

Table 2. Fabric Donations from Marktek, Inc.

Comparable Anatomical Layer	Material Thickness (mm)	Material Resistivity (ohm/sq) (specified by supplier)	Supplier Name
N/A	0.66	100,000	Marktek, Inc.
Skull / Dura Mater	0.5	4700	
CSF	0.5	1500	

-20mV CSD Signal Design and Development

To generate a -20mV CSD signal, we came up with two design options 1) a finely-spaced, discretely-controlled electrode array and 2) a motorized arm with an electrode tip, capable of moving in variable pattern configurations. Because a discrete-controlled array allows for more pattern control and doesn't use moving parts, we decided to create a fine electrode array.

Our chief design considerations were:

- At least 8cm x 3mm (final is 8cm x 1 cm)
- Fine (less than or equal to 1mm) spacing between electrodes
- 800 uniquely addressable electrodes
- Electrodes insulated from neighbors
- Flat and tangent with first adjacent material layer

After initially looking into using micro electrodes from specialized neuroprosthesis companies, we decided to create our own custom array. We settled on a 2x10 array of 40-pin ribbon cables. Connecting 10 sets of 2, 40-pin cable rows created 10 lines of 80 pins (800 total). By cutting the cables in the middle with connectors left on one end, we were able to control each pin individually using wire connections to a control unit. The array was fabricated by super gluing the exposed ends of 2 sets of 10 cables, so that the sides and ends of each ribbon cable were flush with the cables on either side of it. Next, the inner surfaces of the 2 sets were glued together (Figure 4). The cables were then placed within an ABS printed housing unit, containing spacers to center the cables within. Once placed in the unit, an epoxy resin was applied to fix the ribbon cables. Lastly, the end of the assembled unit was machined off and sanded to expose the 800 electrode pins (Figure 5).

Figure 4. Glued ribbon cable arrangement

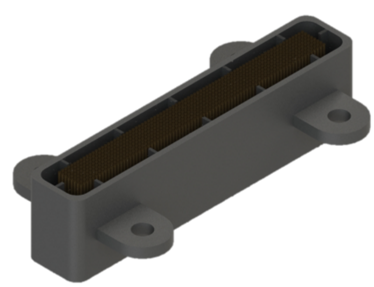


Figure 5. Final fabricated 800 pin electrode array

We needed a potential difference of -20mV between the CSD signal and the rest of the array and brain layer. Therefore, surrounding the array we added an aluminum ground plate, which we connected to a 20mV, high output impedance signal generated by a MCP4725 DAC and 10 ohm current sink resistor (Figure 6). A high impedance ground plate was used to prevent current draw into our array. With the ground plate maintained at 20mV, the CSD signal propagated was held at 0V, creating the -20mV differential needed to simulate a CSD.

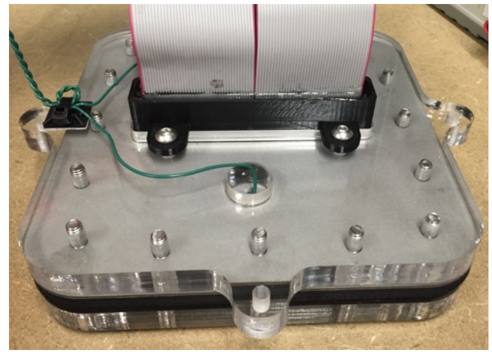


Figure 6. Ground plate

CSD Control Design and Development

With the ability to uniquely control 800 pins, we ran into a new problem: how to control our array with the limited number of outputs from a simple micro controller. Additionally, we needed to find a way to control propagation of small signals on the order of millivolts and disconnect electrodes that are not moving a CSD signal.

To solve these issues, we first searched for a compatible LCD/graphics controller but couldn't find anything to match our specs or price range. Instead, we designed custom demultiplexing circuit boards using the integrated circuit components shift registers and transmission gates. Shift registers allowed us to serially set our entire array using just a few control signals. Transmission gates allowed us to use the outputs of our shift registers as logical control signals for small signal propagation. So when we set a shift register to 5V (High), it opens the transmission gate as a closed switch, allowing -20mV signals to propagate to the ribbon wire array. The additional advantage of this design is that pins not propagating the CSD signal will act disconnected, or floating, allowing them to short circuit with the ground plane.

Ideally, we would fabricate a system on a chip and put all shift registers and ribbon cables on one or a few boards. Given our experience and budget, we created the minimum viable design with 1PCB/ribbon cable, resulting in 20 PCB boards total. Each production quality solder-mask PCB has 5 shift registers and 10 transmission gate ICs for a total ability to control 40 pins per board (Figure 7). In limited control situations, we could technically daisy chain every board to the next and set all pins with just 1 serial input signal. However, in the name of parallelization and speed, each board receives a unique serial input for its 40 pins.

