SUNFEST Technical Report TR-CST01NOV04, Center for Sensor Technologies, Univ. of Pennsylvania, Philadelphia, PA, 2004

University of Pennsylvania
Center for Sensor Technologies

SUNFEST

NSF REU Program
Summer 2004

The Hand-Held Breast Cancer Detector: A 2-D Phased Array System

NSF Summer Undergraduate Fellowship in Sensor Technologies
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ABSTRACT

Presently, there are well known non-invasive methods in the detection of breast cancers. The most important include Magnetic resonance, X-ray, and Ultra-sound mammograms. However, due to their high cost, inconvenience, and time considerations, alternative methods are emerging. The Hand-Held Breast Cancer Detector (HHBCD) is designed to be an inexpensive and convenient way to replace other mammograms for some circumstances. It can detect small size tumors (1mm) up to 1 cm into the skin. The goal of this project is to expand the detection range to 3 cm. The device is based on the interference of two paired anti-phase near-infrared light (NIR) sources, a Photomultiplier tube detector (PMT) that detects a portion of this light, and a 2-D phased array method that discerns inequalities in the breast tissue. Most of the efforts put into the device were dedicated to improved signal interpretation, a more effective light source driver, and a shut-off protection system. The discussed individual parts were built but time did not permit them to be integrated. Successful completion of the device could prove useful for quick tumor detection and as a localization tool.

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INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among women in the United States and worldwide. In 2002, approximately 40,000 women died from the disease in the U.S. alone [1]. Many of these deaths can be attributed to the late detection of cancerous breast tumors; advanced stage tumors much harder to treat. Early detection through mammography and clinical breast exams is essential for effective breast cancer screening. For women between the ages of 50-69, regular mammograms can reduce the chance of death from breast cancer by approximately 30% [1]. Early detection of breast cancer greatly improves treatment options, the chances for successful treatment, and survival [2]. As a result, finely tuned detection devices have been developed to effectively expose very small tumors.

Breast cancer detection devices are powerful weapons in combating breast cancer casualties. Of the many non-invasive devices on the market today, the most important and commonly used are X-rays, magnetic resonance imaging (MRI), and ultrasound (US) mammograms. These devices can uncover tumors that may be too small to feel. While they have been generally reliable, their pitfalls are too great to ignore. Their shortcomings include inconvenience, high cost, and long inspection time. In the case of X-rays, inconvenience comes in the form of painful examination techniques and radiation exposure. For MRI and US, their high cost makes them inaccessible to the masses. Consequently, many women who see no palpable change in their breasts may opt not to get a check up. A new method of detection that can eliminate the drawbacks in current mammograms would bring the benefits of early breast cancer detection to everyone.

The Hand-Held Breast Cancer Detector (HHBCD) is a device that uses Near Infrared (NIR) Light to reveal and localize cancerous tumors in the breast. It is being developed by Dr. Britton Chance at the University of Pennsylvania. This device seeks to eliminate the problems of other non-invasive detection techniques. Due to the use of light as the main tool for detection, the HHBCD is an inexpensive and convenient apparatus for early detection. When perfected, this device will be able to replace existing mammograms for cases where the tumor is located up to 3 cm into the skin.

The objective for the project during SUNFEST 2004 is to assess the effectiveness of the current device and determine changes and improvements to be made.

The purpose, implications, and description of the HHBCD are explained in more detail in **Section 2**. Its principles for tumor detection are presented in **Section 3**. An assessment in performance of the HHBCD is seen in **Section 4**. **Section 5** discusses the recommendations made to fix and enhance the device. **Section 6** explains the changes made. **Section 7** discusses unfinished and future work. Finally, **Section 8** acknowledges the organizations and people who made my contributions to the project possible.

2. THE HAND-HELD BREAST CANCER DETECTOR (HHBCD)

The HHBCD is composed of a small navigation probe, a 12V DC power supply, a circuit interpretation box, a data acquisition (DAQ) card, and a computer. **Section 2.1** describes components and function of the probe. Then, it illustrates the signal read-out on the computer screen. **Section 2.2** clarifies the purpose and future implications of the HHBCD.

