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Design and Validation of an Invasive Blood Pressure Gating System for In Vivo Cardiac MRI of Fetal Pigs

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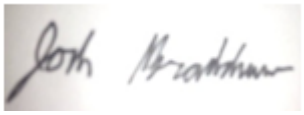
Professor Calamai,

I have prepared this report, “Design and Validation of an Arterial Blood Pressure Gating System for in-vivo Cardiac MRI of Fetal Pigs,” as my 2B Work Report for my work as an undergraduate researcher in Chris Macgowan’s medical imaging lab at the Hospital for Sick Children. This report is the second of three that I must submit as part of my degree requirements. This report was entirely written by me and has not received any previous academic credit at this or any other institution.

Sincerely,

Josh Bradshaw



Abstract

In this report, I present an effective system for generating an MRI gating signal from invasive blood pressure measurements taken in the carotid artery of a fetal pig. The system is comprised of four primary components: the blood pressure transducer, an analog front-end which amplifies the blood pressure signal, a microcontroller which performs real time digital signal processing to detect the cardiac phase, and a computer application that allows the experimenter to monitor the system's operation. First, the system was tested using simulations based on pre-recorded invasive blood pressure traces recorded in adult humans, and fetal lambs. The system's detections of the blood pressure peaks was within the 20ms margin of error for every heart beat in the simulation. Second, the system was tested by surgically implanting the transducer into a juvenile fetal pig. Review of the system logs after the surgery revealed that it produced a flawless triggering signal throughout the test's full duration. The source code and hardware schematics for this system have been open-sourced and are available on the SickKids website.

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Acknowledgements

This project would not have been a success if not for the generous contributions of dozens of hardworking individuals from a wide variety of fields. First and foremost I would like to thank Dr. Chris Macgowan for providing me with support, a generous equipment budget, lab animals, MRI scan time and for allowing me to fully open-source my design. I would like to thank Sharon Portney and Jun Dazai for providing me free access to the Toronto Center for Phenogenetics imaging lab, where I carried out my experiments, created prototypes using their 3D printer and assembled circuit boards. I would like to thank Aneta Chmielewski and Chris Roy for teaching me the fundamentals of MR imaging, and for involving me in their experiments. Finally, I would like to thank Carol Abrahams for going above and beyond to ensure that all of the materials and equipment I needed were ordered in a timely manner.

1

Introduction

1.1 Introduction to Dr. Macgowan's Medical Imaging Lab

Dr. Chris Macgowan's medical imaging lab is currently dedicated to studying maternal and fetal health throughout pregnancy, using magnetic resonance imaging (MRI), with a particular focus on the development of the fetal heart and surrounding vasculature. Researchers in this lab aim to use MRI to learn about physiology, and to develop new imaging protocols for clinical use.

Researchers work towards the goal of usable clinical protocols using a wide variety of techniques. With pulse-sequence programming, researchers are able to modify the algorithm that the MRI scanner uses to produce and sample magnetic resonance signal. Using MatLab, Python, and tools provided by MRI equipment vendors, researchers are able to construct new methods for post-processing the MRI signal, and constructing the images. Finally, researchers occasionally develop and use their own instruments to supplement the signal collection process.

Thanks to the well-established safety of clinical MRI scanners, imaging protocols are typically validated by repeatedly scanning volunteers. During the preliminary stages of protocol development, researchers will typically scan themselves or their colleagues. In later stages, scanning protocols are tested against custom made anatomy models which are produced using 3D printers and plumbing parts. The most promising protocols are then advanced to clinical and animal trials.

1.2 Introduction to Cardiac Gating for Fetal Imaging

The goal of cardiac magnetic resonance imaging is to produce a series of images of the heart throughout the entire cardiac phase, (the cyclical motion of the beating heart) so that radiologists can view images of the heart frame by frame as shown below in Figure 1. The left frame shows the ventricles of the heart in maximum expansion, while the right frame shows the ventricles in maximum contraction.

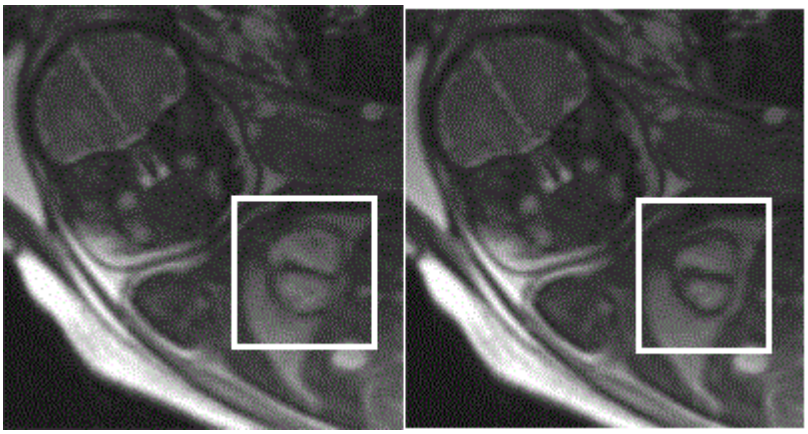

Figure 1: Two frames taken from the same third-trimester human fetal cardiac scan. Image credit: Christopher Roy.

The time required to acquire enough MR signal to construct a diagnostic quality image of a fetal heart is significantly longer than the period of a human heart. This means that data acquisition must be synchronized with cardiac and respiratory motion. This synchronization process is known as gating. The current gold standard for cardiac imaging is to have the subject hold their breath during the scan (typically 5-10 seconds) to eliminate respiratory motion and use the R-wave of the ECG signal to synchronize the data acquisition with cardiac motion, as shown in Figure 2 [1]. In this context, the ECG signal is called the **triggering signal**, because it triggers the system to begin a new **gating window** (also called a system acquisition window in the literature). During sampling, the MR system time stamps the data relative to the start of the gating window. Samples from the same portion of the cardiac phase from different heartbeats are then combined in post-processing to make a complete image of the heart in that state of motion.

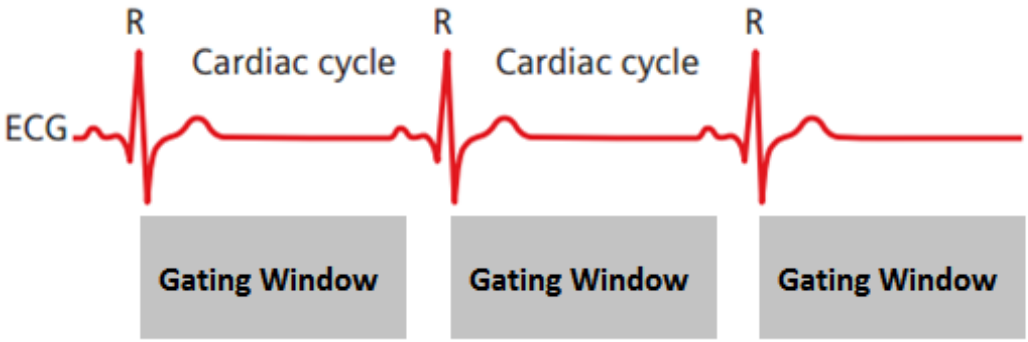

Figure 2: An ECG trace and the corresponding MR signal acquisition windows (gating windows). Adapted with permission from the Siemen`s Magnetom Trio operating manual.

In cases when ECG is impossible or impractical to acquire, blood pressure can be used as a triggering signal. Blood pressure is an inferior triggering signal compared to ECG, because pressure changes lag behind the actual motion of the heart. Additionally, blood pressure waveforms are much less consistent in shape than ECG, which makes accurately distinguishing the heartbeats more challenging [2]. Figure 3 shows an idealized ECG waveform and a corresponding blood pressure waveform.