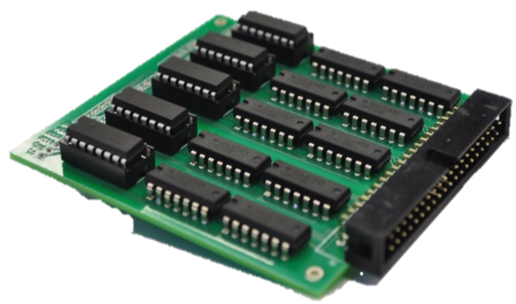


Figure 7. PCB Board Layout

Power, ground, CSD signal, and common clock signals were wired together for each board using long wires and heat shrink (Figure 8). Each serial signal was uniquely mapped to our raspberry pi controller. At this point, controlling our array became a software, not a hardware issue, using the 20 control signals and 2 shift register clock signals.

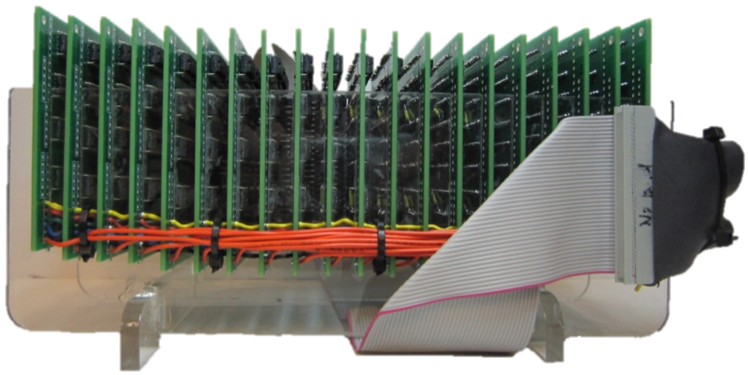


Figure 8. PCB Board Stacking

Software Design and Development

With all PCBs connected to power, ground and the raspberry pi, all remaining CSD pattern work was handled in software. The shift registers work with two clocks, a shift clock and a latch clock. The shift clock controls the movement of bits into registers. All of this shifting occurs without being transmitted to the array, which is the job of the latch clock.

To create complex patterns, we adopted a full refresh scheme, where each movement in the 800 pin array warrants shifting in 800 new bits and latching the new system state. In this way, the software control of the array mimics a graphic controller or video image, which refreshes multiple frames per second. This design was developed in the python programming language, in which we defined a master array of 800 pins divided between 20 instantiations of a 'Board' class. When setting the array, we shift in the 20 boards concurrently for max parallelization, meaning we shift the first pin of each of the twenty boards simultaneously, before moving on to the second pin of each board.

To allow user control of this software, a graphical user interface was created to run on a touch screen (Figure 9). The python graphics framework Kivy was used to handle the multi-touch nature of the interface, which allows for setting of CSD speed and one of three CSD propagation patterns: Linear, Split, and Ring. Upon starting the system, the GUI schedules calls to the PCBs to achieve a moving CSD according to a set pattern. When running, a small window shows the user details of the simulation as well as a real-time display of the CSD motion on the 800-pin array. This propagation can be paused or stopped at any time. The GUI runs continuously and begins automatically at startup.

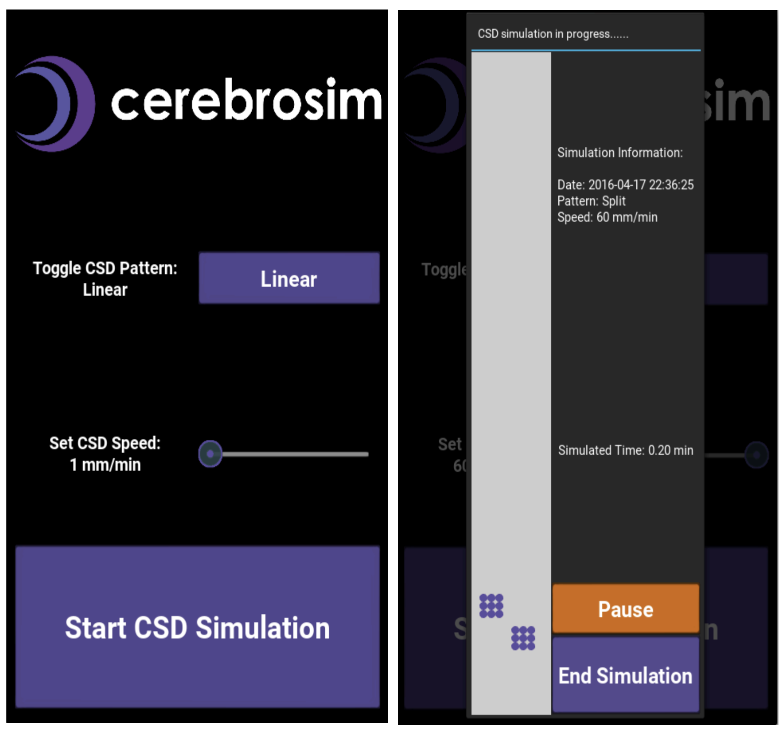


Figure 9. GUI Design

Containment Unit Design and Development

A device was needed to reliably house the material layers and the electrical array together. Two ½-inch acrylic plates with 16 tapped holes were laser cut to clamp the layers together. Acrylic was used since it is long lasting and does not rust. The bottom layer contains a rectangular cutout and four tapped holes to insert and mount the electrode array to the bottom plate (Figure 10). The top plate consists of 16 laser cut holes and a large 12cm x 12cm square hole cut out of the center to allow for the CerebroScope detection device to be applied directly to the resistive fabrics. The fabrics were all laser cut to match the outer, square dimensions of the bottom plate and also contained 16 holes for screw passage. The fabric holes were cut in a slightly tighter pattern than those of the plate, so that the screws would hold the fabrics taut and wrinkle free. When creating the design, we considered how to maximize contact between material layers and pin array. Contact was achieved by sandwiching the fabrics between the two acrylic plates, keeping all of the material layers compressed and immobile.