2.1 Device Description

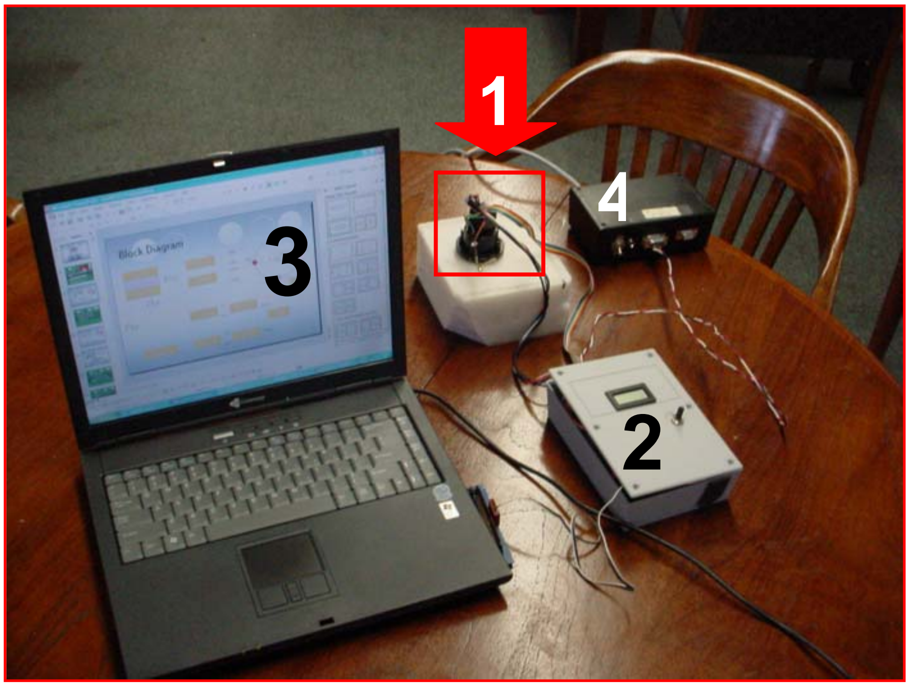


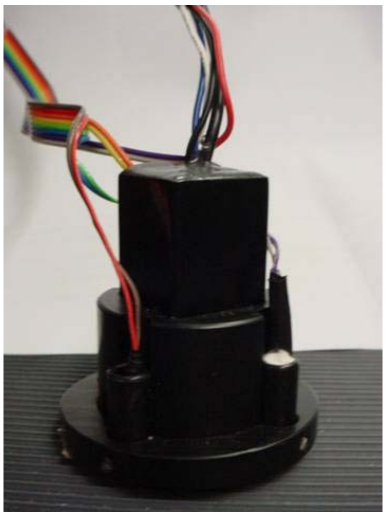
Figure 1: The HHBCD in its complete form. Its elements include 1) a navigation probe, 2) a signal interpretation box, 3) a computer display, and 4) a power supply.

2.1.1 Navigation Probe

The Navigation probe consists of a Photomultiplier Tube (PMT) and four light sources called light emitting diodes (LED's). The PMT is a very sensitive light detector that can be designed to read specific wavelengths. In our case, we have used PMT that operates in the near infrared region (NIR). The LED's are then chosen to produce light (photons) in the NIR region. The intricacies of the PMT and photon diffusion in highly scattering media (breast tissue) merit a report in themselves – references 4, 5, and 6 provide more information for the curious reader.

The PMT produces a measurable electrical signal proportional to the light to which it was exposed [3]. The trajectory of the light is predicted to propagate in the tissue outward from the light source as a spherical wave [4]. This basic understanding in PMT and photon diffusion theory is enough to comprehend the HHBCD's detection method ahead.

The device's probe is home to the PMT and LED's acting as a navigation tool to scan around the surface of the breast. It is circular at the point of contact and is about the size of a toddler's fist. At its center, the probe holds the PMT which is surrounded by two paired LED's placed around it perpendicular to each other as in a cross. These LED's are placed at a distance of 2 cm from the PMT. The fashion in which the LED's are placed permits detection in two dimensions (2-D). **Figure 2** shows the configuration of the PMT in respect to the LED's.



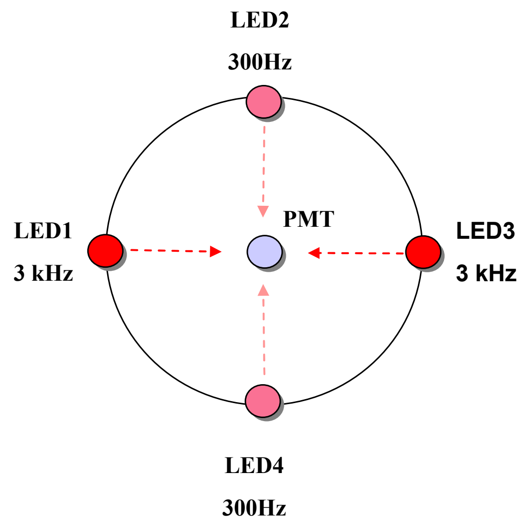


Figure 2: From left to right: picture of navigation probe and a drawing of its face. The components configuration on the face of the probe (phased-array geometry) is easily seen on the drawing. The face is what will come in contact with the breast tissue during inspection.

This arrangement is known as phased array geometry [5]. From this, a 2-D Phased Array system of detection can be implemented when dual out-of-phase sources are used [6]. To detect a small object embedded inside the turbid media, the dual-interfering-source configuration (phased array) is used because it is basically a cancellation technology. To put it more clearly, a phased array system can sensitively detect and locate small objects in turbid media (breast tissue) [5].

With the aid of **Figure 2** it is shown how the interaction of these two components result in the formulation of a signal that can be used for the detection of a cancerous tumors.

Since we have two paired LED's, the circuit contains two frequencies corresponding to each pair: 300 Hz and 3 kHz. This permits the user of the Hand-Held Cancer Detector to know which of the two planes the tumor is located when scanning over the breast.

One must understand two fundamental requirements for effective light localization and detection by the PMT. These include light variation and light intensity.

Light variation, in plain terms, refers to making the LED's light very dim and very bright (by being out-of-phase they change at opposing intervals). This is accomplished by driving the LED by a sinusoidal current. Without proper swing (very dim to very bright), localization cannot be effectively accomplished as the waves are not able to differentiate each other sufficiently for our circuitry to make a clear distinction. We can go back to the color analogy to simplify: without proper swing, the PMT cannot distinguish between green, red, or yellow. As a consequence, localization is lost.

In addition, without a suitably high current in the driver the LED's light intensity might also become insufficient to be read by the PMT. Lack of intensity would then result in losing all capabilities of the HHBCD. Not only would localization be lost but also plain detection of a cancerous tumor.

For simplification purposes, **Figure 3** (in the next page) illustrates only the 1-D case, that is, one plane. The 2-D case would include the plane bisecting the PMT perpendicular to this page. This would allow for two planes of detection simultaneously.