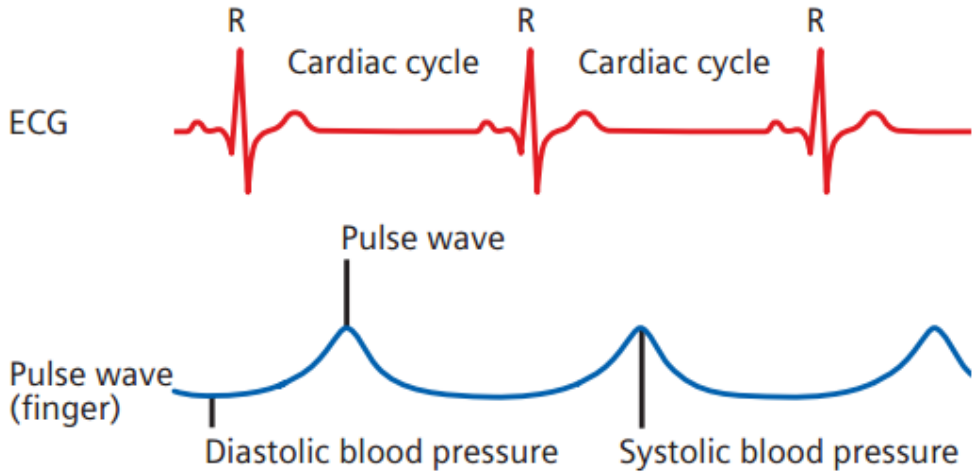

Figure 3: An ECG waveform and the corresponding arterial blood pressure pulse Adapted with permission from the Siemen`s Magnetom Trio operating manual.

1.3 Introduction to the Fetal Pig Cardiac Flow Experiment

The purpose of the fetal pig cardiac flow experiment is to collect time resolved measurements of the blood flow through the hearts of fetal pigs. The motivation for collecting this data is that surgeons at SickKids have recently begun work in the relatively new field of prenatal surgical interventions on fetuses. High resolution images of fetal cardiac physiology are invaluable for the researchers and clinicians working on those surgical protocols.

Unfortunately, conventional fetal imaging modalities such as ultrasound are seldom accurate enough for a cardiologist to distinguish abnormal cardiac development early enough for interventions to be effective. For this reason, a decision was made to attempt to develop and test a new highly accurate methodology for dynamic cardiac fetal imaging on pigs. This data would help us to develop a better understanding of fetal cardiac development, and the challenges associated with taking lengthy MRI scans on fetuses.

The fetal cardiac flow experiment consists of three stages:

1. Scanning still-born Yucatan pig fetuses using long high resolution scans to gain familiarity with the appearance of the anatomy, and collect information about the blood vessel diameters which was required for the development of the experimental and surgical protocols for the later stages.
2. Scanning juvenile pigs to practice the surgical protocol, test the triggering system and collect some preliminary flow data.
3. Scanning late gestation pregnant pigs under full anaesthesia, collecting flow measurements from the fetal heart.

At time of writing, stages one and two have been completed, while stage three is scheduled for fall 2015 to allow for the time required for the pregnant pigs to reach the appropriate gestation.

2

Design Problem

2.1 Problem Definition

The fetal cardiac flow experiment requires lengthy cardiac scans, typically up to fifteen minutes long depending on the resolution required. The length of these scans means that a highly accurate triggering system for the fetal heart is required, because lapses in synchronization between the MRI scanner and the fetal heart result in blur and motion artifacts in the images. Unfortunately, none of the commercially available triggering modules were suitable for the purpose, because none had a MRI compatible transducer small enough to be inserted into the fetal blood vessels. For this reason, the research team decided to build a customized gating device in-house specifically for this experiment, and I was hired to design it.

In coordination with the clinical cardiology team, a transducer was chosen for measuring the fetal blood pressure invasively from the carotid artery (details on the transducer selection process are available in Appendix A). These transducers use an extremely thin fibre optic catheter to measure pressure, and they are extremely accurate. The chosen insertion site for the catheter was the carotid artery of the fetal pig, because the carotids are relatively easy to find and access.

The triggering device was required to process the blood pressure signal from this transducer in real time, and send a triggering signal to the MRI scanner once per heartbeat, which occurred at the pressure peak of the heartbeat.

3

Design Requirements

3.1 Safety Requirements

The MR environment poses unique challenges for circuit design. The scanner produces a continuous base magnetic field of 3T, and a variety of gradient fields which alternate at radio frequency. These fields can be very dangerous. For example, in 1991, a poorly designed pulse oximeter, which had been certified safe for MRI, was launched across the room by the magnetic field, where it impacted a child's head [3]. For this reason, safety was a major consideration in the design process. The major safety requirements are:

1. There must not be any direct electrical connection between the computer system and the subject.
2. There must not be any ferrous metallic components present within the scan room.
3. All electrical connections to the MRI scanner must have overvoltage and overcurrent protection.
4. The amount of conductive material in close proximity to the MRI scanner's bore should be minimized, because the eddy currents induced in the conductive material may cause it to heat up to dangerous temperatures, depending on the material used.

3.2 Functionality Requirements

This gating system must be capable of working in juvenile pigs, and fetal pigs of various breeds. There was a great deal of uncertainty about what effect the chosen anaesthetic would have on the fetal pigs, so I opted to use the highest and lowest observed values in the literature as the specifications. The system must:

1. Send a 5V TTL pulse to the MRI scanner every time a heartbeat is detected.
2. Consistently trigger within 10ms of the pressure peak of the heartbeat.
3. Be accurate over a heart rates from 80-270 BPM (based upon previous recordings in anaesthetized fetal pigs [4]).
4. Function over the blood pressure range of 65-170 mmHg systolic, and 20-50 mmHg diastolic.
5. Operate with less than 20ms of delay.

6. Reject *skip-beats* (missed systolic beats), which are common in fetal pigs [5].
7. Be capable of filtering out the high frequency noise which is inherent to the MRI scan environment from the transducer signals.
8. Correctly handle substantial changes in mean blood pressure, which can be brought on by small mistakes in the administration of the anaesthetic [4].
9. Be agnostic to catheter placement within the carotid artery, to provide the surgeon with a greater margin for error.

3.3 Usability Requirements

Between the surgical team, the animal care team, the MRI scanner operations team and the research team, twelve to fifteen people are involved in each fetal cardiac flow experiment. Hiring all of these individuals is extremely expensive, so generally the full team meets for the first time on the day of the experiment. In this logistically intense environment, it is vitally important that all experimental apparatus be designed for usability to reduce confusion and to avoid wasting valuable time. For this reason, the following usability requirements were established. The triggering system must:

1. Provide immediate feedback if there is a problem acquiring blood pressure data.
2. Have plug and play operation, requiring minimal manual configuration.
3. Give the operator real time feedback on the measured blood pressures, and the triggering signal that's being sent to the scanner.
4. Log the blood pressure and triggering system data with time stamps in a human readable format, so that it can be reviewed quickly.

4

System Design

4.1 System Overview

The block diagram in Figure 4 below provides a high level overview of how information propagates through the system.