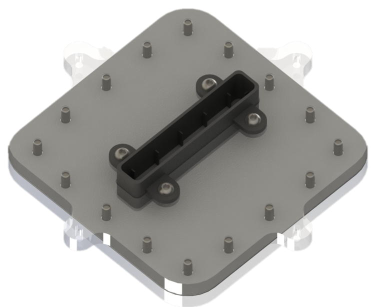


Figure 10. Bottom acrylic layer with inserted electrode array

A Nanuk 915 case was used to contain all the electrical and mechanical components of the design. Nanuk is a lead provider of durable, waterproof cases to military and industry customers. We chose to use the case for its durability, size, and modularity. An internal mounting plate, made of 3/16-inch polycarbonate with a waterproof Buna-N seal, was purchased and customized to meet our housing needs. Using SolidWorks and a laser cutter, we created plate cutouts so the components could be mounted to the plate while the internal parts remained protected from water and other environmental factors during transportation and/or use (Figure 11). The largest cut feature on the plate was made to fit the material housing unit, which is mounted to the plate using 4-6mm hex head screws. The second hole located to the right of the material layers was created for LCD touchscreen, which is mounted securely using 4-3mm machine screws. To the right of the screen is a set of holes that provide an outlet for the fan while still preventing large objects from falling into it. Two sets of inlet holes for the fan are located to the left of the material layers. This allows fresh air to be circulated over the power inverter, the PCBs, and the raspberry pi to keep all of the internal components cool for extended runtimes.

Above the material layers is a laser cut hole that fits an IEC power connector. This type of connector was chosen, because it is relatively cheap and easy to replace. This connector allows the power cable to be disconnected and stored in the case, preventing damage to the cable and the unit itself. To the right of the IEC connector is a round rocker switch that controls the flow of power from a 120-volt AC source to the 5-volt DC power converter. Operation of this switch allows the unit to be completely turned off and on. When this switch is closed, the raspberry Pi will automatically begin its startup sequence. The DAC will also begin its startup sequence to power the 20 PCB boards.

The Raspberry Pi, DC power supply and all loose wiring were secured using zip ties and adhesive zip tie mounts. Upon installing the plate, all of the internal components became fixed. When the lid of the Nanuk case is closed and secured using the two locking latches, all of the internal components are protected from the ingress of dirt and/or water. The case with all of the internals can be easily carried by the provided handle, making transportation of the simulator safe and ergonomic.

Figure 11. Containment housing of final design

Electrical Verification Testing

Verification was performed iteratively and step-wise throughout the design process in every stage before moving on to a more advanced stage. Three levels of electrical verification were performed: conceptual, design and final verification.

Circuit Concept Verification

1) Display more complex CSD patterns (e.g. spreading ring) using 1-2 control signals per row
   - To test CSD complexity, we connected a single shift register to an Arduino and implemented a frame refresh scheme of loading bits.
   - Inputs: varying patterns of shift and latch clocks.
   - Output: successful demo of unlimited pattern control on LEDs.
2) Confirmed –20mV signal transmission gates with 5V logic high control
   - Completion of this test demonstrated the ability to control millivolt transmissions with outputs of shift registers.
   - Input: Tested shift output as transmission gate input with -20mV signal.
   - Output: Signal correctly propagated.
3) Confirmed –20mV signal transmission in electrode array
   - Input: -20mV signal at bottom of ribbon cable.
   - Output: -20mV read correctly with voltmeter at each pin on top of array.
4) Generation of –20 mV signal by voltage inverter and Adafruit DAC chip:
   - Input: Inverter set to invert 5V to -5V. DAC set to trim 5V to 5-20mV. Ground used as 5V input to DAC, -5V used as ground of DAC.
   - Output: FAILURE. Could not get steady -20mV readings.
   - Solution: Changed signal propagation speed such that ground plate = 20mV, signal propagation = 0V (creates -20mV potential difference). Original intention was (ground plate = 0V, signal = -20mV).

Circuit Design Verification

1) Circuit Design and PCB fabrication
   - Ordered 3 prototype PCBs with only 2/5 of full design from ExpressPCB.
   - Inputs: Tested linear CSD propagation on a single board with LED test bench.
   - Output: Successful control of PCB demonstrated.