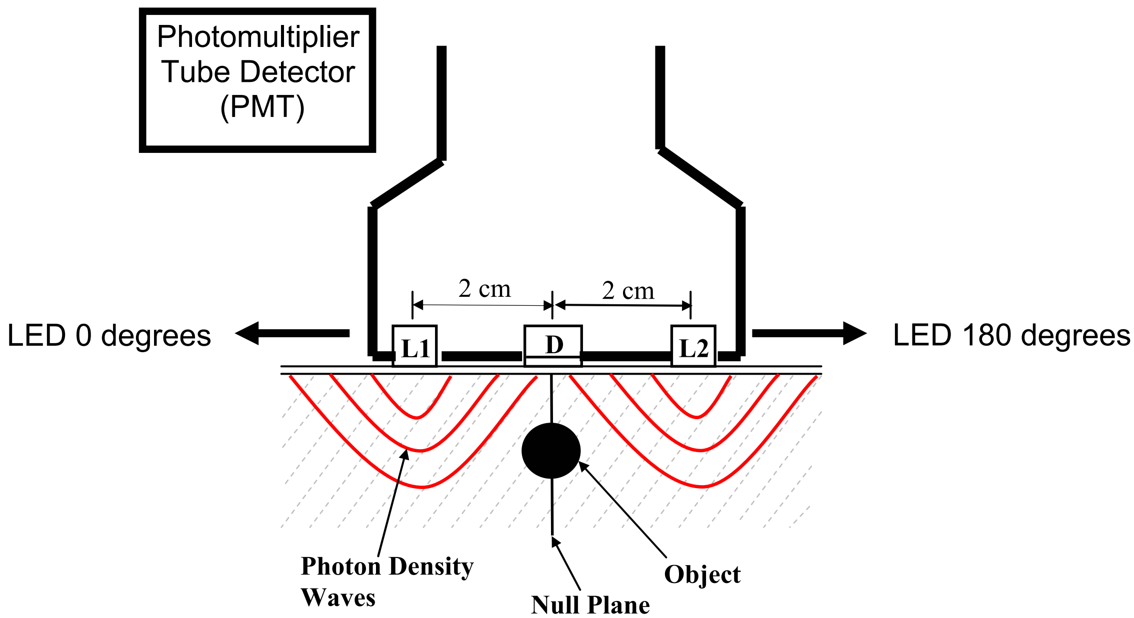


Figure 3: The figure shows a 1-D breast cancer detection. The navigation probe is facing down on a breast surface. As it scans around it will detect a heterogeneous object.

The basic phased array unit consists of a pair of in-phase and out-of-phase amplitude modulated sources (L1 and L2). Thus, a 0° and 180° phase transition is generated in the plane bisecting these two sources in a homogeneous medium, and this pattern can be sensitively perturbed by the presence of an absorbing object to form the signal for detection [5].

Breast tissue is a highly scattering medium. Due to the physical properties of NIR light in highly scattering media, a cancerous tumor will be a strong absorber of light. As a result, the PMT will read a smaller intensity coming back to it than in a completely homogenous solution. For instance, if an object is found to be in front of L1 the PMT will read a higher light intensity for L2 than for L1.

An interesting behavior occurs when the cancerous object is right in front of the PMT: the light intensity of L1 and L2 is the same since the object is affecting both sources equally. This has great significance as this property is used for localization which is explained in the next paragraph.

To explain the way we can localize tumors I use colors in this paper only as a tool to explain the HHBCD's read-out. No colors actually are used in the device, only a graph with various offsets. The real read-out is explained in **Section 2.1.2**.

We can think of HHBCD's read-out to be red, yellow, and green. Each signals different positions of the probe with respect to a tumor. Different read-outs can then be created when the tumor is in front of L1, L2, and the PMT.

For example, when an object is in front of L1 we can think of the read-out as the color red. As the probe keeps moving in the direction where it first yielded red, the object will be in front of the PMT; the HHBCD's read-out will then be yellow. If the probe continues to move in the same direction the object will end up in front of L2; the read-out will then be green. In such a way one can trace the exact location of a tumor by moving around the breast. In other words, a tumor can be detected regardless of having three different read-outs (in this example, colors). However, the advantage of having three different read-outs is useful to determine where the tumor lies in respect to the probe's components. With the localization feature one is able to know a tumor lies directly underneath the middle of the probe (where the PMT is located) when the read-out is yellow.

2.1.2 Computer Read-out

Since the probe itself cannot output a color, a computer screen is integrated into the system to display information. Rather than using colors, the read-out on the computer screen give three different responses in the form of voltage offsets on a graph. These offsets are negative, positive, and neutral (zero). This is depicted in **Figure 4**. As in Figure 3, only one plane of detection is shown for simplification purposes. In actual testing, two graphs appear on the screen, each corresponding to its respective plane.

To make clear the connection between offset and colors we only need to relate the previously used colors with their respective offsets. During the real operation of the HHBCD the graph displays a positive offset when the PMT output was red in the previous color example; a neutral (zero) offset is displayed when the PMT output was yellow; and a negative offset appears when it was green. Experimental data on human