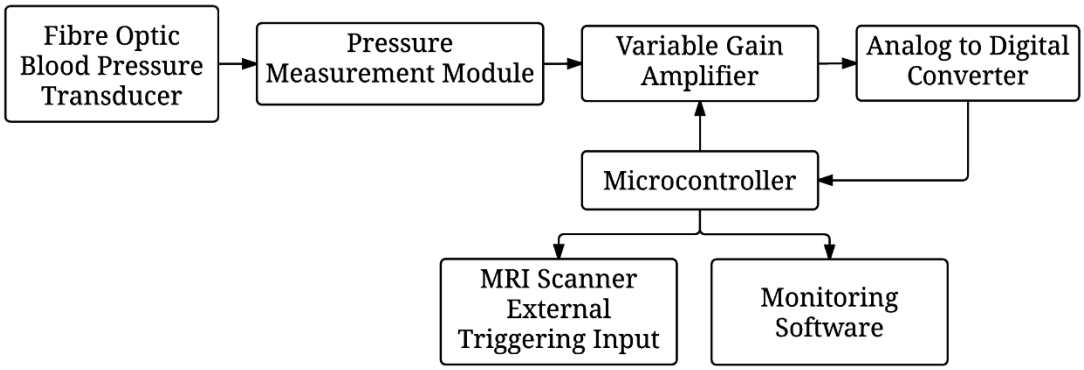

Figure 4: System Block Diagram

The blood pressure signal is collected by an optical pressure transducer, which is inserted into the fetal pig's carotid artery. The optical blood pressure signal is converted into an analog electrical signal by the pressure measurement module (see Appendix A for details), which is then amplified by the variable gain amplifier and measured by the analog to digital converter.

The microcontroller uses a variety of digital signal processing algorithms to filter the signal and detect the pig's pulse. Each time a heartbeat is detected, a triggering signal is sent to the MRI scanner, and a signal is sent to the monitoring software so that the experimenter can verify that the triggering signal was sent at the correct instant.

4.2 Variable Gain Amplifier Design

The analog output signal provided by the Samba Sensor's pressure measurement system had a very small amplitude compared to the full scale range of the analog to digital converter (ADC), so an amplifier was required to increase the signal closer to the full scale range of the ADC.

Unfortunately, the blood pressure of fetal pigs has never been measured from the carotid artery, so it was impossible to determine the correct gain value for the amplifier in advance. This measurement was further confounded, because the effect of our chosen anaesthetic on fetal blood pressure was also unknown. To deal with this problem, I opted to build a variable gain amplifier, with an automatic feedback system to maintain a consistent signal amplitude throughout the experiment. A simplified schematic variable gain amplifier circuit is shown in Figure 5 below.

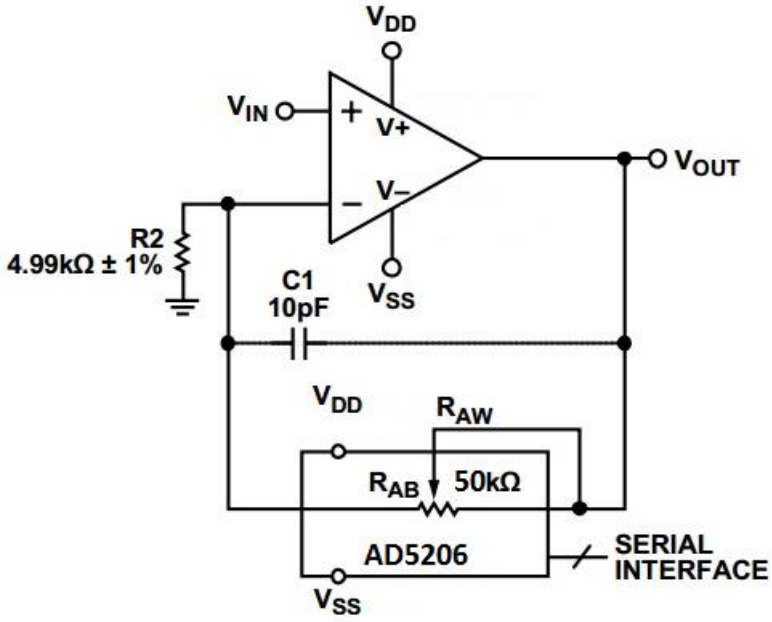

Figure 5: Simplified schematic of the variable gain amplifier used to amplify the signal from the transducer before it is read by the ADC. Schematic is reprinted from Analog Devices reference design #CNO112 with permission [6].

This circuit uses a precision operational amplifier, with a digital potentiometer (AD5206) in the feedback path to allow the gain to be adjusted by the microcontroller as required. The digital potentiometer has 256 counts, giving the amplifier an adjustable gain range of 1-11x. This is sufficient for even the lowest possible fetal blood pressures.

4.3 Gain Adjustment Algorithm

The input of the gain adjustment is a sample from the ADC taken every 100ms. While each sample is recorded, the algorithm compares it to the minimum signal magnitude and maximum magnitude threshold which are 1/5 and 4/5 of the ADC's full scale range, respectively. After a five second windowing period, the signal amplitude is compared

against the thresholds, to see if any gain adjustment is required. The three possible cases are:

1. The signal failed to exceed minimum magnitude threshold during the five second window.
2. The signal exceeded the maximum magnitude threshold during the five second window.
3. The signal exceeded the minimum magnitude threshold, and did not exceed the maximum threshold.

In case one, the gain adjustment algorithm gradually increases the gain during each windowing period, as shown in Figure 6below. The gain increase stops when the signal exceeds the threshold. Same process occurs in reverse for case three. The algorithm is illustrated in the flow chart below.

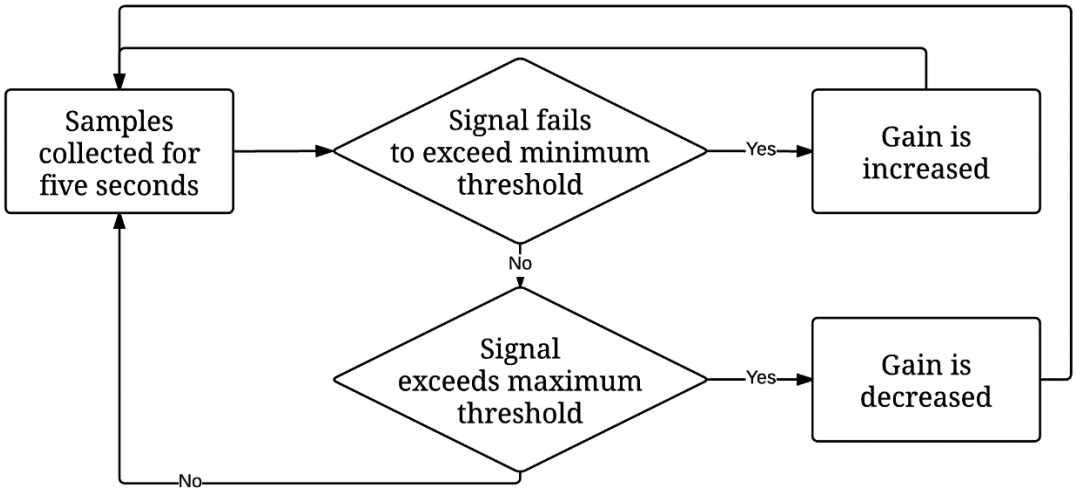

Figure 6: Simplified gain adjustment algorithm decision flow diagram.

The actual functioning of the gain adjustment algorithm is illustrated in Figure 7below. In this test, the triggering system was connected to a function generator which produced a blood pressure waveform with a peak to peak voltage of 700mV. This signal amplitude is based upon recordings on fetal lambs with an identical transducer. As you can see, the gain is very gradually increased in such a manner that it does not disrupt the triggering algorithm, which operates perfectly throughout the duration of the gain increase.