Final Product Verification

1) Scaled PCB board manufacture
   - Ordered 22 production level PCBs with solder mask ready for fabrication.
   - Inputs: Tested linear CSD propagation on all boards using LED test bench.
   - Output: A few small initial errors with propagation.
   - Solution: disconnected short circuit wires in PCB and added jumper cables to rectify design.
2) Device fabrication and post-solder verification
   - Tested post-fabrication correctness.
   - Inputs: Every PCB board with raspberry pi and linear propagation software.
   - Output: Successful fabrication and board operation.

Material Verification Testing

Material verification involved a series of tests to evaluate the resistive properties of the materials used in the final design.

Upon discovering the material discrepancy with respect to the resistive properties of the received fabrics, we spoke with multiple companies on the phone to learn the proper methods of measuring the surface resistivity of fabrics. After trying many methods of measurement, we were able to obtain consistent results by simply placing two 1.5” x 0.5” copper probes parallel to one another, with a 1.5” spacing between their centers, to create one-unit square area between the inner edges of the two probes. We then used a two probe approach to measure the resistance of the fabric per square, by applying downward pressure to each of the copper slabs using two multimeter probes. The detected resistance of the fabric between the two probes was recorded for each fabric. This method of measurement was found to be a reproducible test that confirmed material resistivity based on manufacturing specifications. Although we discovered that the donated materials did not meet the device needs, we were able to confirm that the materials we did receive were what the company spec’d.

In addition to material surface resistivity, we also confirmed multi-level isotropy. We were initially informed by an employee of CerebroScope that the direction used for measuring resistivity values does not matter, since the simulated anatomical tissues are isotropic, i.e. have uniform material properties. Thus, it was important to confirm that the obtained fabrics were also isotropic, to ensure the fabric intent and design accurately simulated the desired biological properties. The isotropic properties of resistive materials were outsourced from Marktek and confirmed through online research. We were told that layered resistive fabrics act like resistors in parallel (i.e. their overall resistance obeys the equation $\frac{1}{R_t} = \frac{1}{R_1} + \frac{1}{R_2} + \cdots \frac{1}{R_n}$ To test this statement, we first measured the resistance of a single layer of fabric in ohm/sq. We then added another layer and measured the resultant resistivity. This process of adding and measuring was repeated until a total of 7 layers were evaluated. The measured values were compared to the expected results (Figure 12). Because the expected and measured values were comparable and followed the same trend, we believe the layered material design is a feasible approach for representing anatomical tissue layers based on resistivity measurements.

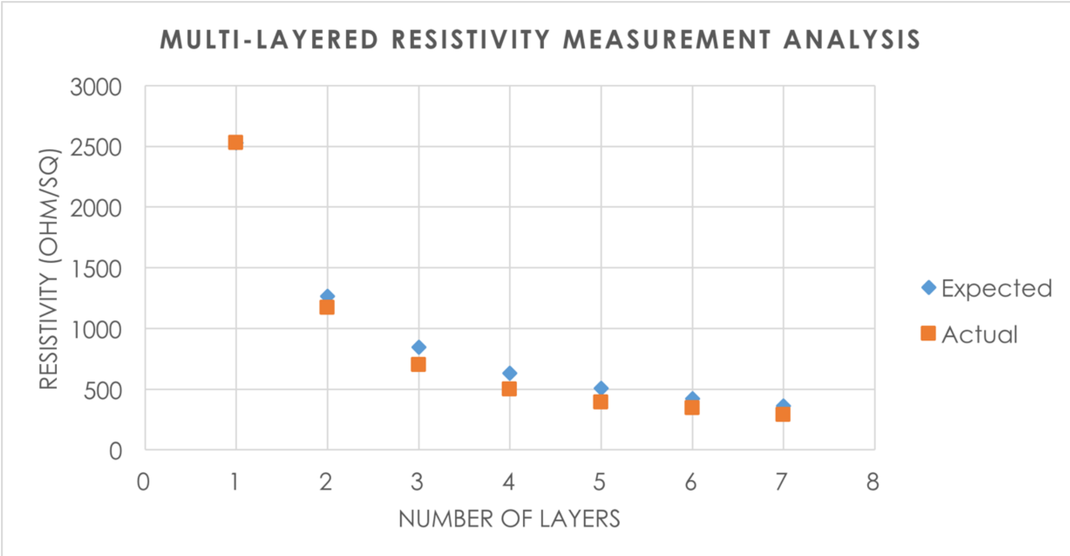


Figure 12. Multi-Layered resistivity expected and measured results

Lastly, we confirmed voltage propagation through the material layers, to ensure that the -20mV signal output by the pins of the simulator's electrode array could propagate through the materials it comes in contact with for accurate representation of the potential difference created by an actual CSD. Voltage propagation was confirmed by placing a voltage source on one side of a resistive material and measuring the output voltage on the other side. The test was performed using our most resistive fabric, as this material presented the highest likelihood of failing the voltage propagation test. The measurement process was repeated using multiple layers of the resistive fabric, to confirm the voltage propagation integrity of our layered material design.

Upon completing the previously described verification tests, we feel confident that if materials of the correct resistive properties are purchased, our device will function as intended.