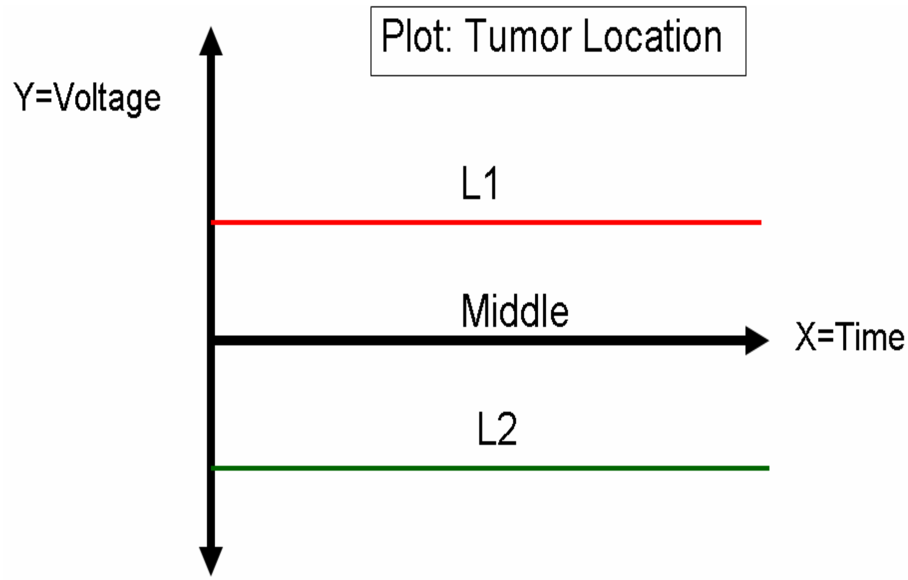


Figure 4: Computer Read-out for the HHBCD. There are three responses: 1) a positive offset occurs when a tumor is in front of source L1, 2) a negative offset when the tumor is in front of source L2, and 3) a neutral or zero offset when the tumor is in front of PMT.

breast phantoms (an object that simulates breast tissue) demonstrates that localization accuracy within several millimeters has been accomplished through this method [6].

In this way, the HHBCD can provide a graphic display that can be interpreted by almost anyone. There is no need for an expensive trained specialist to study the results. If the read-out works as expected for the 3 cm case, creation of a home device would not be out of question.

2.2 Device Goals

2.2.1 Objective

The HHBCD will not replace other non-invasive methods in their entirety. It is currently useful in cases where tumors are as small as **1 mm** and are located up to **1 cm** from the breast surface. If deep enough, the size is small enough that a human hand would most likely not be able to differentiate a change in the breast. Unfortunately, a range of 1cm is insufficient to significantly improve over breast clinical examinations (hand scanning around breast). The final goal is to extend the range to **3 cm** where a tumor is much less likely to be found by touch alone.

2.2.2 Future Implications

The HHBCD offers solutions to a number of problems encountered with existing devices:

1) X-rays: radiation exposure; cold at point of contact, and painful squeezing of the breast.

2) MRI: patient must lie down inside very tight chamber; very long inspection time, very loud rambling noise, and expensive.
3) US: gel must be put on the breast; expensive.

With the HHBCD, the probe is slowly and softly navigated around the breast. Due to the unobtrusive and friendly design of the HHBCD's navigation probe patients will not experience pain or be subject to foreign environments. In addition, the inspection time is fast compared to the methods described previously.

Financial limitations are an important source of lower survival rates among women as those who are financially strapped do not often get mammograms. According to the American Cancer Society, a lack of health insurance is associated with lower survival among breast cancer patients [2]. Breast cancer patients with lower incomes are more likely to be diagnosed with advanced stage of disease and to have lower 5-year relative survival rates than higher-income patients. For example, low-income African American women experience lower survival than higher-income African American women. The presence of additional illnesses, lower socioeconomic status, unequal access to medical care and disparities in treatment are found to contribute to the observed differences in survival between lower- and higher- income breast cancer patients [2].

The HHBCD is inexpensive to build, maintain, and operate. This combination provides for low inspection costs. This could prove invaluable to racial and ethnic minorities and other populations who have not benefited equally from advances in the past. Not only that, it would also contribute to developing countries in much the same way as low-income individuals in the U.S.A. These countries may not otherwise be able to benefit from mammogram technology.

In addition, the HHBCD can also serve as a guide for surgeons to localize tumors for extraction. This is especially important when surgical biopsies are needed. In such cases, a quick and easy-to-interpret signal read-out to localize the tumor is important to verify exactly the tumor's location and minimize the incision made in the breast.

3. DEVICE ASSESSMENT AND RESULTS

This section discusses the assessment performed on HHBCD. We start with full system analysis in **Section 3.1**. After that, we break the analysis into two portions: the LED driver circuit in **Section 3.2** and the signal interpretation circuitry in **Section 3.3**. The results found were then used to determine areas for improvement, discussed in **Section 4**.

3.1 Full System Test and Results

The first step towards improving the HHBCD was to test the device as a whole and find possible problems. The HHBCD block diagram is shown in **Figure 5**.

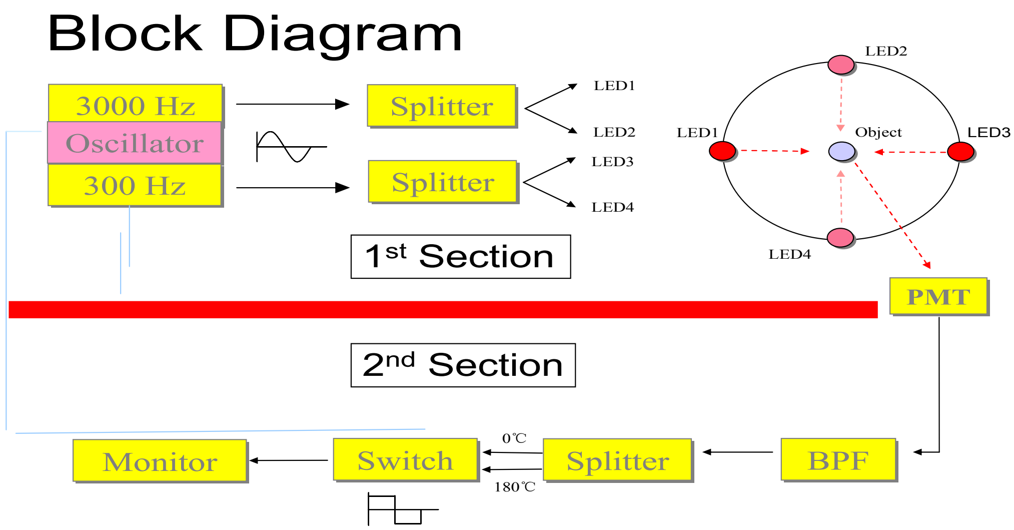


Figure 5: Block Diagram of Hand-Held Breast Cancer Detector. The diagram can be divided into two sections: 1) LED driver and 2) Signal Interpretation/Display.

