Multi-Spectral Brachyseed Oscillator: MARK 1

BME 464L: Medical Instrument Design

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BrachyVision

Abstract: Multi-spectral brachyseed oscillator to monitor seed location during therapy

Brachytherapy is a form of radiation therapy that is used to kill malignant cells by targeting localized areas of tumor with high concentrations of radiation [1]. The radiation doses are delivered to the patient using small brachyseeds, which are placed in close proximity to the tumor. The tumors targeted by brachytherapy are usually in their initial stages of growth, and are not metastatic. However, throughout the course of brachytherapy, the seeds are likely to move, preventing treatment from occurring efficiently. Using imaging modalities such as X-ray and CT would cause the patient to receive excess radiation doses throughout the body, as opposed to the localized radiation meant for therapy. The excess radiation could result in normal cells being harmed. Alternatively, using a device with no excess radiation such as MRI, results in a low-resolution image [2]. BrachyVision has created a portable, brachyseed vibrational device that causes the brachyseeds to oscillate when placed at the targeted site. The device also allows user control of the brachyseeds oscillation. Doppler Ultrasound, which does not result in any harm or excess radiation delivered to the patient, can then be used by clinicians to visualize the seed's vibrations.

The device includes a probe, which allows for the placement of an electromagnet in close proximity to the site to be targeted. The product developed by BrachyVision is intended for use when treating prostate tumors with brachytherapy. Therefore, for increased effectiveness when treating prostate tumors with brachyseeds, the probe will be inserted into the patient's rectum to allow for close proximity to the prostate gland. The probe includes an ergonomic handle designed for the clinician to have increased comfort and control when using the probe. The second part of the device includes a console box with an LCD screen and three buttons. The LCD screen allows for easy user interface to set a frequency from a scale of 0-100 Hz and an amplitude from 0-10 V for the seed's vibration. An additional feature allows for the user to control the backlight of the screen allowing for the device to be used in settings with low lighting. Three buttons on the main screen allow for the user to select options, with buttons for 'UP', 'DOWN', and 'SELECT,' The device is powered using both a 5V AC wall adapter and a 12V AC wall adapter, which can be plugged into all standard U.S. outlets.

Several tests were conducted throughout the process of designing and producing the MARK 1 multi-spectral brachyseed prostate oscillator, including tests to visualize the electromagnetic field, study the power required for the device, and test the strength of the electromagnetic field (EMF). These tests ultimately allowed the conclusion that the device is function (seed movement is observed at an electromagnet-to-seed distance of three centimeters) to be made.

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Section 1 - Customer and Clinical Need:

1.1 Clinical Need

Brachytherapy is one of the most rapidly evolving medical markets in the United States and worldwide, reaching a value of $680 million in 2013 and expected to reach a value of $2 billion by 2030 [1]. Brachytherapy involves placement of small metal beads emitting low-dose radiation at tumor sites. Unlike most common forms of radiotherapy, brachytherapy is unique since it delivers radiation at tumor sites without delivering radiation (and potentially damaging) healthy tissue. One of the main advantages of brachytherapy to other forms of radiation therapy, which also contributes to the therapy's recent rise in popularity, is that it allows clinicians to localize radiation therapy to the specific tumor site(s) of interest without causing harm to remaining patient tissue.

Due to brachytherapy's rapidly increasing popularity, hospitals need to reduce cost and time associated with individual brachytherapy treatments to adequately cater to as many patients as possible. Clinicians need a system that will monitor brachyseed placement over the course of treatment (early stage, low-dose brachytherapy has an average treatment time of 1-2 months). Since brachyseeds are inserted, but not secured, into the appropriate location in the patient's body using a high gauge needle, there is a possibility that brachyseeds will move away from the tumor site over time. The system also needs to be non-invasive, safe, compact and economic.

1.2 Patient Need

Brachytherapy can be used in a variety of cancer treatment applications, such as breast, prostate, cervical and endometrial cancer treatments [3]. The MARK 1's design focuses on prostate cancer applications; however, the technology and associated physical design can be modified to image brachyseeds at different sites in the body. In particular, prostate cancer is most common in males over the age of 55. In 2012, 1.1 million cases of prostate cancer were diagnosed in the US, and 307,000 prostate cancer related deaths occurred [4]. Prostate cancer is easiest to treat during early stages; since brachytherapy provides low-dose radiation and is especially useful for early stage cancer treatment, this type of radiative therapy is an ideal therapy for early stage prostate cancer patients. The ability to effectively monitor therapy progression by detecting brachyseed position throughout therapy, and ensuring that brachyseeds do not move a significant distance away from the tumor site, can significantly reduce the number of prostate cancer related deaths, and can reduce treatment time and costs for patients. A non-invasive brachytherapy monitoring method that does not deliver additional radiation to the patient, such as Doppler ultrasonography, is especially optimal for patient safety.

1.3 Current Solutions

Imaging modalities such as x-ray, computed tomography (CT), MRI and ultrasound are currently used to monitor both the initial placement of brachyseeds into tumor sites and the monitoring of brachyseed position over the course of treatment. Both x-ray and CT imaging involve delivering additional radiation to the patient, which can potentially damage healthy tissue. MRI is non-radiative; however, the imaging modality is relatively expensive, high maintenance and involves rigid patient positioning [1]. The MARK 1 capitalizes on ultrasonography, in particular Doppler ultrasonography, due to its non-invasiveness, low cost and associated patient comfort.

1.4 Relevant Patents

Below is a list of relevant patents for brachyseed position monitoring devices.

Patent	Patent Assignee	Description
US8295910 B1	Jefferson Science Associates, LLC	In situ monitoring of brachytherapy radiation and position using miniature gamma cameras [5].
US8721514 B2	Koninklijke Philips N.V.	External electromagnetic sensing of high-dose radiation brachyseeds [6].
US8021291 B2	Biocompatibles UK Limited	Implantable biomarker applied to brachyseeds for more robust detection using x-ray and CT [7].

Section 2 - Specifications and Constraints:

2.1 Frequency and Amplitude Modulation

To account for differences in human tissue stiffness between patients, the MARK 1's electromagnetic probe must be able to oscillate brachyseeds at frequencies ranging from 40-500 Hz, and at amplitudes ranging from 0-10 V. Clinicians can increase or decrease the frequency of brachyseed oscillation in increments of 1 Hz, and amplitude of brachyseed oscillation in increments of 1 V.

2.2 Non-Invasiveness

A non invasive, radiation free imaging technique that can realistically be used to image brachyseeds is Doppler ultrasonography, which uses high-frequency sound waves to measure changes in velocity, frequency, etc. The MARK 1's hardware delivers alternating currents at user-defined frequencies and amplitudes to the device's electromagnetic probe to produce oscillating movement of magnetic beads ("brachyseeds" used in initial device testing were PTFE stir bars). The changes in velocity caused by oscillation allow brachyseed oscillation (and corresponding position in the body) to be detected using Doppler ultrasonography.

2.3 Size and Weight

The MARK 1's hardware enclosure is meant to be a tabletop device used by clinicians, so portability and compactness were not design constraints considered for the enclosure. However, the electromagnetic rectal probe needs to be as compact as possible to account for human physiology. Since the electromagnet used was 6” x 2” x 2”, the probe was designed to be 7” long with a diameter of 2.5”. The electromagnet’s iron core was the main source of weight, so the probe was 3D printed with ABS plastic to reduce the probe’s overall weight.

2.4 Magnetic Field Strength

The MARK 1’s electromagnetic probe needs to generate magnetic fields of an adequate strength that will allow brachyseeds to oscillate at a distance of 3 cm (the distance between the rectal wall and the prostate). This is mainly dependent on the electromagnet used and associated power and design constraints. An electromagnet with a self-inductance of 8×10^{-4}□, 300 turns at a density of 22 turns per inch, and a maximum magnetic field strength of 7.142 Tesla at a voltage of 12 V was selected to account for minimal internal power dissipation and appropriate magnetic field strength.

2.5 User Interface

Brachyseed oscillation frequency and amplitude can be easily modulated using a user interface on the hardware enclosure consisting of Adafruit’s Graphic ST7565 Positive LCD screen and three weatherproof metal push buttons with LED rings. As clinicians adjust frequency and amplitude settings using the up, down and select buttons, the LCD screen displays a bar graph that gives a visual of the current settings relative to maximum frequency and amplitude settings.

2.6 Microcontroller

The Arduino Uno ATmega 328 was used as the MARK 1’s microcontroller due the number of I/O pins, clock speed of 16 MHz (which was fast enough for robust changes in frequency and amplitude outputs), and flash memory of 32 KB (since the MARK 1 does not involve storing data and producing calculations, the Arduino Uno’s flash memory was sufficient) [8]. One of the Arduino Uno’s limitations included a maximum DC current output of 40 mA from each of the I/O pins, which was accounted for in downstream amplification stages in the hardware.

Section 3 - Final Design:

3.1 Major Design Choices - Hardware

The hardware on the MARK1 includes three main components: connections from the Arduino to the LCD screen, frequency modulation, and amplitude modulation. The LCD screen used was a Graphic ST7565 Positive LCD (128x64) with RGB backlight. This screen is powered off of 3.3 V, therefore a 74HC4050 level shifter was needed to power the screen from the Arduino Uno. Additionally, three buttons were used to allow for the use to pick between ‘UP’ ‘DOWN’ and ‘SELECT.’ The buttons were chosen to have LED rings around them so the device could be used in settings with low lighting. The frequency modulation component of the hardware includes an H-bridge, which is powered through a supply voltage and regulated by four output pins on the Arduino. The H-bridge is composed of four transistors: two TIP-127 PNP

Darlington Transistors and two TIP-120 NPN Darlington Transistors. One TIP 127 and one TIP 120 make up on half of the bridge. Each transistor is turned on/off sequentially with the corresponding transistor on its side of the H-bridge in order to amplify current going through to the electromagnet. The H-bridge allows for current amplification using the transistors but also for current to flow in opposite directions through each branch of the bridge, and ultimately through the electromagnet. This in turn generates opposing magnetic fields from the electromagnet, which causes the seed to vibrate.