Validation Testing

From the initiation of the project to its finish, continuous feedback was outsourced from Dr. Jones to ensure the device design met the needs of the user. Significant changes that were made to the simulator to validation the design included:

1) Scalp Region Size
   - A previous computer simulation of an 3mm expanding-ring CSD showed that the CSD expanded by a factor of 13 by the time it reached the scalp surface. Therefore, in a 10cm x 10cm region, the scalp voltage of a 3mm CSD would then project 2 cm from the edge of CerebroScope's 5cm x 6cm prototype electrode array. This would lead to the location of CSD detection being right on the border of the assembly, if the 6-cm extent of the prototype were centered in the 10 cm assembly (Figure 13) As a result, the assembly was made to be a size of 12 x 12 cm to avoid edge effects.

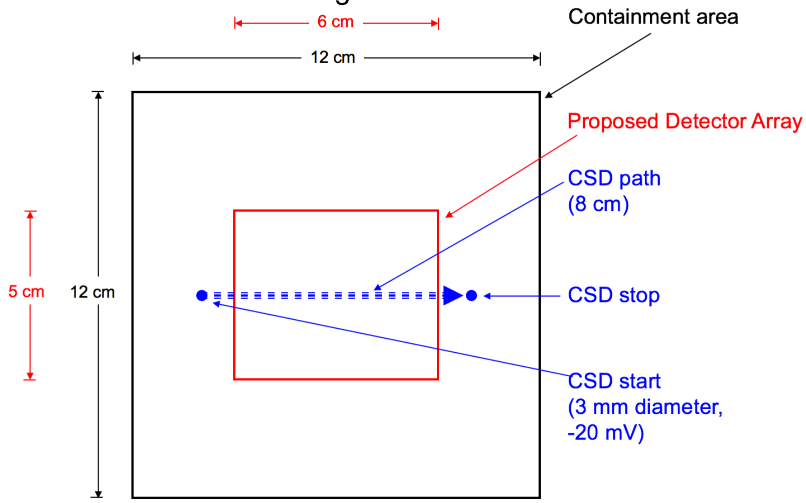


Figure 13. Simulation Region Schema

2) Touchscreen GUI Interface
   - Initially, we had planned to provide CerebroScope control of the CSD propagation through a desktop GUI and manual push-buttons. However, after discussion another opportunity and negotiating the retrieval of additional funding, we implemented the touchscreen GUI described in the section "*GUI Design and Development*." Implementation of a touchscreen was encouraged by Dr. Jones, as he felt displaying the propagating CSD in real time would greatly add to the impact of the device and would assist in future verification of whether or not the electrode array being created by the company is detecting the correct CSD pattern/signal in real-time.

All other specifications remained constant throughout the development of the simulator. Device design was validated periodically throughout the semester on an every-other-week basis, either through email or a face-to-face meeting with Dr. Jones.

Conclusions

Summary of Accomplishments

Overall, we completed our intended goal of creating a mechanical-electrical device that simulates the scalp surface voltage of a brain surface CSD that can be used in the future to bench-test and validate a prototype device that identifies and tracks propagating CSDs on the scalp. Other than the need for materials of different resistivities, our model is an accurate anatomical representation of a -20mV CSD. The CSD has the ability to move in a non-linear fashion, producing multiple known forms of CSD propagation. Implementation of a touch screen user interface allows the user to visualize the propagation and select the path and speed at which the CSD travels.

Other accomplishments associated with our project relate to the modularity and durability of the design. We aimed to create a modular product that allows CerebroScope to add/remove/modify project components as needed. This is especially useful for the revision of the resistive fabrics used in the design, as CerebroScope can purchase and implement new materials of correct resistive properties without influencing overall functionality of the device. Lastly, our product is housed in a durable, watertight case that makes it easy to transport the device with minimal risk of exposure to environments that could potentially damage the product.

Prototype Comparison to Success Measurements

All of the quantitative success criteria were implemented into the final design of the CSD simulator. We implemented all of the essential and non-essential objectives to create a device that simulates a CSD propagation of varying complexity paired with an intuitive graphical user interface. Although bench-testing could not be verified, we believe our simulator will support future non-human testing of CerebroScope's CSD detection device.

Lessons Learned

Many lessons were learned throughout the design, fabrication, and final assembly of our CSD simulator. Lessons we felt most greatly influenced project completion and future work in the engineering field include:

1) Asking Goes a Long Way

By reaching out to material companies early in our project design, we were able to obtain all material layers (except for the dura mater) for free. Had we not obtained donated materials, we would not have had enough funds to support the purchase of the remaining device components.

2) Prototype verification is important to ensure your design works before investing in the large scale product.

Before creating our final product, we tested each aspect of our design before scaling. For instance, we ordered three custom designed PCBs (cost ~$50) to verify the devised routing satisfied our CSD control needs. The initially prototyped design also provided the means to validate the design, as we could show Dr. Jones our low resolution design to ensure it fit his needs before investing in all of the components to create a final product. Once we verified the PCBs functioned as intended, we then made a purchase to scale to our final PCB design (cost >$400). Had we purchased all of the PCBs up front before verifying the design and found that the schematic did not work or fit the needs of the user, we would have wasted $400 of our budget.