Testing of the device was done by using a breast phantom. It is always necessary to test the HHBCD in a dark room as the PMT's high sensitivity to light makes it very vulnerable to damage when exposed to room light [3]. Such a problem was taken into account; its solution is discussed in **Section 4**.

The probe was navigated on the breast phantom and objects of about 4 mm were placed inside the phantom at a distance of 2 cm from the probe. This is 1 cm farther than its usual working parameters; the distance was chosen to investigate what components would need to be changed to expand its range to our goal of 3 cm.

Our results on the computer read-out did not show significant offsets or provide a stable signal. This led us to believe the LED driver which provides the sinusoidal current was not strong enough to either provide enough intensity or swing. Also, there could be factors of noise other than light caused by damaged circuits.

We considered two sections – the LED driver and the signal analysis section- separately. We worked on them in that order to discover whether the problem was rooted in the light source or in the signal interpretation circuitry.

3.2 LED Driver Test and Results

Reconstruction of the LED driver (**Figure 5**) was done on a breadboard to measure voltages at various stages. This was performed to test the circuit and more easily make required changes. Using an oscilloscope, careful measurements were made starting from the voltage source, then moving to the oscillator circuit, following the transformer (which splits the signal to make two out-of-phase signals), and finally testing the LED's.

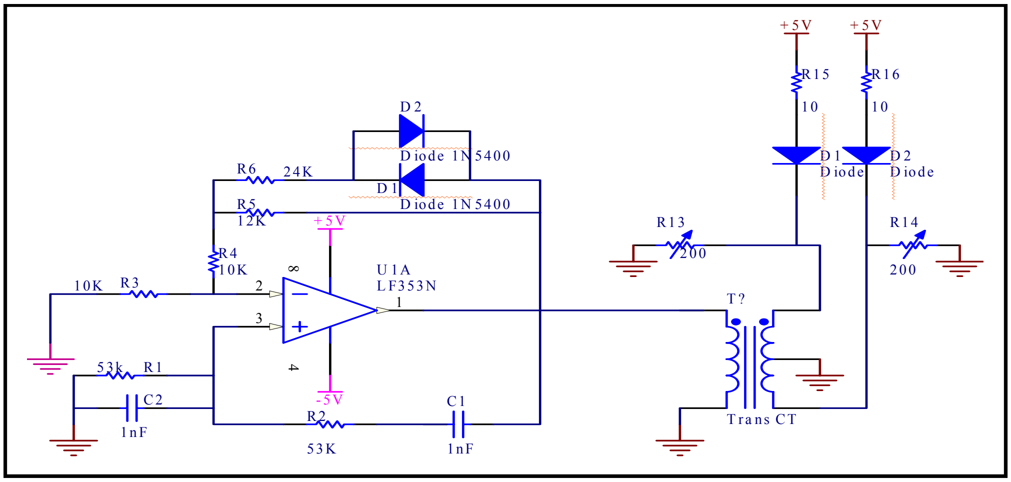


Figure 5: Old LED driver circuit; a load-down effect was caused by the transformer causing a low current intensity on the LED's.

Two problems were found:

1) The low resistance seen by the transformer's output created a load-down voltage effect.
2) The voltage swing generated by the oscillator was low,

A load-down effect is nothing more than an improperly low transfer of voltage to the circuit. In other words, the transformer's output resistance was higher than the resistance it saw. Thereby, by voltage division principles, not all of the voltage was fed to the LED's. The low voltage swing was occurring due to voltage limitations that resulted from a low voltage supplied (5 V) to the op-amps in the oscillator circuit.

After the problems were found in the LED driver, it was obvious there would not be good light swing or light intensity. The low voltage caused by the load-down effect resulted in low power to the LED's. To make matters worse, even with enough power to create good light intensity the low swing would result in a loss of localization capabilities at a distance of more than 1 cm. Solutions to these problems are briefly discussed in **Section 4.**

3.3 Signal Interpretation Test and Results

Once it was discovered the LED driver was not functioning properly it was important to test each component in the signal interpretation circuitry (Section 2, Fig. 4). Testing of this circuitry did not take place until after the LED driver was fixed.

The signal interpretation circuitry consists of the following items (in the order encountered by the PMT output signal):

1) Current-to-voltage converter
2) Band-pass filter

3) Non-inverting amplifier
4) Transformer (splitter)
5) Analog Switch

We tested each component individually by running it with the corrected LED driver. Each element's voltage was sampled using an oscilloscope. The approach was to systematically track any unusual change of signal block by block. Our intention was to discover possible sources of noise that might contribute to the unstable read-out mentioned in **Section 3.1**.

By testing each individual component we discovered the following problems:

1) The band-pass filter was not filtering out undesired frequencies.
2) The Transformer (splitter) was deficient.

The band-pass filter being used was of first order. A first order filter does not attenuate other frequencies as effectively as higher-order filters [7]. As a result, some of the 300 Hz frequency was not completely cancelled at the 3 kHz filter and vice versa. This resulted in an unwanted signal – or noise. The deficient transformer was affecting the signal by distortion. It seems the transformer had been tampered with which resulted in its malfunction.

4. SUGGESTED IMPROVEMENTS

Based on the findings in **Section 3**, a number of improvements were made. The old LED driver was changed and tested on a breadboard but not rebuilt on a circuit board. The resistance seen by the transformer was increased to eliminate the load-down effect and somehow provide sufficient light swing and intensity. These details are explained with the discussion of the redesigned LED driver circuit in **Section 5**. A higher-order filter was recommended to replace the old band-pass filter in order to better attenuate unwanted frequencies. Finally, the faulty transformer will simply be replaced when the new system is constructed.