The amplitude modulation stage of the hardware consists of an output pulse width modulated signal from the Arduino. The user through the buttons and settings on the LCD screen can set this signal. The signal then passes through a low pass filter with a cutoff frequency of 5.3 Hz. This filtered signal is also amplified in this stage by a factor of 2. The output of this stage serves as the adjustable voltage input into a voltage regulator, which is powered by the 12V power supply. The output of the voltage regulator serves to increase the adjustable voltage input by 1.25 V, which then goes on to serve as the supply voltage to the H-bridge transistors. Therefore, the user can initially set the amplitude at which the seed's vibration will occur.

3.2 Hardware Schematics and Descriptions

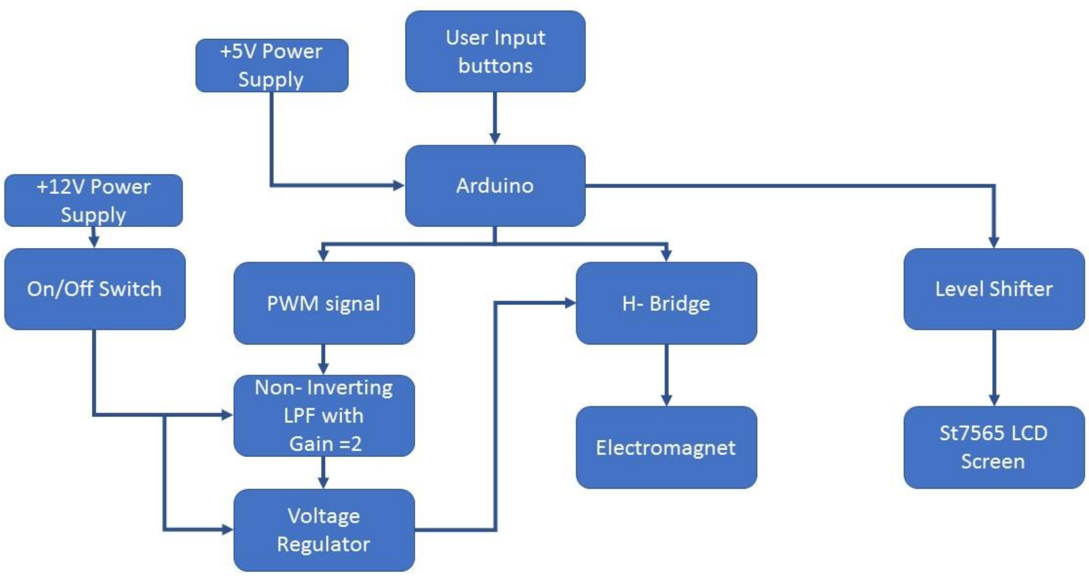


Figure 1: Hardware block diagram

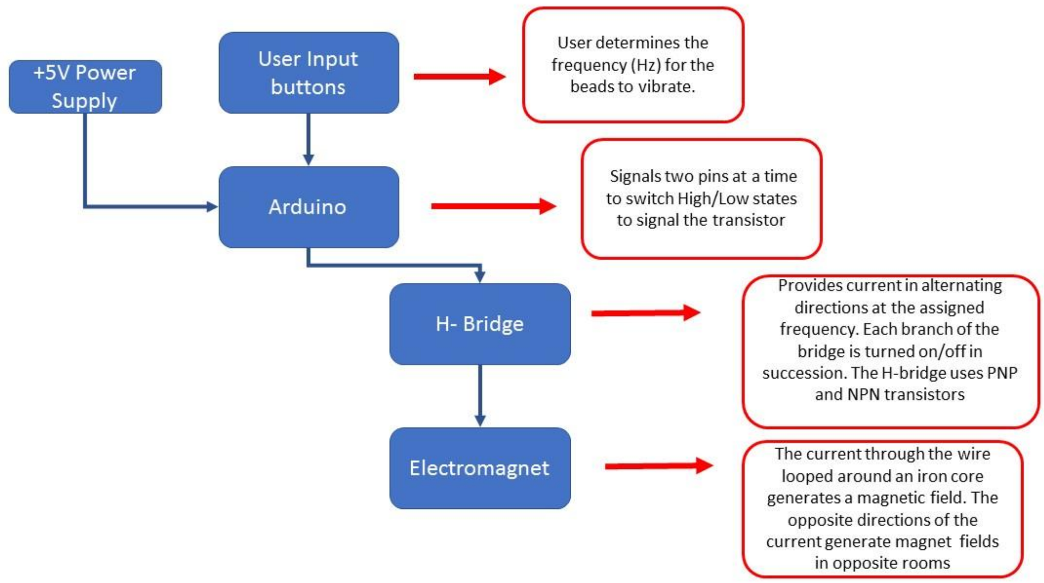


Figure 2: Block diagram for frequency modulation

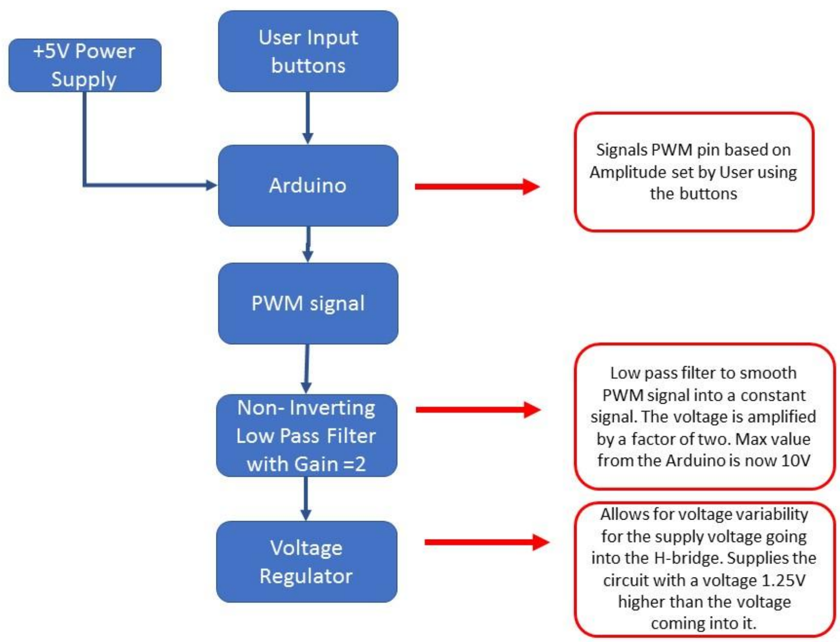


Figure 3: Block diagram for amplitude control

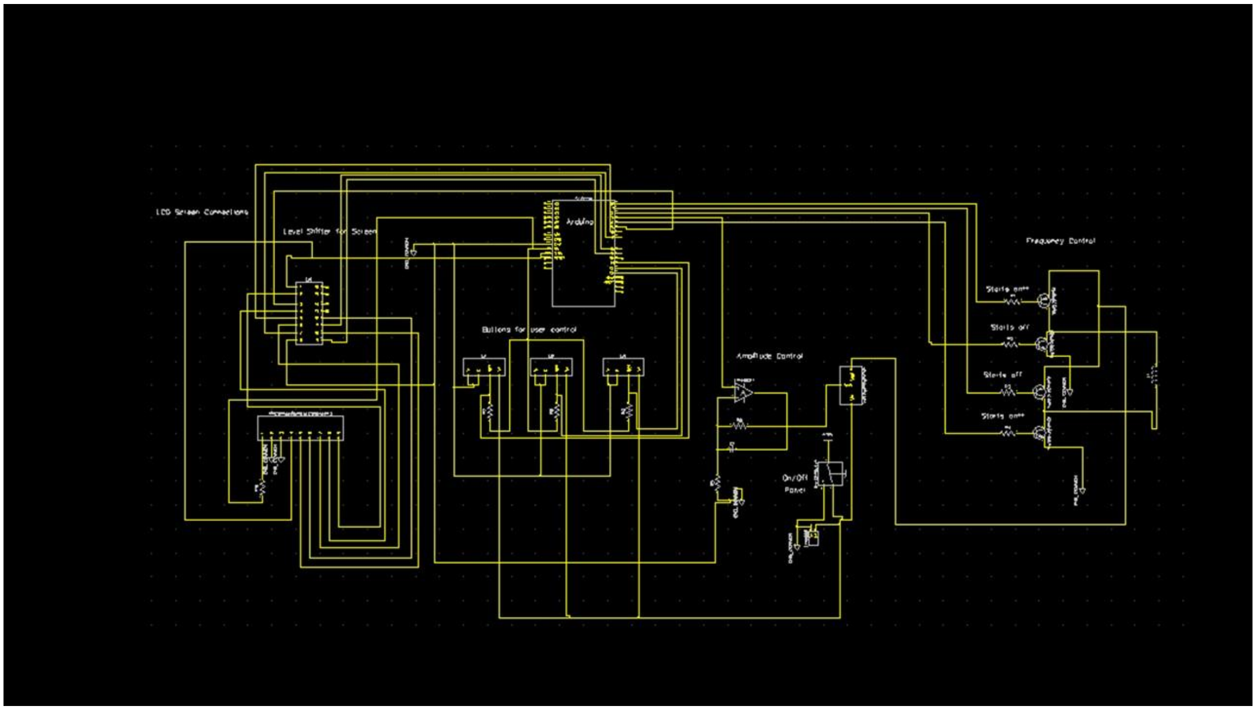


Figure 4: Hardware schematic

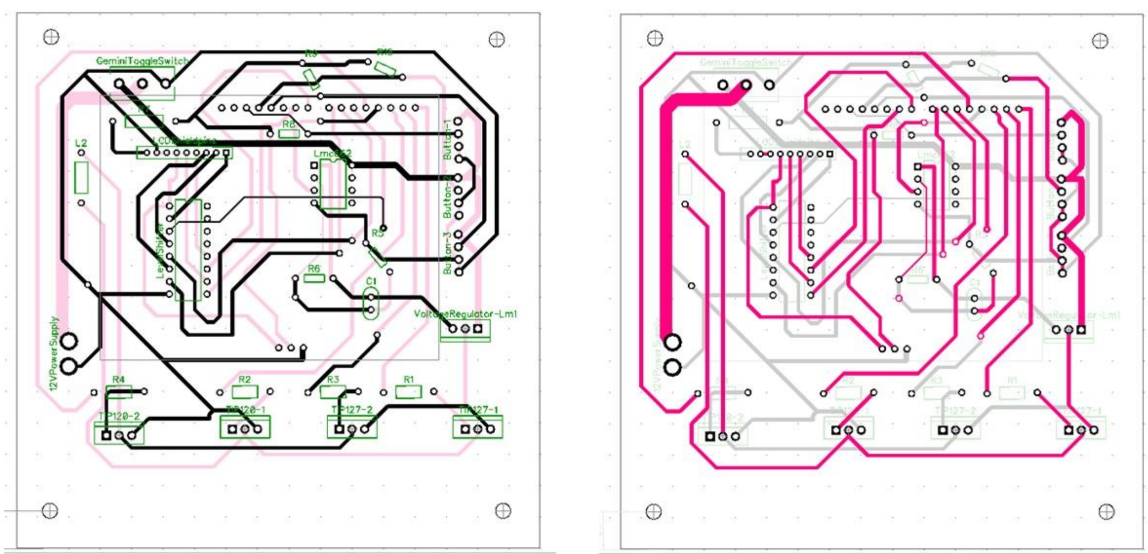


Figure 5: Hardware PCB layout. Front of board (left) and back of board (right)

3.3 Major Design Choices - Software

An Arduino Uno was used to produce time varying amplitude and frequency outputs (via pulse-width modulated outputs from four designated Arduino pins) that ultimately provide an alternating current to the electromagnet and generate the magnetic field used to oscillate brachyseeds. In addition, the Arduino communicates with a ST7565 LCD screen to provide a user interface, in which the user can modulate the LCD backlight brightness, output frequency, and output amplitude of the magnetic field.

3.4 Software Schematics and Descriptions

See Appendix 2 for details.

3.5 Major Design Choices - Physical Design

The MARK 1's physical design consists of two major components: a hardware enclosure with user interface and an electromagnetic probe. These components were 3D printed with ABS plastic using the BME lab's MakerBot 3D printers, and were designed using SolidWorks.

Hardware such as the Arduino Uno microcontroller and the printed circuit board are stored inside the enclosure. There are a series of active electronic components used in the MARK 1's hardware (such as transistors and voltage regulators) that tend to get warm during use; as a result, we have mounted heat sinks onto these components and designated a heat vent on the side of the enclosure to accommodate for heat dissipation and transfer within the device. The MARK 1's hardware enclosure also includes three power input slots - two for the 5 Volt Arduino Uno power supply and a 12 Volt power supply to power the active electronic components, and one for the toggle switch. Finally, there is an output slot for the wires at the H bridge's output to eventually be connected to the electromagnet. As previously mentioned, the hardware enclosure (5” x 7” x 4”) is intended to be a tabletop device and therefore did not have stringent size constraints. However, the user interface needs to be readily accessible by users as the probe is being used; therefore, the LCD screen and buttons were placed on the enclosure’s lid. The enclosure has a lid that can be taken on and off in the instance of hardware malfunctioning for convenient troubleshooting.