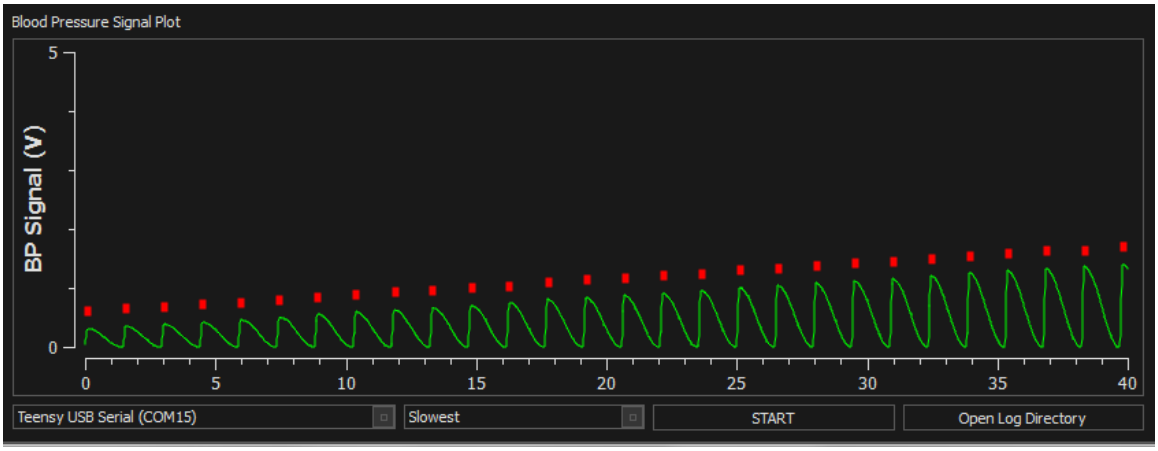

Figure 7: Gradual increase in gain to amplify a low amplitude blood pressure signal. The red markers indicate when the triggering signal was sent to the MRI scanner.

4.4 Blood Pressure Signal Preprocessing

The top plot in Figure 8shows an arterial blood pressure waveform which was measured invasively in a fetal lamb. Notice that after the main pressure peak, there is a second reflection peak, which results from closing of the aortic valve.

This waveform is relatively noisy, and the peak is not particularly easy to identify. For this reason, it is necessary to apply a filtering algorithm to simplify peak detection. First, a first order low pass filter with a cut-off frequency of 25Hz is applied, to smooth the small spikes in the pressure waveform, as shown in Figure 8 below. The first order low pass filter's equation is given below.

$$y[n] = \frac{u[n]}{20} + \frac{u[n-1]}{20} + \frac{9y[n-1]}{10}$$

Next the slow sum function is applied. The slope sum function is defined as:

$$z_i = \sum_{k=i-w}^{i} \Delta u_k, \quad \Delta u_k = \begin{cases} \Delta y_k & : \ \Delta y_k > 0 \\ 0 & : \ \Delta y_k \leq 0 \end{cases}$$

Where the optimal value of the windowing constant k is the number of samples in the rising edge of the signal [2]. For the fetal pig application, I chose k=15, based upon visual

inspection of pre-existing fetal lamb blood pressure recordings, which are very similar to fetal pigs in terms of blood pressure and heart rate.

The plot in Figure 8 below illustrates a fetal lamb's blood pressure, and the corresponding slope-sum filtered output for that blood pressure waveform.

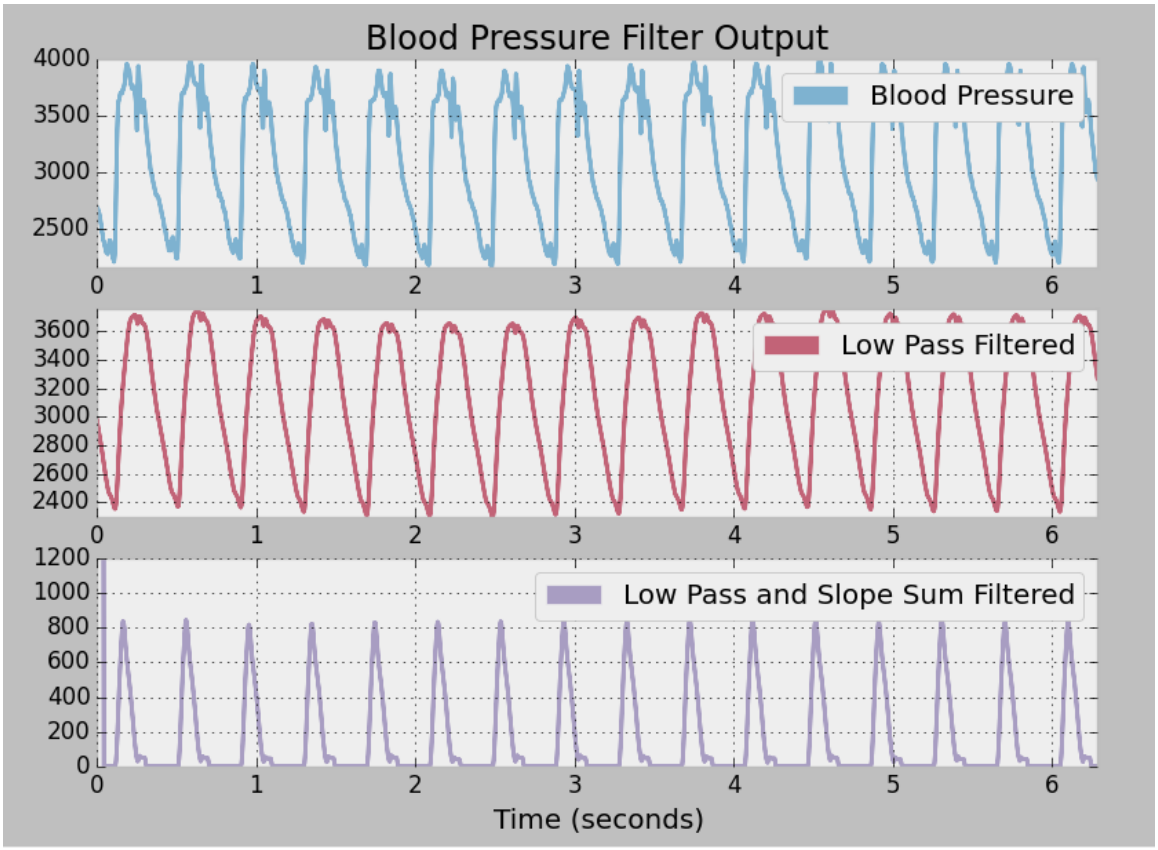

Figure 8: The top plot shows the fetal lamb blood pressure waveform. The middle and bottom plots show the outputs of the low pass filter and slope sum filter respectively. The lamb blood pressure trace was provided by Dr. Johnathan Mynard. The recording equipment used to produce this plot was not capable of providing absolute readings, so the units of measurement are simply ADC counts.

Notice that the low pass filter removes the high frequency ridges from the blood pressure wave form, leaving only the low frequency content that corresponds to the expansion and contractions of the hearts ventricles.

The slope sum function improves the signal by establishing a consistent baseline of zero, eliminating the effects of DC drift in the measurement instrument. The slope sum function also sharpens the peaks, which makes the problem of automatic peak detection far less ambiguous.

4.5 Blood Pressure Pulse Detection Algorithm

The blood pressure pulse detection algorithm is a state machine. The high level overview of the algorithm is given by the flow chart in Figure 9 below.