There are many effective high-order band-pass filters. One would simply need to choose a known design and construct it onto the circuit. For example, a simple way of accomplishing this would be by cascading (connecting in series) various first order band-pass filters. This would increase its order each time one new band-pass filter is connected. Since choosing a band-pass filters is not a concern, they are not covered further from this point on in the report.

After identifying problems in the HHBCD and recommending solutions, it was necessary to choose between two courses of action:

1) Reconstruct the device and test it.
2) Postpone reconstruction and design new improvements.

I chose the second option as due to time constraints. Working on new components would add scope to the Hand-Held Breast Cancer Detector. For this reason, reconstruction of the HHBCD was delayed in hopes of coming up with new components that would be included in the reconstruction of a new device.

The suggested improvements address protection and noise elimination. The PMT is sensitive to light and physically fragile. If exposed to too much light, the PMT will get permanently damaged. Also, due to its fragility, if not handled with care its parts can be broken. Finally, interference was created by having the LED's on at 300 Hz and 3 KHz. Solutions to these problems are explained in **Section 5, 6**, **and 7**.

5. REDESIGNING LED DRIVER CIRCUIT

To explain the redesigned LED driver circuit let us go back to the initial problem. The old LED driver was loading-down the voltage provide to the LED's resulting in low intensity. Also, there was not enough swing in the sinusoidal current driving the LED's crippling the capabilities of the HHBCD for localization.

The problems encountered were solved by the redesigned circuit in **Figure 6.**

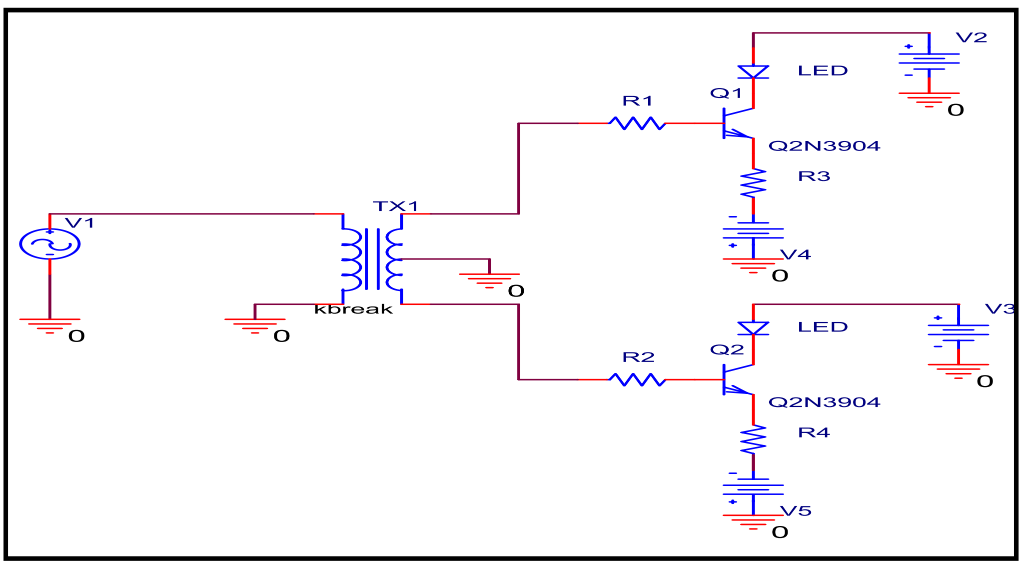


Figure 6: Redesigned LED driver. It consists on the addition of a transistor with a high base resistance and the placing of the LED's on the transistor's collector side.

The circuit's improvement was due to the implementation of Bipolar Junction Transistors (BJT). Their contributions were important in the following two ways:

1) A high resistance was placed at the base of the transistor thereby significantly decreasing the load-down effect. This is due to the voltage division principle: the voltage will travel to the highest resistance. Since the resistance seen by the transformer was much higher than its own output resistance, almost all the voltage moved on to the transistor base.

2) BJT transistors could provide more current and swing as they can increase small currents by a factor of approximately a hundred. This provided for more swing in the LED's as well as greater intensity (due to higher power). This is a result of being able to keep a constant voltage across the LED terminals (V3 in Figure 6) and the ability to increase a small current in the base to a large current at the collector side of the transistor. Since an LED intensity is regulated by current (LED's maintain a constant voltage as they act like diodes), its light intensity increased. Also, due to the small current changes required at the base to create large currents at the collector, a good swing (variation of high to low intensity) could be achieved.

To summarize, the addition of the transistor to the design was enough to correct the problems encountered during testing while not having to completely redesign the LED driver.

6. COMPLETED UPGRADE: VOLTAGE SHUT-OFF PROTECTION SYSTEM

The incredible sensitivity of the PMT makes it very vulnerable to damage when exposed to too much light. When using the HHBCD, one must operate in a dark room. If the HHBCD were to be operated in an environment other than a dark room, other light would interfere with the signal to be read from the NIR light sources. Such precautions can be arranged without much difficulty. Lamentably, a safeguard to an unexpected strong source of light did not exist in the HHCBD. Unanticipated situations can include turning on the room switch, or lifting up the window curtains where inspection is being performed. A protection device that could save the PMT from strong light was constructed. A picture of the circuit that corrected this problem is shown in **Figure 7**.