The rectal probe is 7” long probe with a diameter of 2.5”, with a 6” long handle of the same diameter. One major design consideration was a comfortable grip on the probe handle; to account for this, a curved probe that is easy to grip was designed. In addition, the wires and electromagnet need to remain in place within the probe during use. Wires are passed through the probe handle through a tunnel 0.5” in diameter handle into the probe. The electromagnet is contained within a cavity consisting of two plastic walls 1” high on either side of the electromagnet, allowing the component to stay still during use.

3.6 Physical Design Schematics and Descriptions

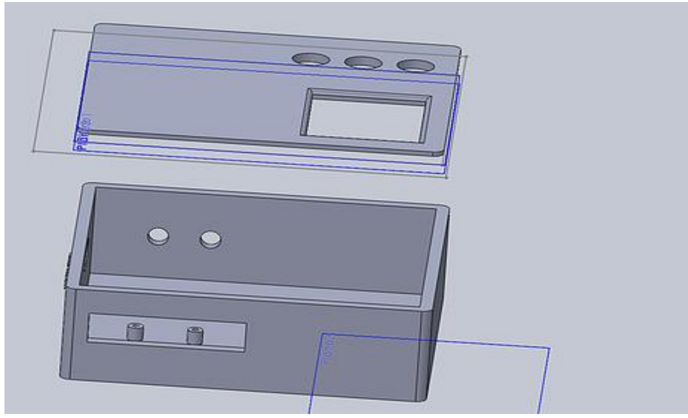


Figure 6: Hardware Enclosure - SolidWorks Drawing

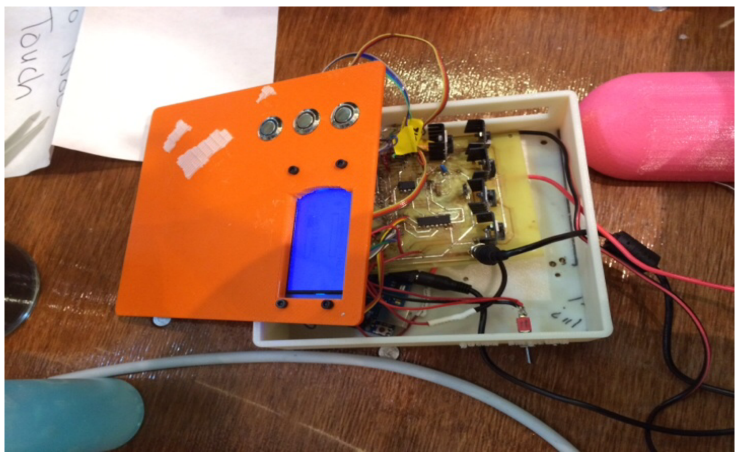


Figure 7: Hardware Enclosure - 3D Printed Part

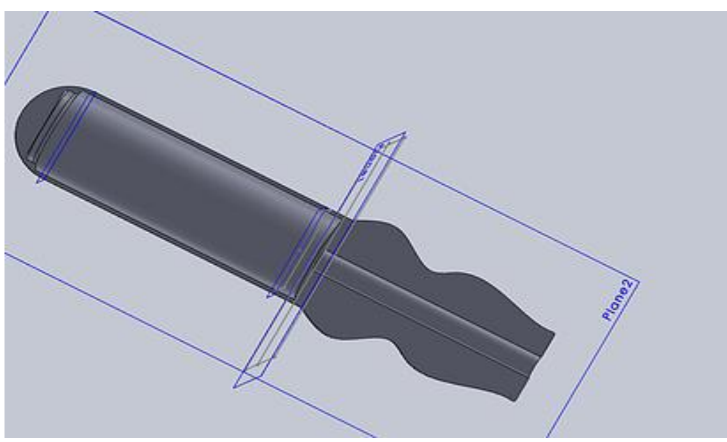


Figure 8: Rectal Probe - SolidWorks Drawing

Figure 9: Rectal Probe - 3D Printed Part

3.7 Parts List and Budget

Below is a table detailing the costs associated with each of the parts used in the MARK 1's design. Throughout the semester, $232.82 out of $400 originally allotted toward the project was spent on the MARK 1's development. Some of the products bought were not used in the MARK 1's final design, while other components that were used in the design were available in the lab (and therefore did not need to be bought).

Quantity	Part Description	Price	Extended Price
4	Weatherproof Metal Pushbutton with Red LED Ring - 16mm Red/Blue Momentary	$4.95	$19.80
2	DIY AMP Mono TDA7293 Amplifier Board BTL 85W Audiophile	$18.50	$37.00
4	TIP 120-NC Fairchild Semiconductor - Transistor BJT	$0.66	$2.64
4	TIP 127-FS Fairchild Semiconductor - Transistor BJT	$0.66	$2.64
1	Graphic ST7565 Positive LCD (128x64)	$17.50	$17.50
1 pack of 10 bars	PTFE Stir Bars - 5 mm x 2mm	$26.00	$26.00
1 pack of 10 bars	PTFE Stir Bars - 3 mm x 3 mm	$26.00	$26.00
1 pack 10 potentiometer	Potentiometers 9mm 200Kohms Single Cup	$1.34	$13.40
1	AC to DC Adapter - 110V AC to 5V DC	$10.75	$10.75

	Converter w/ Standard 4 Pin (500mA Max)		
2	SPDT Mini Power Switch	$1.50	$3.00
1	Arduino Uno R3	$24.95	$24.95
2	LM 338 Voltage Regulator	$2.01	$4.02
1	Electromagnet with Iron Core, 6" x 2" x 2"	$35.12	$35.12
Assorted Parts	Screws and Washers - Physical Design	$10.00	$10.00

Total: $238.82

Section 4 - Final Testing Procedures:

Please note that all Testing Protocols and data sheets can be found in full detail (set ups, etc) in the Testing Directory in the Team MARK GitHub Repository under 'All Testing Protocols and Pictures'. Below are brief overviews.