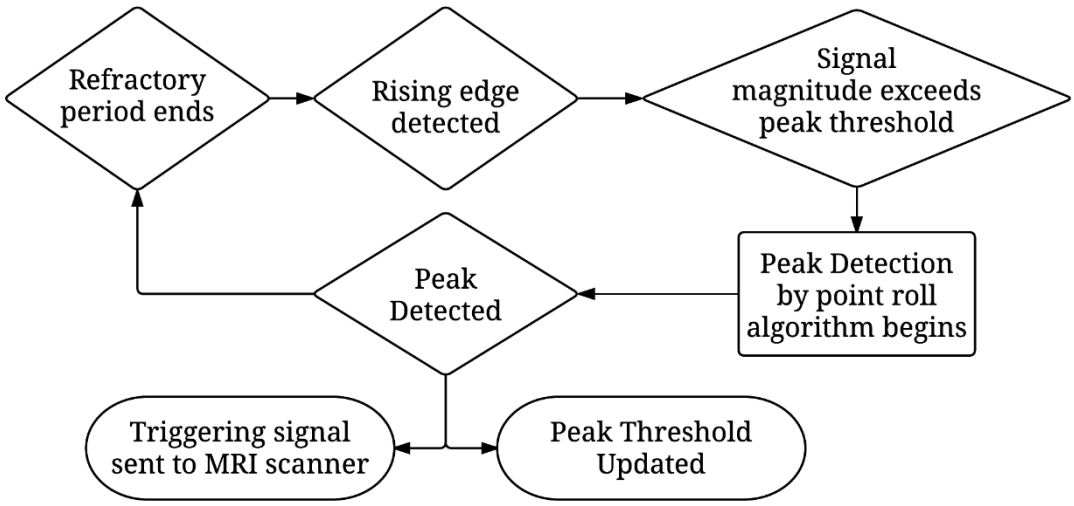

Figure 9: Peak detection state machine algorithm.

To ensure that the peak detector only triggers on unique blood pressure pulses, a refractory period is applied between peaks, and the algorithm does not begin peak detection until the rising edge is detected and the signal magnitude is greater than the peak threshold. The peak threshold is calculated as ½ of the average of the last five peaks.

The point roll algorithm for peak detection works by continuously generating an approximation to the first derivative based on the last four samples. A peak is detected when the derivate approximation changes from a positive value to a negative value.

4.6 Monitoring Software

The monitoring software serves three purposes. Firstly, it allows the animal care technician to continuously monitor the blood pressure signal to ensure that the animal subject is healthy and responding properly to any drugs. Secondly, it allows the MRI scanner operator to monitor the animal's pulse and the triggering signal, so that they're continuously aware of whether the scanner is properly synchronized with the fetal heart. Thirdly, the software logs the triggering signal information to a data file, so that it can be

compared with the MRI scan during post processing to manually remove portions of scan data that were corrupted by irregular heart motion.

The main window of the monitoring software in use is illustrated in Figure 10below. The green line is the blood pressure signal, and the red markers indicate when the triggering signal was sent to the MRI scanner.

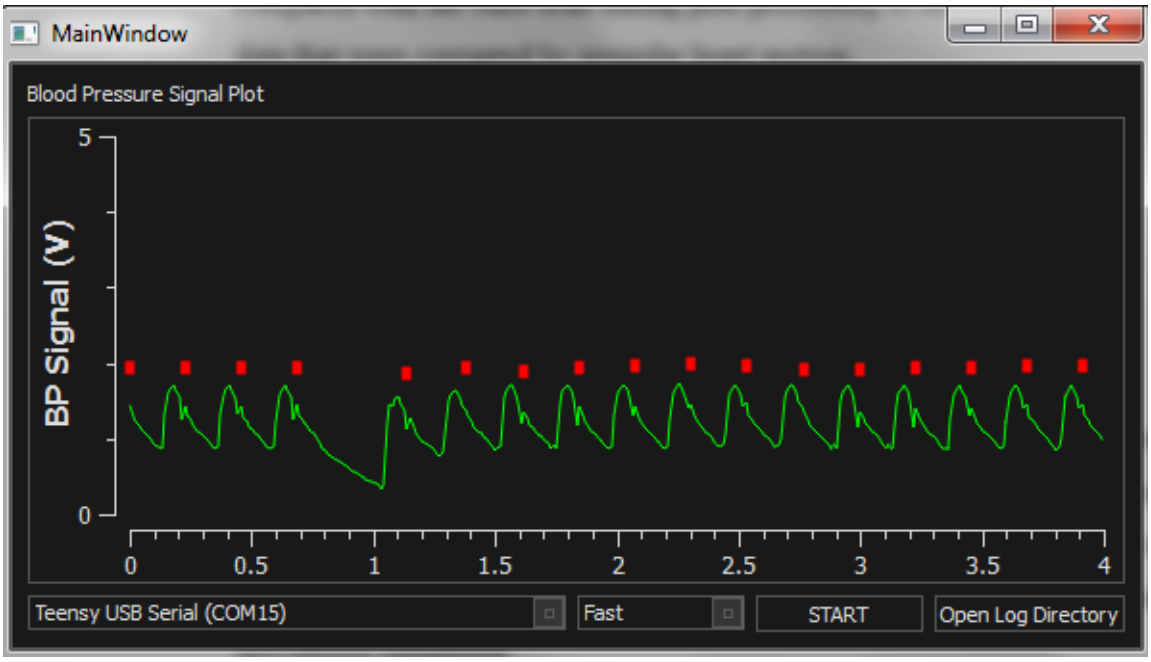

Figure 10: The monitoring software display during a test on a fetal lamb blood pressure recording.

4.7 PCB Design

The PCB was designed to be inexpensive to manufacture in small batches, so that other MRI labs can manufacture their own units based on the open-source schematics. All of the parts used come from major manufacturers who guarantee their ongoing availability, and all of the components are large enough to be placed and soldered by hand.

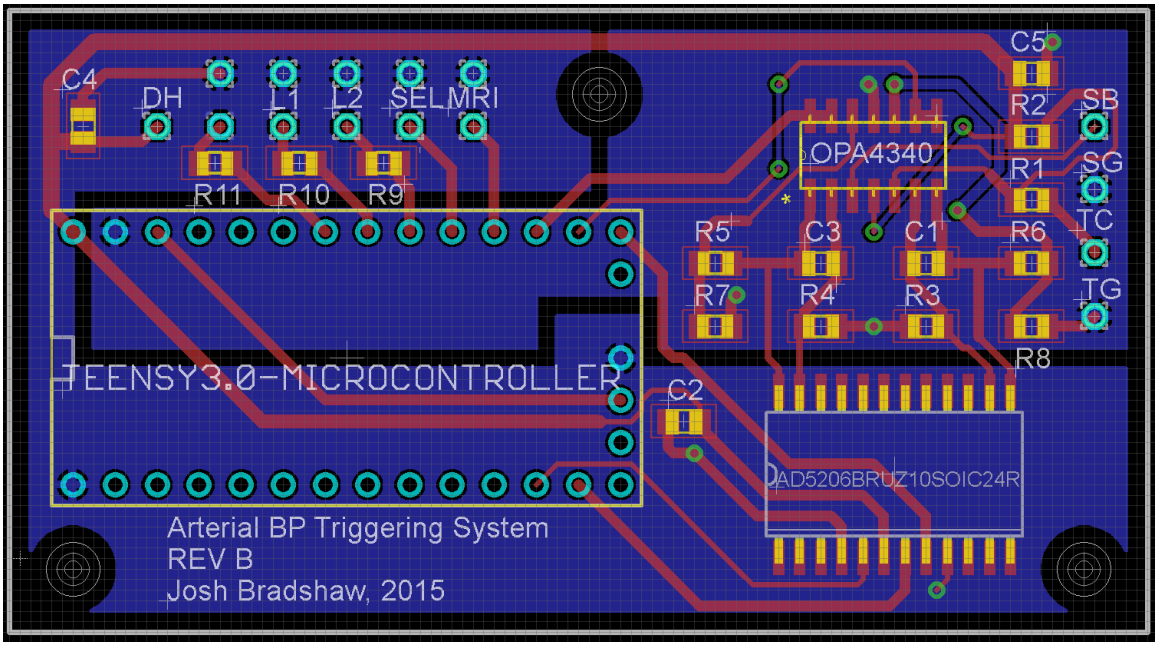

Figure 11: Simplified PCB Schematic. Red denotes traces on the top layer, and blue denotes traces on the bottom layer. Yellow denotes surface mount pads, and green denotes plated holes through the board.