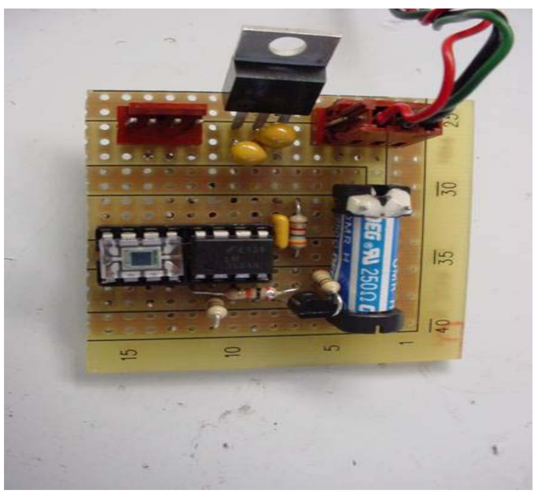


Figure 7: A picture of the voltage shut-off protection system. It was designed to protect the PMT from light overexposure by turning its supply voltage off when exposed to room light.

Ahead, the shut-off protection circuit schematic is shown in **Figure 8** with its explication to follow.

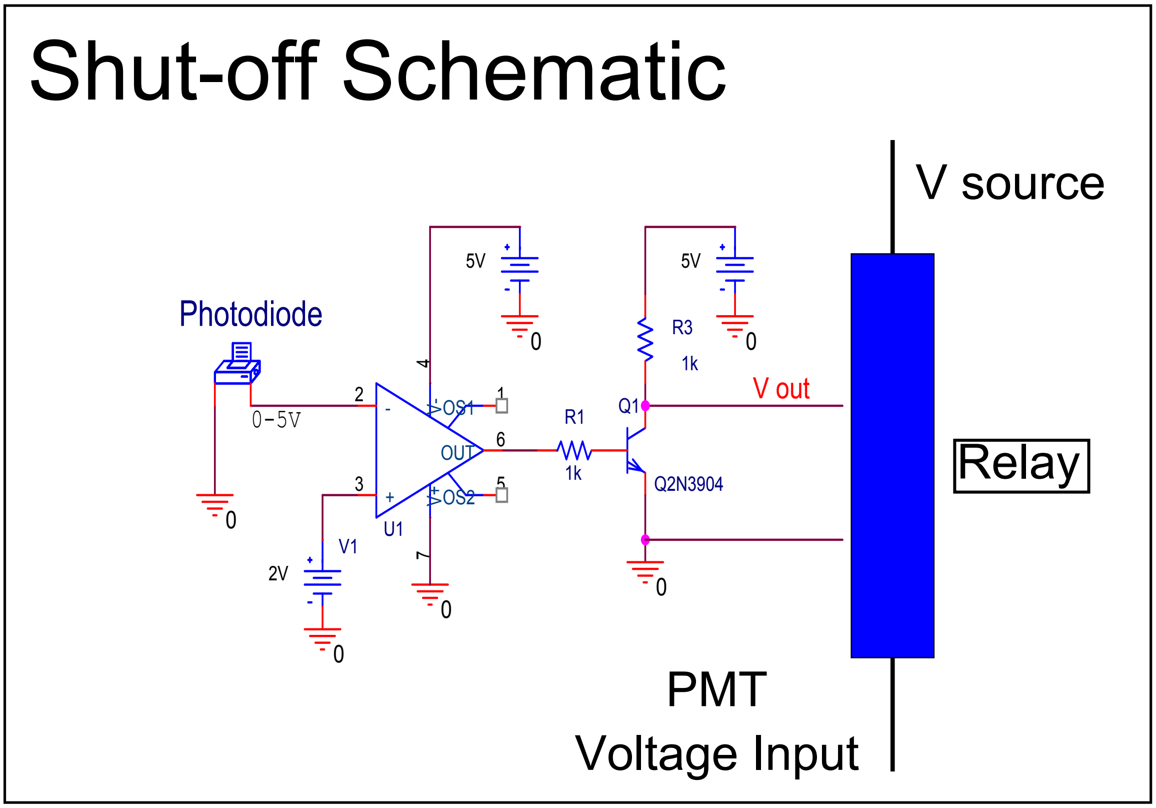


Figure 8: Schematic for the voltage shut-off protection system. Four components are used: 1) an OPT101 (photodiode), 2) a LF353N op-amp, 3) a 3904 transistor, and a 4) mechanical relay.

The circuit in **Figure 8** is effectively impedes voltage supply to the PMT in approximately less than one second. It is comprised of a photodiode (OPT101), an op-amp (LF353N), a BJT transistor (3904), and a mechanical relay.

The photodiode outputs 5 volts (V) when exposed to a strong light – room light qualifies. The output is connected to the inverted input of an LF353N op-amp. The positive input of the comparator is held at 2 V. By having a static voltage at one terminal and varying at the other a comparator is formed [7]. A comparator outputs a voltage equal to its power supply. Which power supply it uses depends on what input terminal is higher in voltage. In our circuit, the negative power supply of the comparator (Vee) is connected to 5 V and the positive power supply (Vcc) is 0 V. In such a configuration, the comparator output is 5 V when the photodiode is exposed to strong light and 0 V when very dim light is present.

When the base of the transistor is 0 V (no light), the transistor is forced into cut-off mode [8]. In this state, the NPN junction acts as an open circuit forcing the voltage supply of the transistor to appear across the input of the mechanical relay. This allows flow of the power supply to the input voltage pin of the PMT. Thus, the device would be in operation mode.

Where the base of the transistor is 5 V (strong light), the transistor is forced into saturation mode [8]. This is a consequence of the low resistance placed in the collector of the transistor. The low resistance permits high current to flow through it which creates a high drop in the resistance. The input of the relay then becomes approximately 0.3 V which shuts-off the relay and quickly stops current from flowing through it. If the PMT is connected to the relay, its voltage supply is abruptly ended by the shut-off protection system.