4.1 Testing Protocol 1: Basic First Pass

1. Align the electromagnet with the table top
2. Line up PTFE stir bar seeds parallel to the electromagnet 5 cm from the center of the magnet. They should be in 20 cm intervals along the length of the magnet
3. Starting from 0A, slowing increase the current passing through the electromagnet, pausing and recording when any of the seeds moved.
4. Continue till the device begins to overload or until the seeds are no longer moving
5. Repeat for a total of three trials
6. Increase the seeds-to-magnet distance by 1 cm and repeat
7. Repeat until the seeds-to-magnet distance is 10 cm

4.2 Testing Protocol 2: Iron Shavings

1. Tune the power source to provide the magnet ~0.5A
2. Outline the electromagnet on a piece of plain white paper
3. Place the paper on top of the electromagnet
4. Gently and evenly sprinkle iron shavings on top of the paper
5. Turn the electromagnet on and gently tap the paper to align the shavings to the electromagnet field
6. Take a picture
7. Clean up

4.3 Testing Protocol 3: Power Testings

1. Set-up

2. Turn on device and tune software
3. Record the max current and voltage and take a picture of the M-mode or PW-mode screens
4. Increase the voltage by an increment of 0.5V, wait for stabilization, and repeat the data recordings
5. Repeat for three total trials
6. Repeat until a clear sinusoidal pattern is visible on the M-mode or PW-mode screens, after which the voltage should be increase by an increment of 0.5V three more times.
7. Turn device off
8. Calculate power
9. Decide which power source should be ordered

4.4 Testing Protocol 4: Amplitude Modulation

1. Set-up device, ensuring the amplitude is set to the lowest setting (0)
2. Set-up and turn on Gaussmeter, with the tip of the probe 3 cm from the end of the electromagnet
3. Record the amplitude setting and the measured EMF. The measured EMF that is recorded should be the highest observed, since it will be oscillating.
4. Increase the amplitude setting by 0.5. Wait for stabilization and record data.
5. Repeat until the amplitude setting is maxed out.
6. Repeat experiment and then run statistical analysis (one-way ANOVA).

4.5 Testing Protocol 5: Electromagnetic Field Strength

1. Arrange the device and testing set-up
2. Record the distance between the electromagnet and seed
3. Prepare the Gaussmeter
4. Turn on the device, set the frequency to 5 Hz and power source voltage to 6V
5. Record the current through the magnet, the seed-to-magnet distance, the measured EMF, and any observations about the seed movement. Record three measurements of measured EMF and current.
6. Increase the seed-to-magnet distance by 0.5 cm.
7. Allow time for stabilization, the record data again
8. Repeat until the seed-to-magnet distance is 3 cm. Record all the necessary measurements.
9. Turn the device off.
10. Calculate the expected electromagnetic field strength based on the equation.
11. Perform statistical analysis on the data as follows:
    a. Significance testing comparing the strength of field of the different distances (ANOVA)
    b. Significance testing between the measured and calculated electromagnetic fields (two-tailed t-test)

Section 5 - Final Testing Results:

Many conclusions could be drawn from the tests conducted during the production of the MARK 1. During the first pass basic test, the magnetic field lines were clear, and the power of the magnetic field (before the Gaussmeter was obtained) could be slightly observed due to the seeds aligning roughly the same regardless of the tested distances, as seen in the Figures before. However, some seeds repeatedly aligned to the field faster (ie. at lower currents) than others, notably the seeds at positions 40-80 cm.

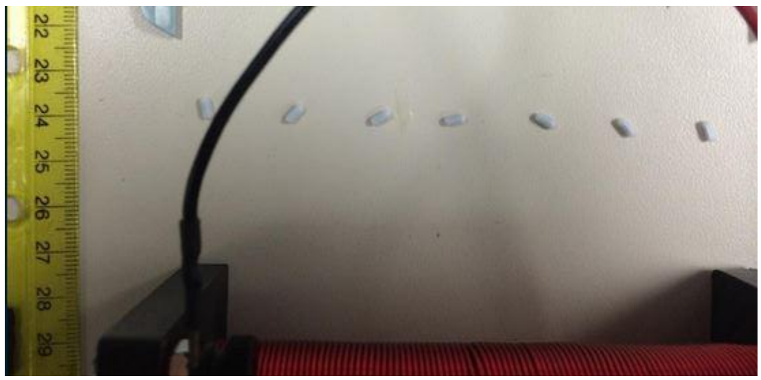


Figure 10: First pass test, seed-to-magnet distance of 6 cm. Note seed position alignment to magnetic field, allowing for basic visualization.

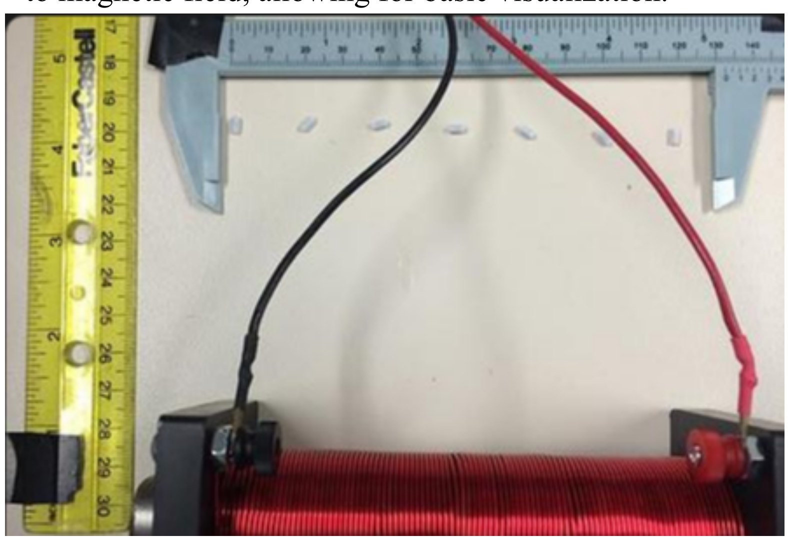


Figure 11: First pass test, seed-to-magnet distance of 6 cm. Note seed position alignment to magnetic field, allowing for basic visualization.

The iron shavings test also allowed for visualization of the electromagnetic field, but provided a more complete picture. It should be noted that the electromagnet had to be hooked up directly to the power source because the oscillations made visualization hard. The field lines when the device is fully hooked up are exactly the same, just switching direction as dictated by the Arduino.

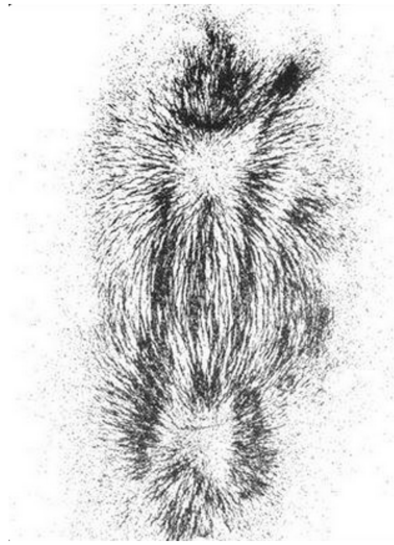


Figure 12: Picture of EMF lines as visualized with iron shavings. The two poles can clearly be observed, with lines connecting them in an arc.

Amplitude modulation, once functional, was tested briefly. As amplitude is increased, the measured EMF should have increased as well, which was observed. A one-way ANOVA was done to test whether there was a significant difference in the measured electromagnetic field as the amplitude was modulated. With a significance value of 0.05 and a returned p-value of $4.49*10^{-6}$, the difference was significant and the amplitude modulation is functional.

ANOVA Table

Source	SS	df	MS	F	Prob>F
Columns	3.69098	10	0.3691	24.29	4.48879e-06
Error	0.16715	11	0.0152		
Total	3.85813	21			

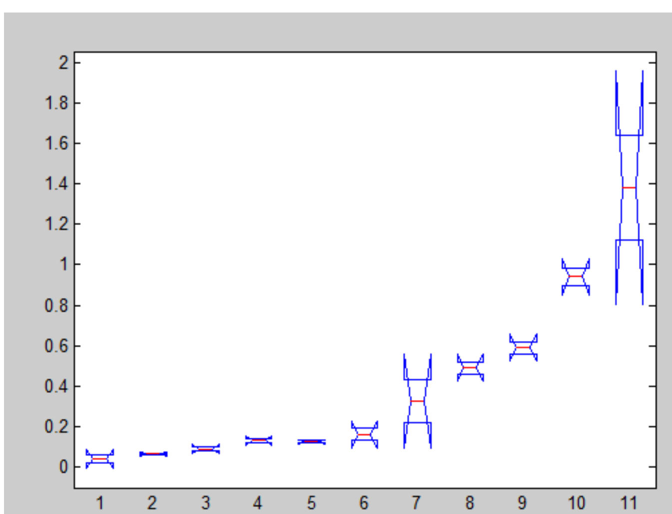


Figure 13: one-way ANOVA chart and table for amplitude modulation testing statistical analysis

Power testing was conducted to choose which type of power source should be purchased for the device. Based on observed seed movement and on the M-Mode and PW-Mode images, it was determined that a 10 W power source would be required. This was because the best ‘wiggle’ was noted at 6V, with a calculated power of roughly 8 W. Keeping the plastic probe that the electromagnet would ultimately be encased in, a 10 W power supply was determined as the best choice. This was an exciting test to run, as seed movement could clearly be visualized, and it allowed for the use of the ultrasound machine. Select images can be found in the Figures below.

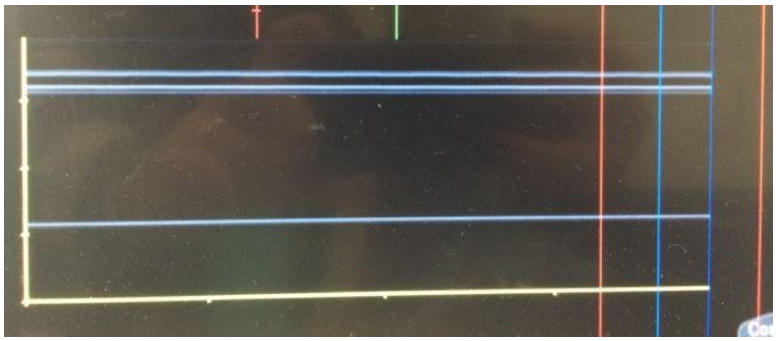


Figure 14: Power testing at 3V. No regular, repeating pattern can be observed in the M-mode of the ultrasound, meaning that there was no seed movement at this point.