3) Project management tools, such as a Gantt Chart and Milestone Trend Analysis (MTA), are extremely useful in devising tasks and quantifying project status/progress.

Although most of us had previous experience using gantt charts to manage projects, this class further confirmed how imperative organizational tools are in managing project status, progress, and team goals. Both the gantt chart and MTA provided a means to monitor and predict the status of our project. These tools greatly helped us time manage and distribute tasks to team members that best supported the achievement of project milestones. When adversity caused goals to be set back or changed, the gantt chart and MTA also aided in the rearrangement and redistribution of tasks to maximize efficiency. Lastly, these organizational tools provided an accurate, visual representation of our project status in real-time, which was effective in updating others of our project status.

Recommendations and Future Work

To improve the functionality and usability of the CSD simulator, we recommend the following:

1) Purchase materials that more closely fit the resistivity, thickness, and permittivity properties of the anatomical layers of the CSF, skull, dura mater, and scalp.

Obtaining materials that more closely represent the known resistivity values of the anatomical layers of the cerebral spinal fluid, dura mater, skull, and scalp will help produce a more accurate representation of the simulated propagation of the CSD through the anatomical layers. This will lead to a signal the better represents what would be present on the scalp surface.

2) Add the anatomical layers that were ignored in this design (including muscle and the hard and soft bone of the skull).

Implementation of additional layers normally present in a true anatomical model will also lead to a more accurate representation of the simulated propagation of a CSD.

3) Modify the containment unit of the device to have the dimensions and curvature of a human skull

This design refinement will improve the accuracy of the simulated propagation of the CSD signal and the contact between the CerebroScope High Density Electrode Array and the simulated scalp surface.

4) Improved control of the CSD propagation patterns

Additional means of propagation control would allow the user to specify the desired simulation to more closely obtain the propagation of interest. The interface should allow the user to select from the following:

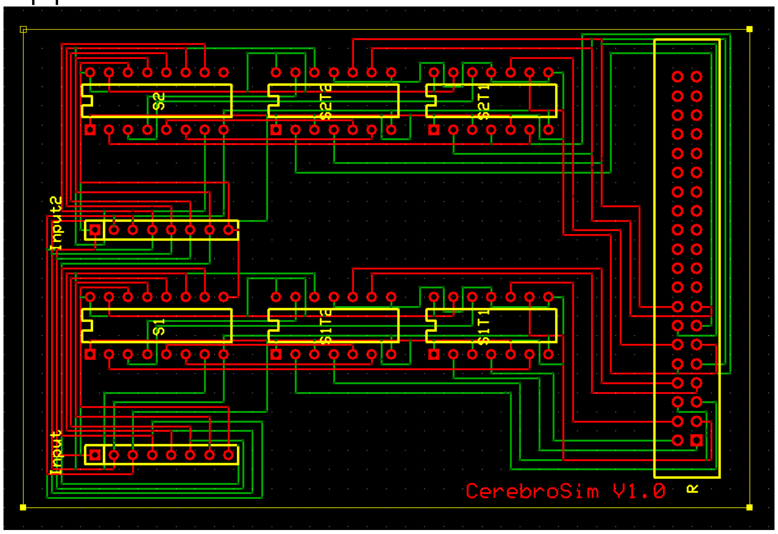
- CSD morphologies of a circle or expanding ring
- CSD dimensions of 2, 3, or 4 mm diameter
- CSD propagation speeds of 2, 3, 4, 5 mm/min
- CSD propagation track of a straight, wavy, or irregular line
- Choice whether or not to provide a region of depressed voltage (15 mV) that would correspond to infarcted brain that a globular, circle-type CSD would travel along its edge.

5) Validate the device with the scalp-mounted, CSD-detection system produced by CerebroScope