A simplified drawing of the PCB is shown in Figure 11. To ensure best possible signal integrity, the analog and digital ground planes were separated, to prevent crosstalk between the microcontroller and the sensitive amplification circuitry [7]. Additionally, the power rails are filtered by a variety of bypass capacitors, to minimize the effects of 60Hz hum from the mains power lines that run throughout the control rooms of the MRI scanners [8].

The circuit board was assembled by hand using MRI compatible solder. The fully populated circuit board is shown in Figure 12. The assembly was performed by hand using a soldering iron, but a reflow process would have been more optimal, given how small the passive components are.

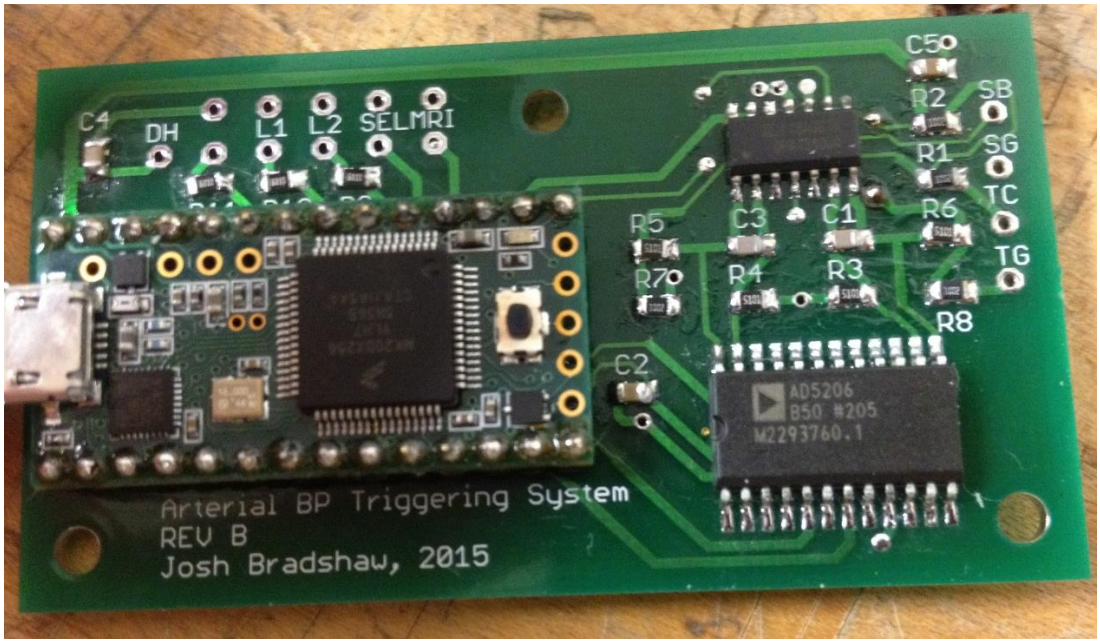

Figure 12: Fully populated circuit board.

4.8 Enclosure Design

The enclosure for this box was hand machined out of aluminum. The case was originally designed for audio equipment, and it meets IP54 standards for shielding, dust and water proofing. The completed enclosure is shown in Figure 13.

Figure 13: The aluminum enclosure for the triggering unit, complete with connectors for the transducers and an output connector to the MRI scanner.

5

Validation and Analysis

5.1 Triggering Algorithm Validation through Simulation

The unit was tested against 15 recordings from the MIT SLPDB database [9] of non-invasive blood pressure recordings, and 12 recordings taken in fetal lambs. The signals were programmed onto an arbitrary waveform generator, which was directly connected to the triggering unit. Validation was carried out by visual inspection by two graduate students who are experienced in cardiac MRI. The plot in Figure 14 below shows the trigger output for a blood pressure waveform recorded in a fetal lamb.

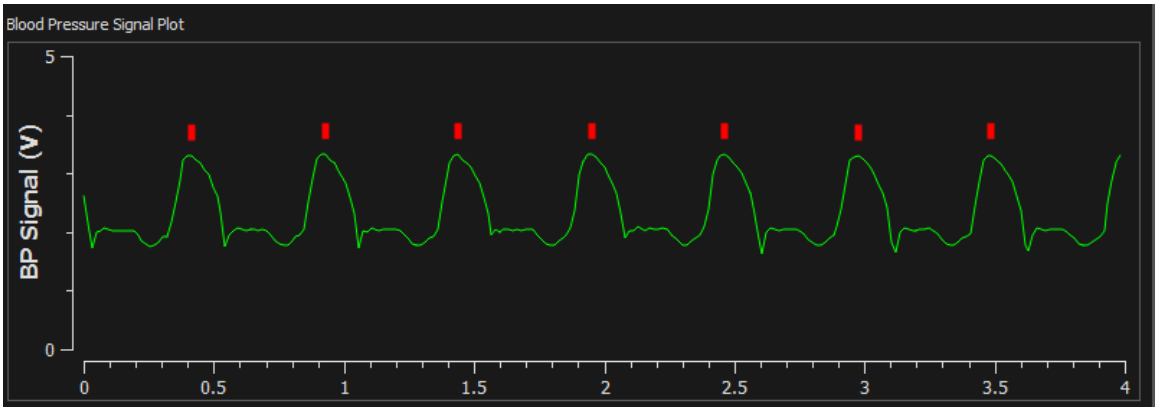

Figure 14: Test of the triggering system on an invasive recoding taken in a healthy fetal lamb.

The recordings contained a wide variety of different blood pressure waveforms. In this somewhat extreme example, the fetal-lamb is skip-beats, induced by Dr. Johnathan Mynard by tapping the heart with forceps.

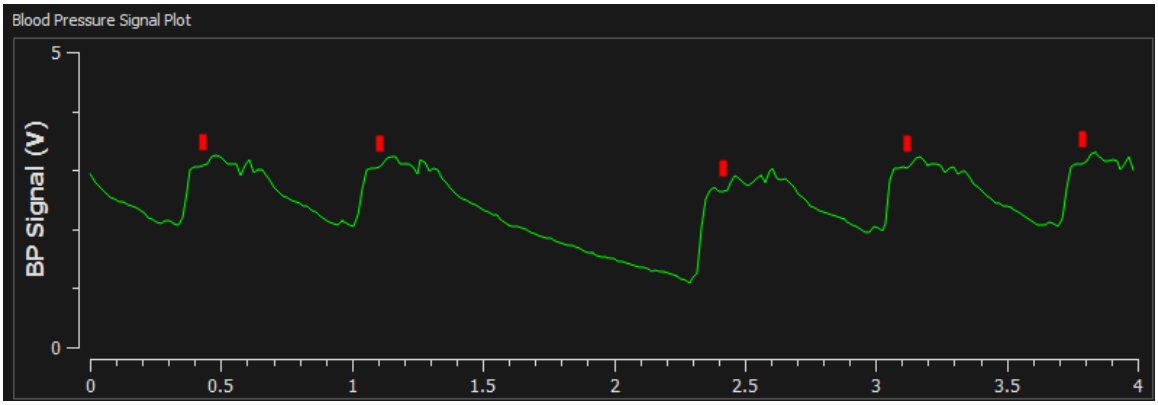

Figure 15: Test of the triggering system on an invasive recording of a fetal lamb experiencing a cardiac malfunction.

As you can see in the plot in Figure 15 above, the triggering unit is very robust, and it triggers very consistently even when the blood pressure waveform is distorted.