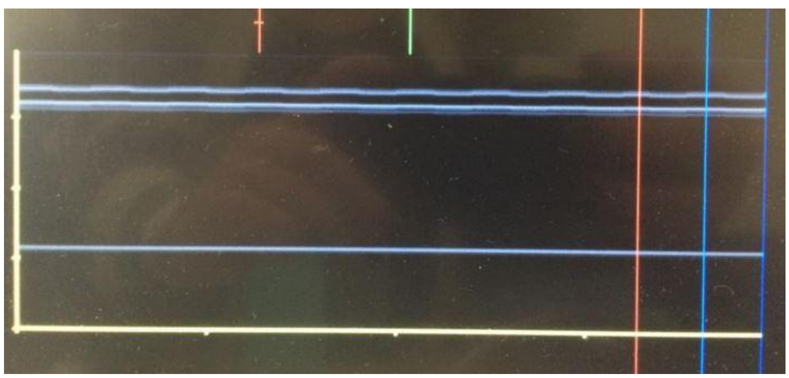


Figure 15: Power testing at 5V. A pattern is now observable, but it is not very strong.

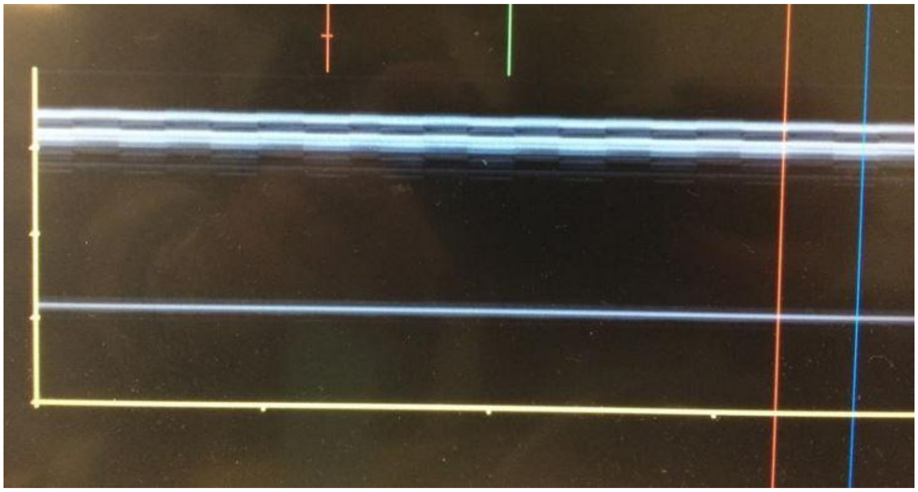


Figure 16: Power testing at 6V. A clear pattern is observed.

Finally, the most important test run was that of the electromagnetic field strength. Functionality of the device was defined as seed movement at a seed-to-magnet distance of 3cm. Because this was observed, the <u>MARK 1 can be considered a functional device</u>. Two statistical tests were run to analyze the data recorded from this experiment. A two-tailed t-test on the calculated and measured electromagnetic field strengths yielded a p-value of $1.727*10^{-6}$. Because this is below the significance value of 0.05, the difference between the two is significant and cannot be attributed to random chance. Interestingly, the measured EMF was higher than the calculated EMF. Running a one-way ANOVA was done to test if there was a significant difference between the different measured EMFs for the various seed-to-magnet distances. With a significance value of 0.05 and a calculated p-value of $1.33*10^{-9}$, the difference is significant. This makes sense because the equation predicts the EMF to drop off at a rate of R^3 with increasing distance. This equation can be found on GitHub, under All Testing Protocols. This may be due to the fact that the equation only takes geometry into condition, so there may be something inherent to the electromagnet (type of wire, thickness of wire, core material, etc.) that is causing the measured EMF to be higher than calculated.

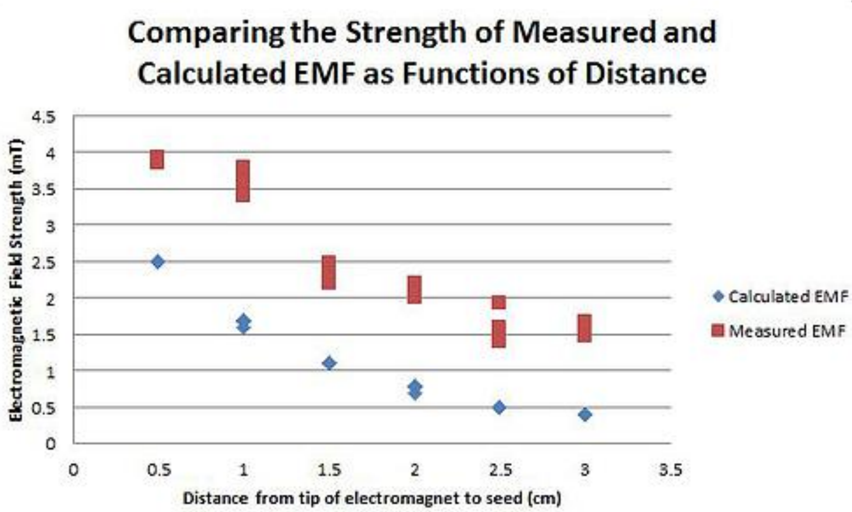


Figure 17: Measured EMF compared with Calculated EMF as a function of distance between seed and electromagnet. Measured EMF is significantly higher.

Section 6 - Design Iterations:

6.1 Current Amplification Stage (Hardware)

Upon deciding use an electromagnet to generate the vibration for the bead, the next step was to determine how to generate a high enough current to create the field strength that would be needed. Our first option was to use a voltage controlled current source to then be amplified using an audio amplifier. The current needed for the electromagnet was 0.5A and therefore the current source would need to provide that current. However attempting to make an audio amplifier circuit was not successful and ordering one would cause us to lose control over that components functionality. Therefore that idea was dismissed.

We then moved to the H-bridge idea to provide alternating current to generate fields in opposite directions to move the bead. The first H-bridge design involved four TIP-120 transistors (NPN- Darlington Pairs). For each branch of the bridge, one transistor would be powered using the 5V supply and the other transistor would be grounded. Both collector pins on the transistor would connect to one side of the electromagnet.

After completing this circuit design and building the circuit, it was found after testing that this circuit did not function as expected. Upon review, it was found that the base current being supplied was not enough to turn the transistor on. This resulted in a design modification to include 2 TIP-127 transistors and 2 TIP-120 transistors, with a 127 and 120 serving as one branch of the H-bridge. This allowed for the transistors to be turned on using the 5V supply voltage and work to control frequency.

The next step was to modulate amplitude. To do so, the supply voltage going into the H-bridge needed to be controlled. The team decided to use a voltage regulator, which would provide a voltage that was 1.25V greater than a variable voltage input into the regulator. Using the Arduino PWM pin to provide a signal that was then low pass filtered, this voltage was then fed into the voltage regulator and then as the supply voltage for the H-bridge. However, the 5V maximum output from the Arduino was still not enough to provide large enough amplitude in the bead’s vibration. The team then decided to amplify the voltage by a factor of 2 using an active amplifier. This was combined with the low pass filter.

6.2 LCD Screen and Associated Library (Software)

The general methodology behind the code stayed relatively consistent throughout the design iterations, but several elements underwent changes. For example, between software versions 1.0 and 2.0, the team received the ST7565 LCD screen, which we used to replace the Arduino LCD shield in order to present a more appealing user interface to the potential users. So version 2.0 is essentially the same implementation of the code as version 1.0, but it includes the capability of interfacing with the more complex screen. To achieve this, an open-source user made Arduino library was utilized in order to create menu screens on the LCD screen. Furthermore, several methods were added to the code in order to generate menu screens.

However, this user-made library had several downsides. It was impossible to create more intuitive menus that better fit the desired functionality within the framework of this library. Furthermore, a glitch in the library caused the second menu item screen to appear first, which was undesirable. Additionally, cursor movements as a result of button presses was poorly coded in his library, causing button movements that were very “jumpy”, making it difficult to accurately navigate the menu screens. Most importantly, the void loop called an “update” function during every cycle that re-wrote the LCD screen output. Writing to this LCD screen is very time consuming, and therefore the speed at which the frequency pins could be modulated was limited to less than 16 Hz due to the loop cycling through at the slow rate of 16 Hz. In order to bypass this roadblock, a menu item was implemented that “escaped” from the void loop, and continually outputted the frequency and amplitude settings until told to stop. While this increased the maximum modulation speed of the frequency pins, the output could only occur on this screen, which was un-intuitive and not user friendly.

To overcome this, for version 3.0, the user-made library was abandoned. Instead, customized menu screens were written to better fit the functionality of the MARK 1 device. A short delay was added after the button presses so that the cursor movement in response to button presses were smooth, and so that one button press yielded one cursor movement. Furthermore, if statements were employed such that the LCD screen output would only be updated if a button was pressed. This drastically reduced the amount of time necessary to cycle through the void loop when no buttons were pressed, which allowed the frequency to be accurately modulated at frequencies greater than 500 Hz.

6.3 Frequency and Amplitude Modulation Pins (Software)

The final change made to the code was to the implementation of the pin changes to create frequency modulation of the H Bridge. Initially, an ‘if’ statement checked to see if the current time was within a certain tolerance of the time at which the current frequency dictated that a change should occur. If so, then the pin states were switched. This method was prone to errors though: The tolerance limited the speed at which the frequency pins could be modulated. The frequency could be modulated no faster than the tolerance level. Furthermore, the tolerance had to be precisely calibrated so that pins would switch at least once but no more than once each time that it was supposed to. The tolerance required to do this, however; is frequency dependent, and thus this method resulted in a frequency modulation highly prone to “missing” a change in frequency. Because accurate frequency modulation was vital to our device working properly, this error was unacceptable.

To rectify this problem, a function was written that defined a variable as sin(Frequency*time)/abs(sin(Frequency*time)). That is, this variable is a square wave, oscillating between -1 and 1 at the current frequency. This function then checks to see if the sign of this variable is the same as it was last cycle: if not, then this indicates that the frequency pins’ states must be changed. This method proved to be both much more robust as well as faster than the previous method.