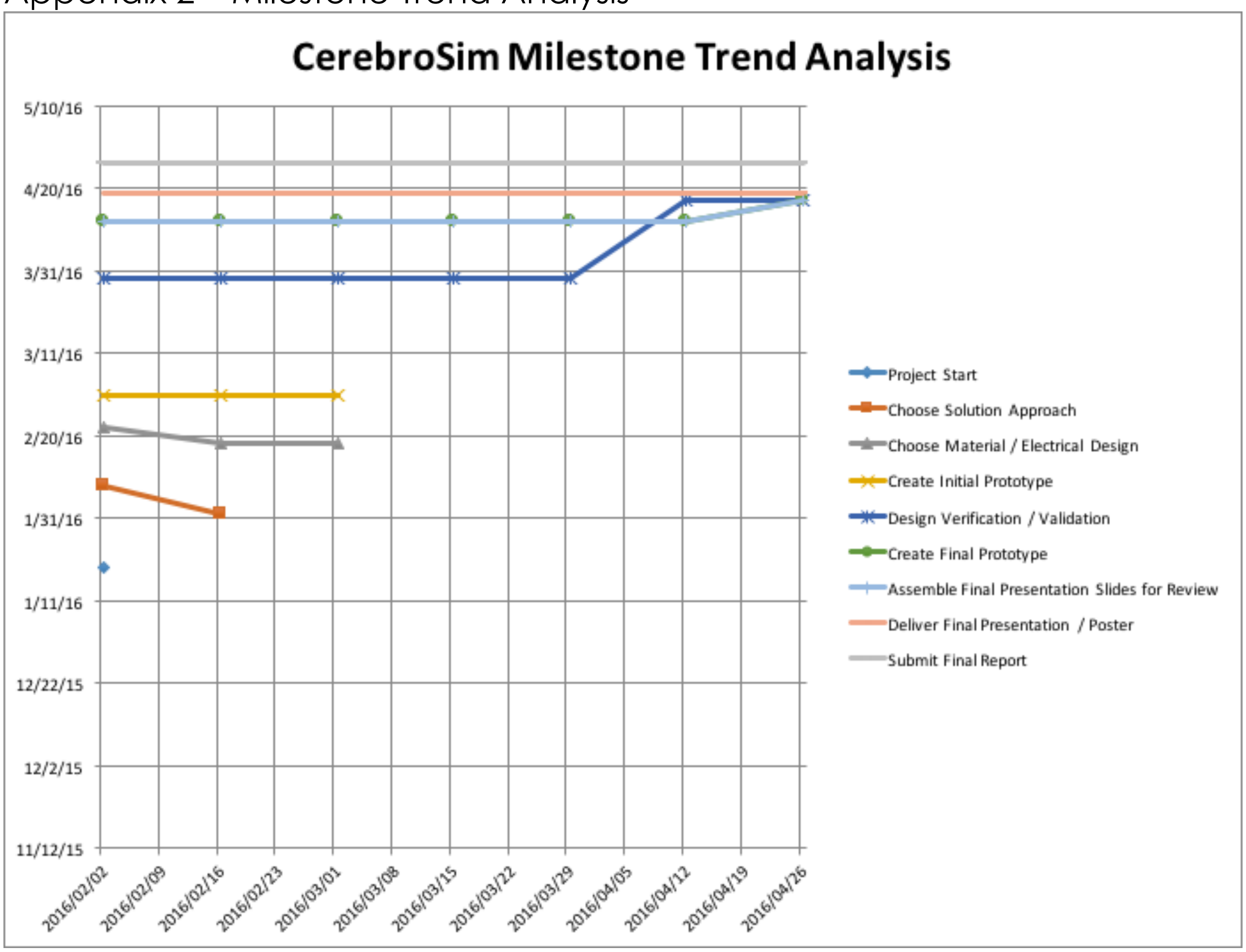
Upon creation of CerebroScope's detection unit, validation is necessary to ensure the simulator provides the means to bench-test CerebroScope's High Density Electrode Array and satisfies the requirements to be considered as an accurate method leading to the future detection of real-time scalp potentials in patients with acute brain injury.