The shut-off protection system effectively discontinues power to the PMT. Unfortunately, to completely save the PMT under room light conditions our system would have to turn off the power supply in less than 10 nanoseconds [3]. Our device can only do it in less than a second which is too slow. However, with the use of optical band-pass filters at the face of the PMT, much of the light could be prevented from reaching our highly sensitive detector. Since the photodiode will still see the light and shut the power to the PMT, this design would still be capable of significantly protecting the PMT from light overexposure.

7. FUTURE WORK

The following work has been accomplished:

1) Full System Test and Results
2) LED Driver Test and Results
3) Signal Interpretation Test and Results

This work resulted in 1) a new LED driver, 2) a higher order band-pass filter, 3) the replacement of a transformer, 4) and a voltage shut-off protection system. These items were completed and are ready for reconstruction. However, a time-shared system to reduce noise and a new probe casing design remain under construction. They are briefly described in **Figure 9** and **10**.

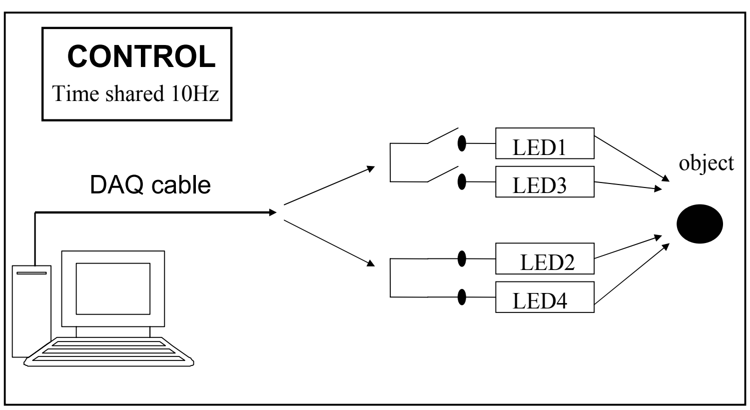


Figure 9: A computer controlled time-shared system. An LED pair is turned on while the other pair is off at a rate of 10 Hz. If successful, the filters in the signal interpretation will work independently. Thus, the LED's will not interfere with each other, stabilizing the read-out on the computer screen. A program that can do this is under development.

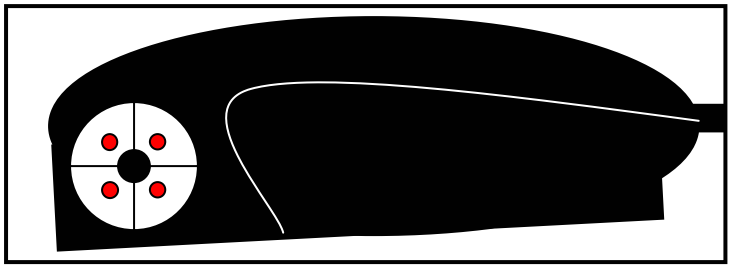


Figure 10: A rough drawing of a new probe casing idea. Its main purpose is to place the PMT at a location other than the probe. The plan is to use fiber optics from the PMT area of detection to the Black dot seen in above Figure. The attenuation inside the cable is believed to be negligible due to the short distance from the box to the probe. Also, the probe is made in the shape of a computer mouse (familiar feel) to facilitate its handling.

If these two devices are completed successfully, the project can then move to the integration and construction of the new HHBCD. Once the circuitry has been reconstructed, testing on a breast phantom must be done. That would be followed by testing on human subjects.

8. ACKNOWLEDGEMENTS

This is my time to thank everyone, from the bottom of my heart, for making SUNFEST 2004 a truly motivating and enriching experience. I would first like to thank UPENN for hosting the program. The National Science Foundation for funding the program and trusting that young students like me will one day give fruits to their investment. Thank you Dr. Van der Spiegel for selecting me to participate in this prestigious program. I feel very fortunate and thankful that you trusted in me. To Dr. Britton Chance, for being kind enough to offer a project for undergraduates out of pure joy for teaching. To the grad students in the lab of room 203 in the Anatomy/chemistry building, especially Sammy, Simon, Kiran, and Lan Lan. Thank you Sammy for being so patient and helpful to me.

I want to thank Dr. Pappas, Dr. Kassam, Dr. Lee, Dr. Santiago, and Salvador for helping me in the search to better accomplish my goals.

I want to thank Delores, Shelley, and Denise for being so nice and informative every time I needed any kind of help. Delores, thank you for you football insight.

Finally, I want to thank God, my family, and my princess. Without your love, none of my work would mean anything.

Thank you.

9. REFERENCES

1. American Cancer Society: Cancer Facts and Figures – 2002, *American Cancer Society* (2002).

2. American Cancer Society: Breast Cancer Facts and Figures – 2003-2004, *American Cancer Society* (2004).

3. Hamamatsu: Photomultiplier Tube Detector Technical Manual – 2003, *Hamamatsu* (2003).

4. J. B. Fishkin and E. Gratton, Propagation of photon-density waves in strongly scattering media containing an absorbing semi-infinite plane bounded by a straight edge, J. Opt. Soc. Am. A, 20 (1993) 127-140.

5. Y. Chen, *Contrast Enhancement for Diffuse Optical Spectroscopy and Imaging: Phase cancellation and targeted fluorescence in cancer detection*., Dissertation in Bioengineering, University of Pennsylvania (2003).

6. Y. Chen, C. Mu, X. Intes, and B. Chance, Adaptive calibration for object localization in turbid media with interfering diffuse photon density waves, Applied Optics, 41 (2002) 7325-7333.

7. S. Franco, *Design with operational amplifiers and analog integrated circuits*, McGraw-Hill, New York, 3rd ed., 2002.

8. S. Schwarz, *Electrical engineering: an introduction*, Oxford University Press, New York, 2nd ed., 1993.