Finally, it was determined that a non-trivial amount of time was needed to allow the transistors on the “open” half of the H Bridge to close before it was safe to open the other side. If the other side of the H Bridge was opened during this time, then “shoot through” currents would flow through the short circuit created by the opening transistors and the not-yet-closed transistors. This resulted in massive spikes of current through the transistors, causing them to heat up quickly. To avoid this, a delay was implemented in the frequency function such that the opening side of the H-Bridge opened a little after the closing side closed. This delay successfully limited the shoot through currents from occurring.

6.4 Electromagnetic Probe (Physical Design)

Initially, the team made an electromagnet with a 2.5” iron core and 30 gauge copper wire found in the BME lab to reduce the probe’s size and weight. However, when current was passed through the hand-made electromagnet, the magnetic field generated was not nearly strong enough to attract, let alone oscillate, a neighboring PTFE stir bar. The team then made the decision to invest in a stronger, albeit larger, electromagnet that can generate a stronger magnetic field. Some components of the larger electromagnet that make it more capable for this application include the size and material of the iron core, number of windings and winding density, and wire gauge. The larger electromagnet had a larger and more magnetic iron core, greater number of windings and tighter winding density, and lower gauge (i.e. thicker diameter) copper wire.

Section 7 - Ethical Concerns:

7.1 Global Availability

One of the main questions that must be asked when dealing with medical devices is how realistic and widespread its application will be. Will it only be accessible in a state-of-the-art hospital, or is it something that could be made available in a third world country? Is it an extremely expensive technology, or is it affordable (both to produce and maintain)? $222.82 of the $400 budget was used to create this device. However, this was done with the help of a great amount of technology which was provided, including 3D printers, an ultrasound machine, and a gaussmeter, all of which are commercially very expensive. Considering this, the device would not be easy to recreate without a fair amount of resources. Past that, however, it is easy to power and maintain and could be used anywhere there is a wall outlet to provide power. It is easy to use and does not require extensive training, making it fairly globally available.

7.2 Probe: Discomfort versus Benefit

The size of the rectal probe makes the issue of risk versus benefit an important one for the MARK 1. The size would cause a patient pain and discomfort, and the probe needs to be properly cleaned to maintain hygiene. The situation needs to be fully explained to the patient before a decision is made to ensure that the benefit that the device provides outweighs the discomfort.

Section 8 - Safety Concerns:

8.1 Use of electromagnet

If there is a power surge of some sort, it could lead to a spike in the electromagnetic field, potentially harming the patient. There could also be unintended effects of the electromagnetic field on the body.

8.2. Internal movement of the seed

Since testing cannot be conducted in actual patients, the amplitude of the seed cannot be totally understood in the context of tissue. Too large a vibration may cause damage.

8.3. Seed material

The brachyseed material must be biocompatible, and must be carefully chosen so it does not trigger an immune system response, leading to inflammation and ultimately more harm than good.

Appendices

Appendix 1: User Manual

Mark 1 BrachySeed Oscillation System
User Manual and Troubleshooting Guide

Device Operation

Operating the Probe Transducer

1. The rectal probe transducer produces electromagnetic fields to induce brachyseed oscillations. To avoid this field causing interference with cell phones, computers, or other electronic devices, the probe should be properly placed BEFORE turning on the device
2. To place the probe, insert the probe rounded-end first into the patient's rectum. Take care to ensure that the side of the transducer is as close to the prostate as possible

Turning on the Device

1. To turn on the device, plug the extension cord into a standard 120V 60Hz wall outlet. Then, turn the power switch on the device to the "On" position.

2. The LCD will turn on, and display several startup screens, showing the device name and logo

Adjusting the Brightness

1. The first menu to appear will be the backlight menu. This menu controls the brightness of the LCD screen backlight. The menu consists of 3 menu items: “Up”, “Down”, and “Finished”, as well as a graphical representation of menu brightness

2. The bar at the bottom of the screen displays the current backlight brightness in relation to the maximum and minimum values. The greater the brightness of the backlight, the more filled in the bar will be. At the left of the bar is the number correlated to the backlight brightness: there are 11 levels of backlight brightness, ranging from 0 to 10. A backlight brightness of 10 is the maximum brightness of the backlight.

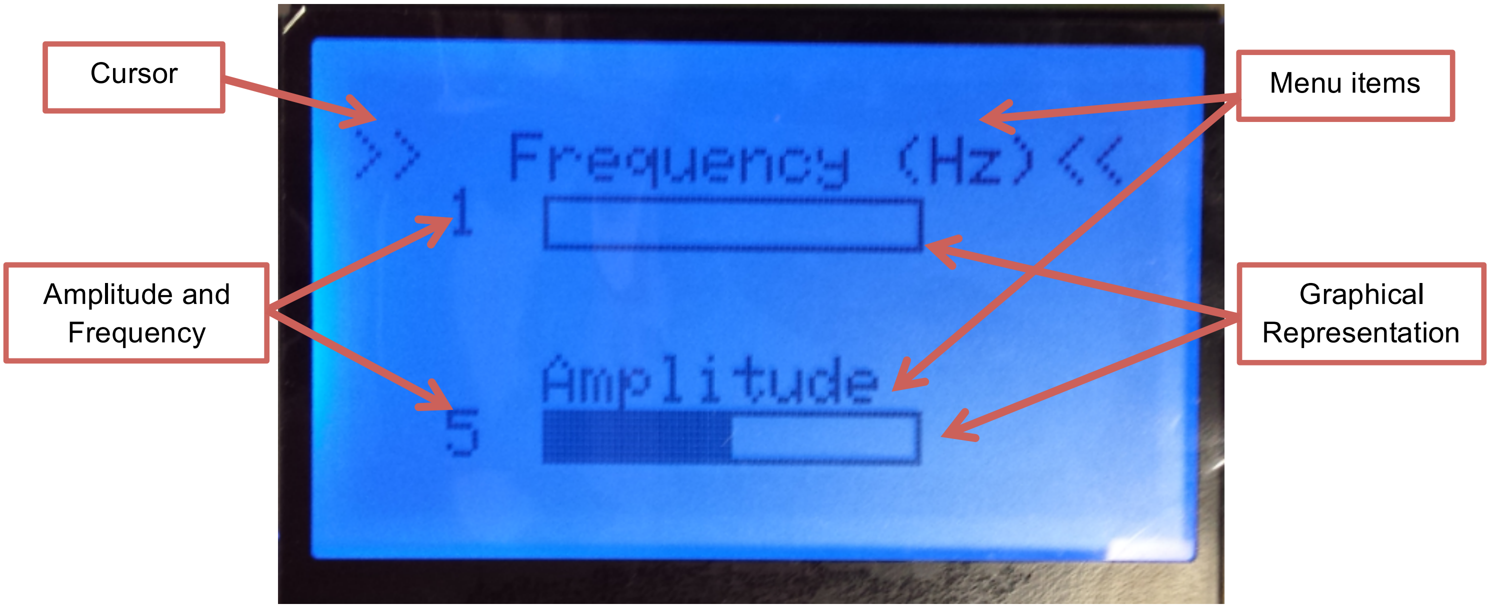
3. To adjust the backlight brightness, use the buttons to navigate the screen. The "UP" button moves the cursor upwards on the screen by one menu item, while the "DOWN" button moves the cursor downwards on the menu. The "SELECT" button is responsible for accessing the functionality of that menu item. For example, to increase the brightness of the backlight, use the "UP" and "DOWN" buttons to navigate to the "UP" menu item, and press "SELECT". Doing so will increase the backlight brightness by one increment.

4. Adjust the backlight until the screen brightness allows for easy screen visibility in the current lighting conditions.

5. To exit this menu, navigate to the "Finished" menu item, and press select. Note that this is the only opportunity to change the backlight brightness.

Changing the Frequency and Amplitude

1. After exiting the backlight menu, the main menu will appear. This menu displays frequency and amplitude menu items, along with visual representations of the current frequency and amplitude settings in relation to the maximum and minimum values, similar to the one seen in the backlight menu.



2. The frequency can vary from 0 to 50 Hz in increments of one Hertz. The amplitude has arbitrary units, and can vary from 0 to 10 in increments of 1. The frequency has a default value of 1 Hz, and the amplitude has a default value of 5. The frequency setting controls the rate at which the transducer will cause the brachyseeds to oscillate. The amplitude setting controls the strength of the magnetic field producing the oscillations: higher amplitudes should lead to larger oscillations that penetrate deeper into the tissue.

3. To adjust the Frequency or Amplitude, use the buttons to navigate the screen. Pressing the "Select" button moves to select the other menu item than the one the cursor is at currently. So for example, if the cursors are next to the "Frequency" menu item, then pressing the select button will move the cursor next to the "Amplitude" menu item. The "UP" and "DOWN" buttons are responsible for increasing and decreasing the value of that menu item by one increment. For example, to increase the frequency, use the "SELECT" button to navigate to the "Frequency" menu item, and press the "UP" button. Doing so will increase the Frequency by one increment.

Sending output to Transducer

1. Once the main menu is reached, the Mark 1 system will be constantly outputting the specified frequency and amplitude settings! So once the desired settings are set in the device, no further action is required!

Troubleshooting guide

Q: The LCD screen won't turn on

A: Possible solutions:

1. Make sure that the power cord is plugged firmly into a standard 120V 60Hz wall outlet.
2. Make sure that the power switch is turned to the "ON" position.
3. Check to see if there are breaks in any of the power cords: if there are, then they may need to be replaced.

If the device will still not turn on, then there may be some loose or damaged circuitry within the device. Please contact BrachyVision product support at 303-815-2195.

Q: The screen turns on, but I can't see any oscillations on my ultrasound

A: Possible solutions:

1. Make sure that the Frequency and Amplitude settings are both non-zero. If either setting is zero, then no oscillations will occur.
2. Increase the Amplitude incrementally, as it is possible that the brachyseeds require a larger magnetic field in order for movement to occur.
3. Sweep through the frequency range incrementally. Brachyseed movement is frequency dependent, so certain frequencies will allow for visualization with the ultrasound. If you are using Doppler, then the frequency should be set at or above 40 Hz for optimal visualization.
4. Make sure that the ultrasound probe is directed towards the prostate. Ensure that ultrasound gel is applied to the area of probe contact to ensure optimal ultrasound conduction.
5. Ensure that the rectal probe is inserted correctly into the patient's rectum, and that the distance from the prostate to the side of the probe is minimized.
6. Check to see if there are any loose wires going from the control box of the device to the transducer. If there are, discontinue use of the device immediately and contact BrachyVision product support at 303-815-2195.