In later testing, the waveform generator's output frequency was adjusted to simulate different heart rates. Figure 16 shows a plot of the triggering system's operation at 315 BPM.

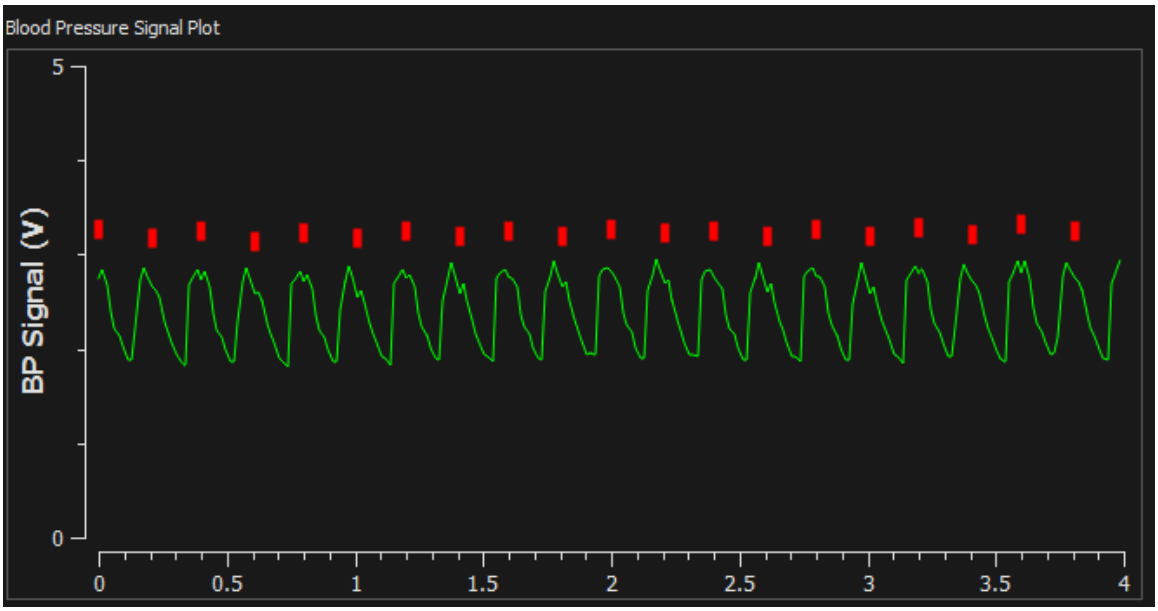

Figure 16: Triggering system performance at maximum heart rate.

5.2 Trial run on a Juvenile Pig

The first tests on living animals were carried out on juvenile pigs. The surgical procedure is documented in Appendix B. The gating module was operated for ten minutes during the surgical procedure. Plots of the gating signal are shown in Figure 17 below.

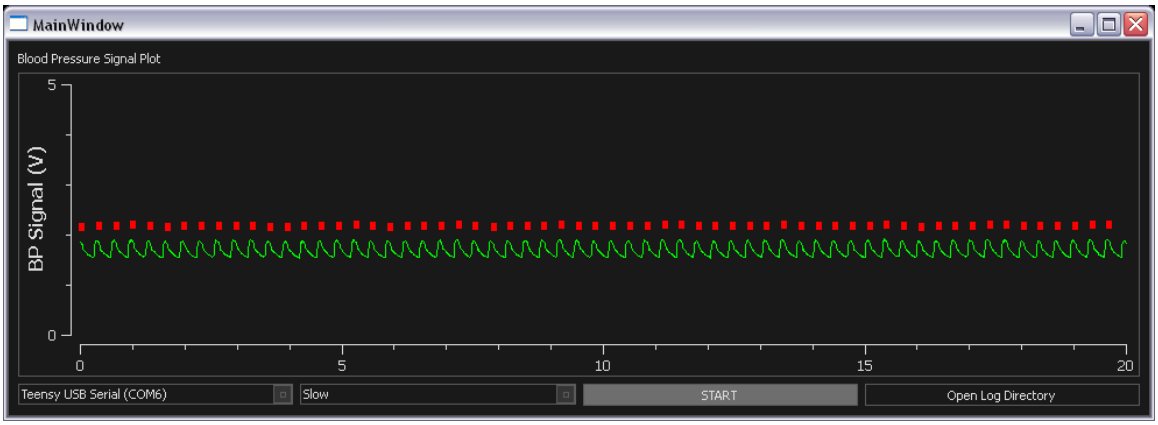

Figure 17: Triggering signal plot taken during surgical procedure on a juvenile Yorkshire pig.

As you can see, the system was functional throughout the procedure, and the pig's heart beat was very consistent. The mean interval between triggering signals was 435ms, which corresponds to a 137BPM heart rate. The standard deviation of the interval between triggering signals was 21ms.

Some minor issues were observed in this test. One issue is that the transducer`s baseline was set to the system default of 0 mmHg. This caused the recorded signal to have significant DC offset, reducing the effectiveness of the gain adjustment algorithm. The recording also differed from our expectations, because our cannula was too long to allow the catheter to reach the heart, so the signal amplitude was lower than it ideally could have been.

Despite these issues, this test was judged to be a success. The triggering signal was sufficiently accurate on every heartbeat that there would not have been any problems whatsoever with the synchronization between the pig`s heart and the MRI scanner if we had been scanning throughout the recording.

6

Conclusions and Recommendations

6.1 System Performance

The system consistently performed as well as a human observer succeeded at detecting blood pressure peaks, and triggered the MRI scanner perfectly both in simulation and during trials on pigs. In terms of core functionality, this triggering system is sufficiently accurate and reliable for its intended purpose in the fetal cardiac flow experiment, so its use will be continued throughout the remaining animal experiments.

6.2 System Shortcomings and Further Work

Given the tight time constraints and lack of prior knowledge about the problem, there is still room for improvement in the triggering system. These problems are relatively simple, and they can be addressed by a future co-op student.

The first major disadvantage of the system is that it depends on solid-state pressure transducers, which are extremely expensive. Very recently, inexpensive MRI compatible fluid filled differential pressure transducers, such as the Transpac IV, have become available. With some MRI compatible amplification circuitry, these inexpensive transducers could be interfaced with the triggering system, which would reduce the overall cost of each animal trial significantly.

Another minor problem is that the triggering unit's variable gain amplifier does not provide zero-baseline offset voltage correction. This feature was deemed unnecessary during the initial tests, because the pressure measurement system can be adjusted to correct any offset voltages. Unfortunately, the fast pace of the experiment and the logistics of inserting the catheter into the animal makes adjusting the zero of the pressure measurement system very impractical, so it should be done using the triggering unit's amplification circuitry instead.

Also, the system's triggering software is hard-coded to work optimally for fetal pig hearts. The application area of this device could easily be expanded to a wide variety of other animals, such as rats and lambs, if the monitoring software's user interface was

expanded to allow the user to adjust the device's triggering parameters without needing to manually change the microcontroller code.

Finally, while the build quality of the circuit board itself was excellent, the hardware design of the unit is sub-optimal, because it requires manually soldering six cables to the PCB and the connectors. In a future revision, the assembly time of the unit could be reduced substantially by using an extruded aluminum case and using the PCB as the front panel. This way, the connectors could be directly soldered to the PCB, and the PCB silkscreen layer could be used to label the connectors and to provide basic instructions [10].