Appendices

Appendix 1 - PCB Schematic



Appendix 2 – Milestone Trend Analysis



Appendix 3 – Gantt Chart

First Day of Week (Mon=2): 2

WBS	Tasks	Task Lead	Start	End	Duration (Days)	% Complete	Working Days	Days Complete	Days Remaining
1	**Project Identification and Initiation**	All	1/12/16	1/21/16	11	100%	8	11	0
1.1	Initiate contact with Dr. Jones	Angela	1/12/16	1/13/16	2	100%	2	2	0
1.2	Perform literature research	Team	1/12/16	1/22/16	11	100%	9	11	0
1.3	Create project question list	Team	1/12/16	1/22/16	11	100%	9	11	0
1.4	Meet with Dr. Jones	Team	1/12/16	1/22/16	11	100%	9	11	0
2	**Initial Report**	Team	1/19/16	1/26/16	8	100%	6	8	0
2.1	Define Problem Statement	Team	1/19/16	1/26/16	8	100%	6	8	0
2.2	Define Needs Statement	Team	1/19/16	1/26/16	8	100%	6	8	0
2.3	Define Project Overview	Team	1/19/16	1/26/16	8	100%	6	8	0
2.4	Define Project Motivation	Team	1/19/16	1/26/16	8	100%	6	8	0
2.5	Define Product Requirements	Team	1/19/16	1/26/16	8	100%	6	8	0
2.6	Define Objectives / Goals	Team	1/19/16	1/26/16	8	100%	6	8	0
2.7	Devise "plan of attack"	Team	1/19/16	1/26/16	8	100%	6	8	0
2.8	Create Gantt Chart	Team	1/19/16	1/26/16	8	100%	6	8	0
2.8.1	Define task schedule	Team	1/19/16	1/26/16	8	100%	6	8	0
2.8.2	Define project milestones	Team	1/19/16	1/26/16	8	100%	6	8	0
2.8.3	Define key deliverables	Team	1/19/16	1/26/16	8	100%	6	8	0
2.9	Create powerpoint	Team	1/19/16	1/26/16	8	100%	6	8	0
3	**Mid-term Presentation**	Team	1/26/16	3/1/16	29	100%	26	29	0
3.1	Order Supplies	Team	1/26/16	2/8/16	14	100%	10	14	0
3.2	Execute Ideation Session	Team	1/26/16	2/8/16	14	100%	10	14	0
3.3	Pretyotype at least 3 models	Team	1/26/16	2/8/16	14	100%	10	14	0
3.3.1	Design electrical signal hardware / software mechanism	Brian and Zach	1/26/16	2/8/16	14	100%	10	14	0
3.3.2	Decide upon materials and fabrication methods	Brian and Zach	1/26/16	2/8/16	14	100%	10	14	0
3.4	Provide Status Update #1	Team	1/26/16	2/9/16	15	100%	11	15	0
3.5	Test Material Resistivities	Team	1/26/16	2/9/16	15	100%	11	15	0
3.5	Meet Dr. Jones to discuss prototypes	Team	1/26/16	2/18/16	24	100%	18	24	0
3.6	Choose prototype design	Team	2/9/16	2/22/16	14	100%	10	14	0
3.5	Machine Containment Unit	Angela and Bill	2/9/16	2/22/16	14	100%	10	14	0
3.6	Provide Status Update #2	Team	2/9/16	2/23/16	15	100%	11	15	0
4	**Status Update 4**	Team	3/2/16	4/19/16	35	100%	35	35	0
4.1	Order Remaining Materials	Angela	3/2/16	3/15/16	14	100%	10	14	0
4.2	Add materials to containment unit to satisfy thickness requirements	Angela and Bill	3/2/16	3/21/16	20	100%	14	20	0
4.3	Fully assemble containment unit	Team	3/2/16	3/21/16	20	100%	14	20	0
4.4	Meet with Chris Horwitz from Electrogrip to gain material	Team	3/2/16	3/18/16	17	100%	13	17	0
4.5	Create and test bench for PCB and software	Brian and Zach	3/2/16	3/21/16	20	100%	14	20	0
4.6	Verify generation of multiple CSD patterns	Brian and Zach	3/2/16	3/21/16	20	100%	14	20	0
4.7	Verify PCB design	Brian and Zach	3/2/16	3/21/16	20	100%	14	20	0
4.8	Provide Status Update #3	Team	3/2/16	3/22/16	21	100%	15	21	0
4.9	Verify material resisitive properties are comparable to	Angela and Bill	3/22/16	4/4/16	14	100%	10	14	0
4.10	Scale design from 16 to 40 pin PCB's with mounting holes	Brian and Zach	3/22/16	4/4/16	14	100%	10	14	0
4.13	Solder PCBs	Team	3/22/16	4/4/16	14	100%	10	14	0
4.14	Manufacture metal contact to ground brain	Team	3/22/16	4/4/16	14	100%	10	14	0
4.18	Provide Satus Update #4	Team	3/22/16	4/5/16	15	100%	11	15	0
5	**Final Presentation**	Team	3/22/16	4/19/16	29	100%	21	29	0
5.1	Finalize software API and	Brian and Zach	3/22/16	4/11/16	21	100%	15	21	0
5.2	Assemble final prototype	Team	3/22/16	4/11/16	21	100%	15	21	0
5.3	Create GUI	Team	3/22/16	4/11/16	21	100%	15	21	0
5.4	Build wall power unit	Brian and Zach	3/22/16	4/11/16	21	100%	15	21	0
5.5	Creat power, control signal breakout board	Brian and Zach	3/22/16	4/11/16	21	100%	15	21	0
5.6	Draft Final Presentation and request feedback from Dr. Winter	Team	3/22/16	4/12/16	22	100%	16	22	0
5.7	Provide Final Presentation	Team	3/22/16	4/19/16	29	100%	21	29	0
6	**Final Poster**	Team	3/22/16	4/19/16	20	100%	21	20	0
6.1	Choose Template	Team	3/22/16	4/5/16	15	100%	11	15	0
6.2	Assign roles and section responsibilities	Angela	3/22/16	4/5/16	15	100%	11	15	0
6.3	Request feedback from Dr. Jones	Team	3/22/16	4/10/16	20	100%	14	20	0
6.5	Submit Final Poster		3/22/16	4/19/16	29	100%	21	29	0
6.6	Present at Design Expo		3/22/16	4/22/16	32	100%	24	32	0
7	**Final Report**	Team	3/22/16	4/26/16	15	100%	26	15	0
7.1	Assign roles and section responsibilities	Angela	3/22/16	4/5/16	15	100%	11	15	0
7.2	Create Report Layout	Angela	3/22/16	4/5/16	15	100%	11	15	0
7.4	Submit Final Report	Angela	3/22/16	4/26/16	36	100%	26	36	0

Appendix 5 – References

[1] Rates of TBI-related Emergency Department Visits, Hospitalizations, and Deaths — United States, 2001–2010. (2016, January 22). Retrieved http://www.cdc.gov/traumaticbraininjury/data/rates.html

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[4] Severe TBI. (2016, February 08). Retrieved from http://www.cdc.gov/TraumaticBrainInjury/severe.html