Q: The cursor is not moving in response to button presses

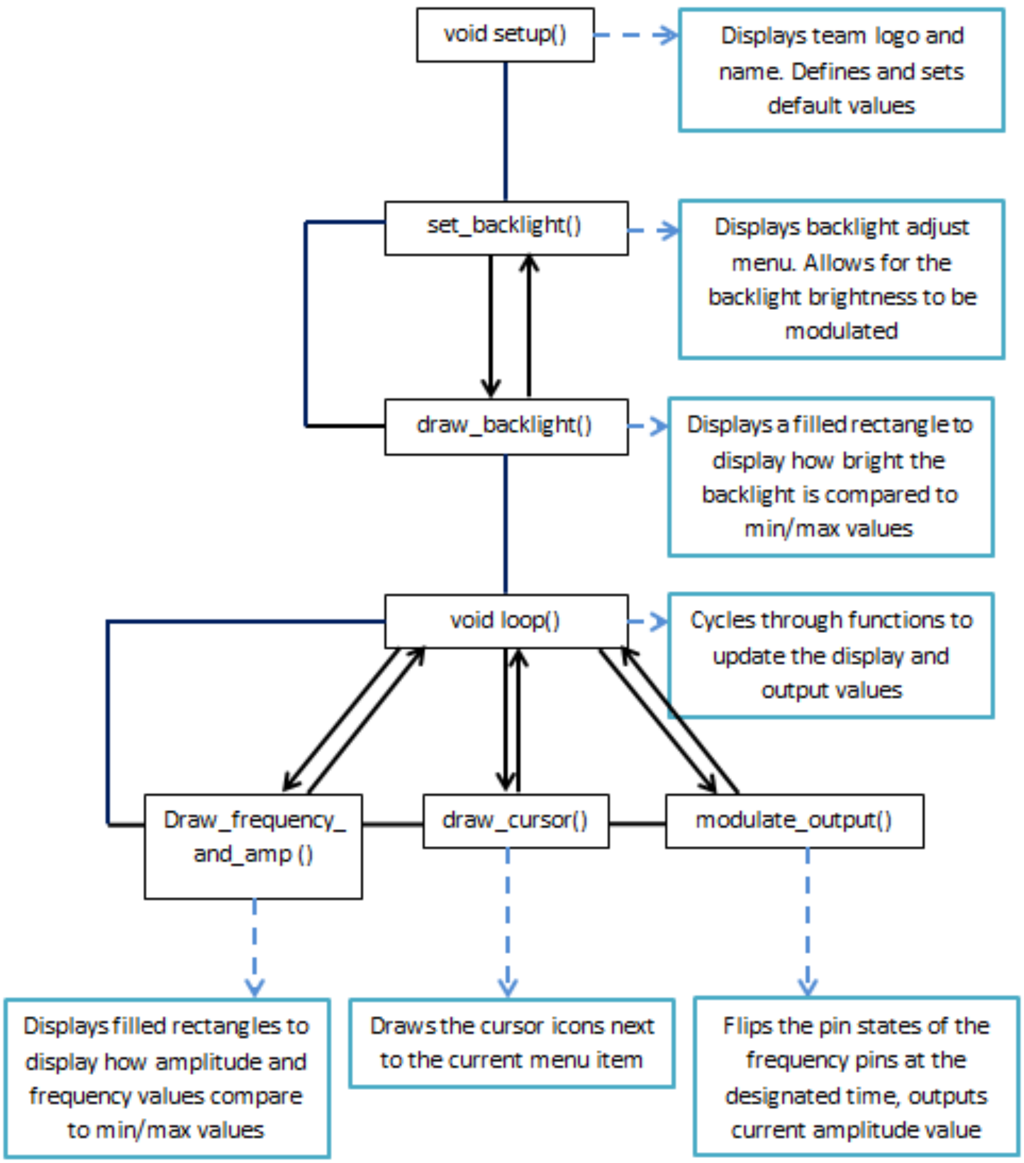
A: Possible solutions:

1. Make sure that the buttons are being pressed down firmly, until you can hear them "click".
2. Turn the device off and then back on. The Arduino powering the device is working really hard, and so sometimes it can get tired. In these cases, a restart is required.