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Appendix A

Transducer Selection

The chosen method for acquiring a blood pressure signal for these experiments was to surgically implant a catheter into the fetal pig's carotid artery. The transducer had to meet these minimum requirements:

1. Must be certified by the American Society for Testing and Materials (ASTM): to meet MRI safety and compatibility standard F2503.
2. Must be capable of measure blood pressures in the range 0-300mmHg.
3. Must be designed for use in surgical applications, meeting either clinical or pre-clinical safety standards.
4. Must function reliably for at least one hour after implantation without requiring any adjustments that would require a surgical staff member to enter the MRI scanner.
5. Must have a catheter diameter <2mm to fit inside the artery in question.
6. Must have a catheter length of >10cm to allow the surgeon to insert the catheter without exteriorizing (removing the fetus from the womb).

The instruments that meet these requirements on the market are:

1. Baxter Edwards Truewave fluid filled pressure catheter.
2. Samba Sensors Preclin solid fibre optic pressure sensor.
3. Transonic T-402 ultrasonic flow probes.

All of these transducer's stated specifications far exceeded our requirements, so the primary deciding factor became cost. SickKids already owned a Samba Sensor's pressure measurement unit, so we opted to primarily use that unit.

Appendix B

Surgical Procedure for System Validation

The surgical procedure was developed in coordination with the cardiology team at SickKids. To develop the protocol, we began by taking high resolution MRI scans of a stillborn Yucatan pig fetus, to determine the diameters of its major arteries. From these scans, we determined that the carotid arteries (shown at the shop of the scan in Figure 18 below) would be greater than 3mm.

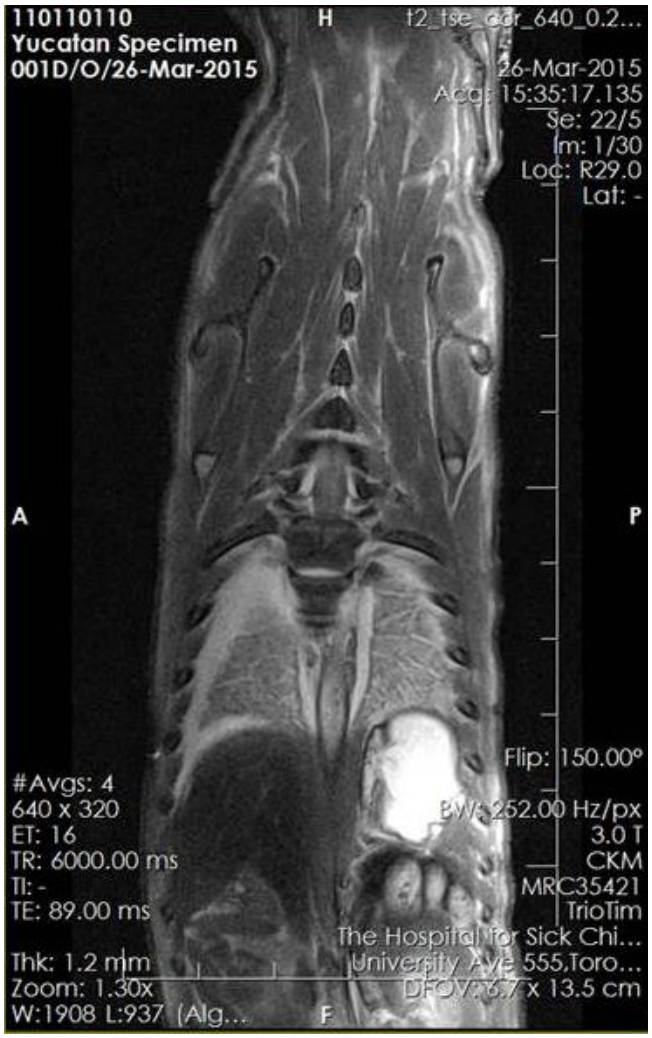

Figure 18: High resolution MRI of a stillborn Yucatan pig fetus.

Next, we worked with a cardiologist from the SickKids catheter lab to choose the surgical equipment. We opted to use a very fine cannula, shown in Figure 19, designed for use in human children to insert the catheter into the artery.

Figure 19: Cannula, complete with valve system for delivering fluids.

The pig chosen for this experiment was a seven day old male of the Yorkshire breed. We chose this specimen, because it is a very good analog for the size and vasculature of a late gestation fetal pig of the Yucatan breed, and it cost significantly less to care for than a pregnant pig.

The pig was placed on the operating table in supine position, supported by cushions on both sides. Gas based anaesthetic of 2% isoflorine gas was delivered through a ventilator, and a small hot water pad was placed over its abdomen to prevent hypothermia. The full operating room setup is shown in Figure 20.

Figure 20: Operating room setup.

After the pig was anaesthetized, the veterinarian adjusted the ratios of nitrous oxide and oxygen in the gas mixture to slightly increase its heart rate to more closely resemble the normal resting heart rate of a fetal pig.

Once the pig was stable, the surgeon made a small incision and located the carotid artery. In a continuous well-practiced motion, he punctured the artery, inserted the cannula, and placed sutures around it to stop the bleeding. The pig lost a small amount of blood during this procedure, so supplementary fluids were introduced via a syringe.

After the cannula was secured in place, the surgeon inserted the pressure transducer (the blue wire). A small piece of silicon tubing with a yellow handle was placed around the catheter prior to insertion to protect the tip while it was pressed through the valve.

Next, I connected the catheter to the Samba Sensors pressure measurement module and started the gating module. Data was recorded for ten minutes. The photograph in Figure 21 below shows the full equipment setup.

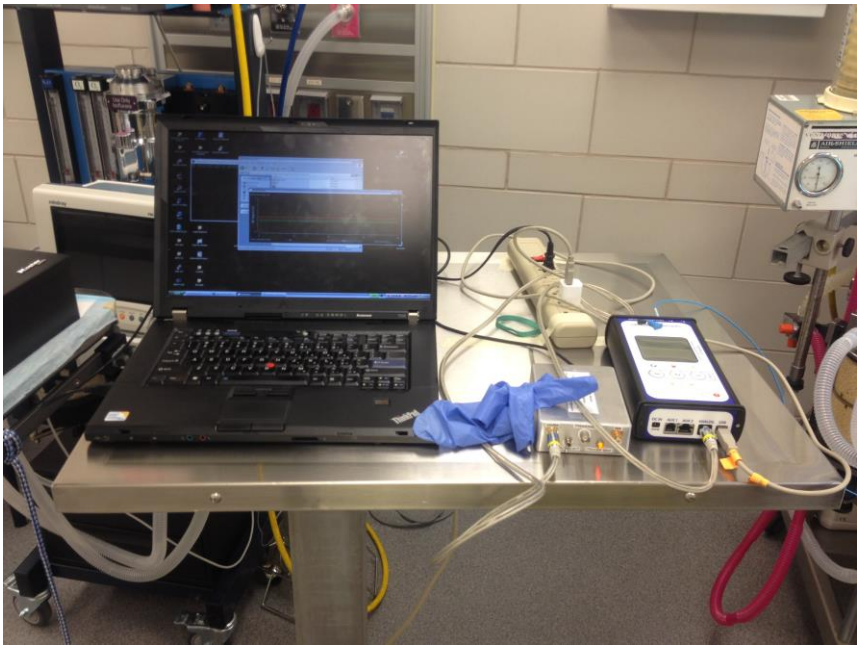

Figure 21: Complete instrumentation setup for testing the gating module. The equipment from right to left is: Samba Sensors pressure measurement module, triggering system, and a laptop running the monitoring software.

After ten minutes of recording, the gating module was disconnected and the pressure probe was replaced with a fluid based transducer to test anaesthesia options. From this test, we determined that slightly increasing the isoflourine concentration to 2.2% resulted in a lower mean blood pressure of ~42mmHg and slower heart rate of 140BPM. Lowering the isoflourine concentration to 1% resulted in tachycardia with peak heart rates of 210BPM and a significantly increased mean blood pressure of ~50 mmHg.