Appendix 2: Software Flowcharts

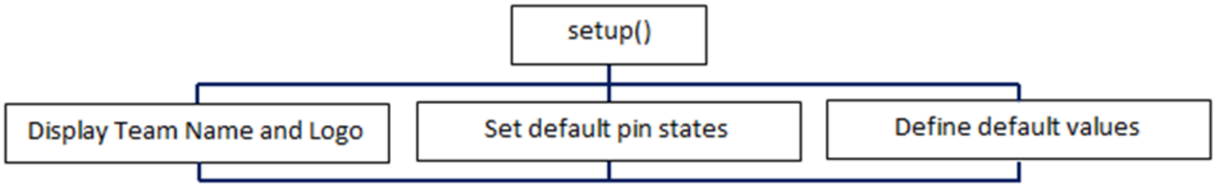
Code Flowcharts

General Code Flow

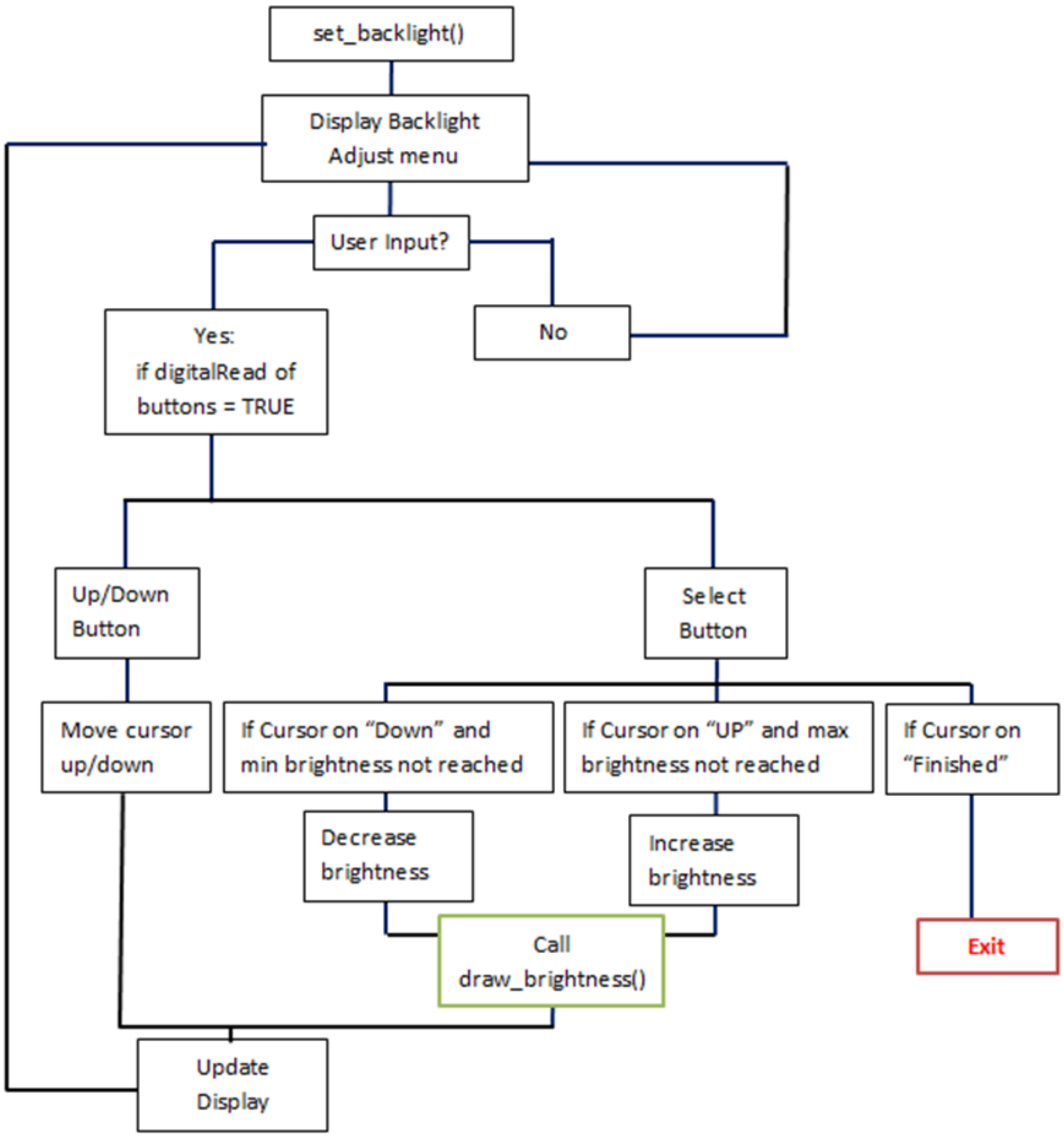


In Depth Code Descriptions

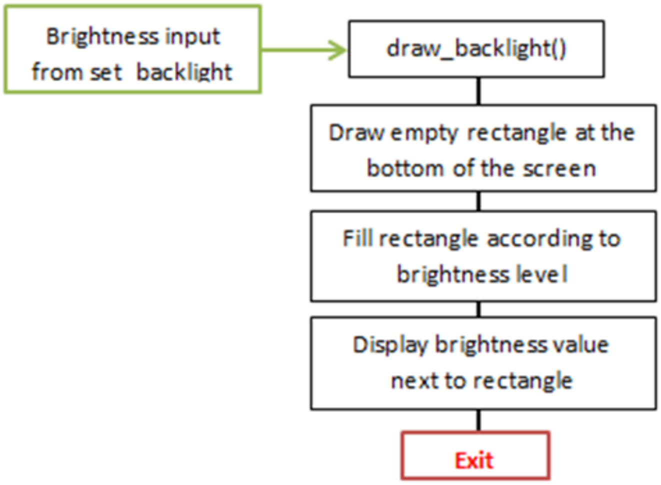
Setup Function



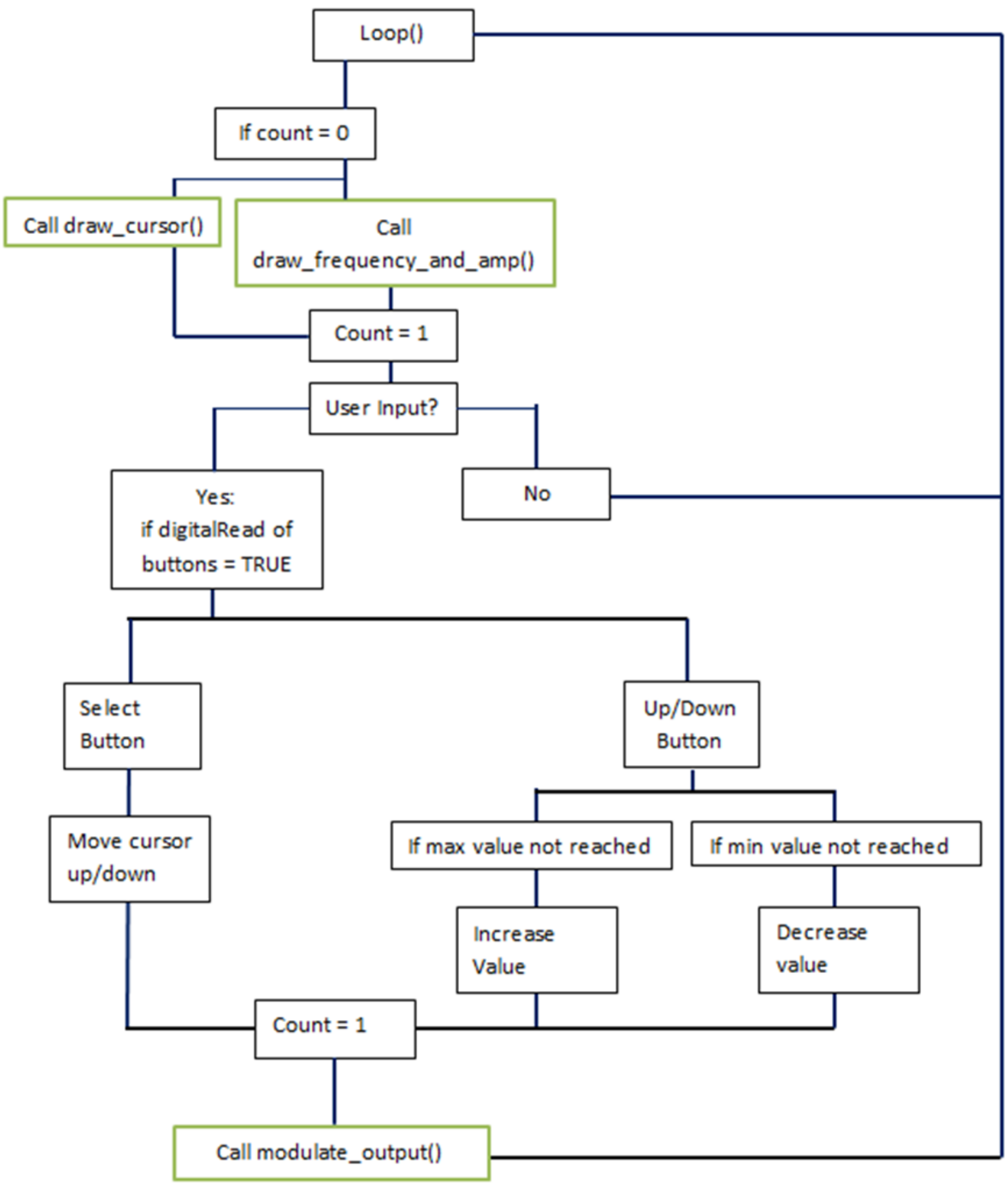
Set backlight Function



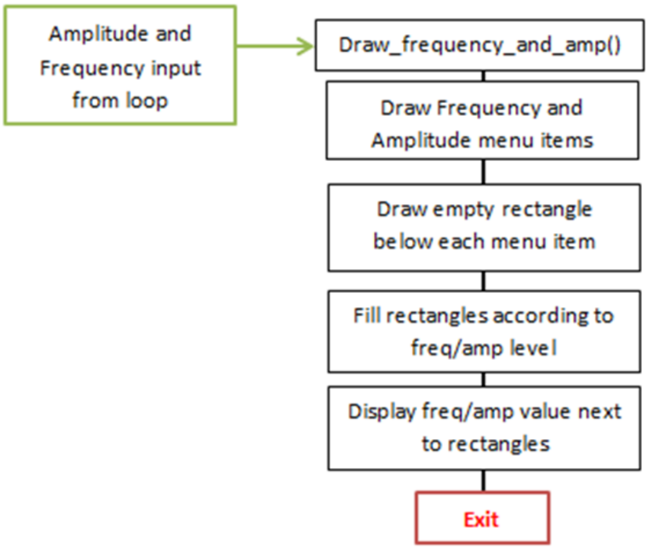
draw_backlight Function



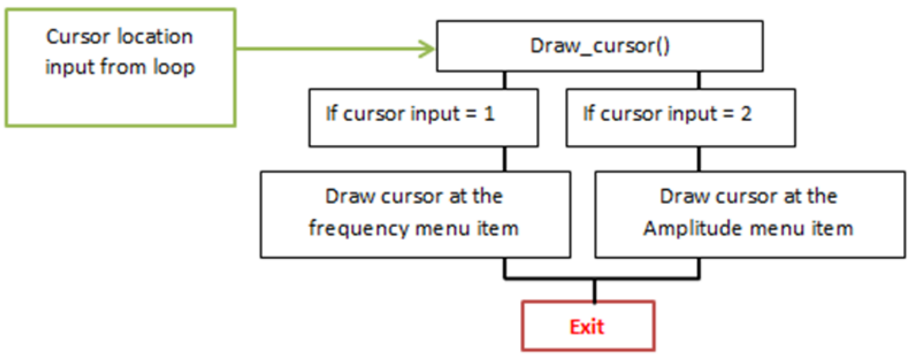
Loop Function



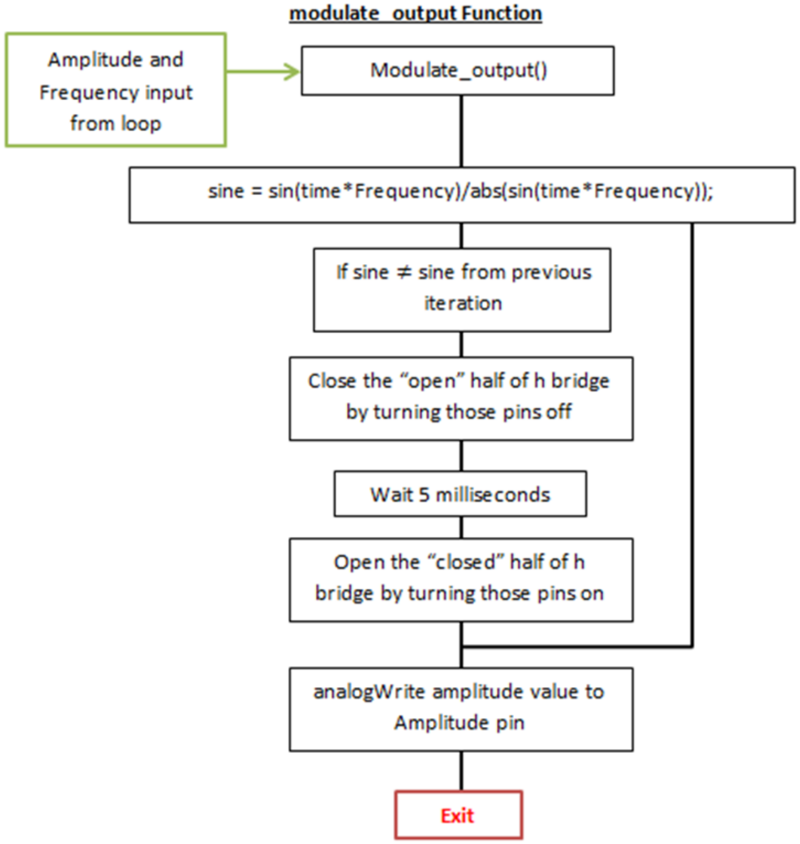
draw_frequency_and_amp Function



draw_cursor Function



modulate_output Function



Appendix 3: Link to Website

The BrachyVision team invites you to check out our website for more information about our MARK 1 device. Visit us at: http://brachyvision.wix.com/brachyvision!

References

[1] http://www.isotopeworld.com/products/brachytherapy/

[2] Thomas SD, Wachowicz K, Fallone BG. MRI of prostate brachytherapy seeds at high field:A study in phantom. Medical Physics. 2009; 36(11):5228–5234. [PubMed: 19994533]

[3] https://www.americanbrachytherapy.org/resources/brachyapps.cfm

[4] http://www.mayoclinic.org/tests-procedures/brachytherapy/basics/definition/prc-20021316

[5] https://www.google.com/patents/US8295910?dq=brachytherapy+monitoring&hl=en&sa=Xei=tI6IVIFHwtuwBNzHgOAD&ved=0CCQQ6AEwAQ

[6]https://www.google.com/patents/US8721514?dq=brachy+seed+position+monitoring&hl=en&sa=X&ei=DJGIVLm-H4vasATYuoCQBA&ved=0CDkQ6AEwBA

[7] https://www.google.com/patents/US8021291?dq=brachyseed+position+monitoring&hl=en&sa=X&ei=2pGIVIbjIcfdsASfnYK4Aw&ved=0CDQQ6AEwAw

[8] http://arduino.cc/en/Main/ArduinoBoardUno