Quad Rat Vitals Monitor

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***Abstract*—In the course of our client's research, PET imaging of rats is often used. During each scan, four rats are anesthetized and manually kept under anesthesia for the course of two to three hours. Because the current system of anesthesia requires manual adjustments, the vitals of each rat should be monitored constantly. Currently, our client is using a veterinary pulse oximeter designed for "small animals" (such as dogs, cats, and monkeys). However, since the rat has a relatively much higher heart rate, the machine often displays inconsistent readings, greatly reducing the efficiency of anesthesia delivery. Our novel design would allow for the display and recording of SpO_2 levels, heart rates, respiratory rates, and body temperatures of four rats simultaneously during PET imaging experiments, in order to maintain appropriate anesthesia dosages on each of the four rats independently. Design and construction of the respiratory rate and temperature components of the device have been constructed and tested, and are able to simultaneously, on four rats, accurately monitor and record rectal temperature (32-42° C) and respiratory rate (around 20 breaths/min) so that the researchers are able to determine the adequate dosage of isoflourane to keep the rats anesthetized.**

I. Background

In the course of our client's research, PET imaging of rats is often used. During each scan, four rats are anesthetized and manually kept under anesthesia for the course of a few hours. Because the current system of anesthesia requires manual adjustments, the vitals of each rat should be monitored constantly. Currently our client is using a veterinary pulse oximeter designed for "small animals" (such as dogs, cats, and monkeys). However, since the rat has a relatively much higher heart rate, the machine often displays inconsistent readings, greatly reducing the efficiency of anesthesia delivery. Our novel monitoring device allows for the display and recording of SpO_2 levels, heart rates, and body temperatures of four rats simultaneously during PET imaging experiments in order to maintain appropriate anesthesia dosages on each of the four rats independently. The device will need to be able to, simultaneously on four rats, accurately detect heart rates up to 500 bpm and blood oxygen saturation levels with an accuracy of ±2% so that the anesthesiologist is able to determine the adequate dosage of isoflourane to keep the rats anesthetized (Fig. 1). In addition to monitoring the heart rate and SpO_2 levels, our client would also like us to design the device to be able to monitor and record rectal temperature (32-42° C) and respiratory rate (around 20 breaths/min). If the device is able to effectively monitor the rats at the set specifications (up to 500 bpm, ±2% SpO_2, 32-44° F, and detect breathing at around 20 breaths/min), we hope to implement a computer controller to automate the anesthesia delivery system.

Figure 1. Isoflurane delivery system. Knobs are manually adjusted by an operator to mix appropriate amounts of isoflurane and oxygen in administering the proper concentration of anesthesia.

To detect SpO_2 and heart rate, companies such as Nonin and Nellcore produce pulse oximeter currently on the market. However, they are almost exclusively for humans. There are also some veterinary oximeters on the market. However they are not suitable for use with rats and mice. Rats have an average pulse rate of 300 beat per minute while under anesthesia, which is more than fivefold of what human would have. Our client is currently using a pulse oximeter designed for dogs and cats on rats, and the pulse rates shown on the device are often out of range compared to the approximate normal values. The reason is due to the algorithm of signal processing as there is less blood passing through the artery with each beat and there is much less waiting time between peaks, compared to dogs, cats, or monkeys. Currently there is a pulse oximeter specialized for rats and mice, named MouseOx, which is produced by Starr Life Science, however the cost for this device is estimated to be more than $7,000 USD[1].

Heart rate can be detected because the arterial blood vessels expand and contract with each heartbeat. This is shown on the waveform of the pulse oximeter. By measuring the time distance between two consecutive peaks, we can calculate the pulse rate by taking the inverse of the time between two peaks.

II. Materials and Methods

A. Circuit Design

We used a circuit described in Webster, 1997 [2]. Because of the use of light in the absorbance measurement, we need a "light-to-voltage" conversion using current as the input signal. The classes of photodiode amplifiers suitable for pulse oximetry applications are the classical resistor-feedback transimpedance amplifier and the capacitor-feedback switched integrator. This circuit is also commonly use with piezoelectric sensors, which also gives out a small current in response to a stimuli. This is the first stage of our circuit (Fig. 2).

In the pulse oximeter case, the light shining on a photodiode produces a small current that runs to the amplifier-summing junction and through the feedback resistor. Given the very large feedback resistor value we used (4.7 MΩ), this circuit is extremely sensitive to changes in light intensity. A small capacitor (390 pF) is used to control gain peaking caused by the diode capacitance.

The second stage of the circuit is a differential amplifier, which is used to filter out the common noise from the input. The third stage is a non-inverting amplifier with a gain of 22 so the output signal can be observed on the oscilloscope.

For the thermistor circuit (Fig. 3), we used the thermistors from digital human thermometers purchased from Walgreen's (which is closely related to what our client currently uses) and use a non-inverting amplifier to get the signal. We place the thermistor at the positive input of the op-amp. When the temperature causes the thermistor resistance to change, the voltage across the thermistor also changes. This signal is then displayed on the front panel.

B. LabVIEW

LabVIEW (LV) was used to analyze, display, and store the output signals from the circuit. LV was chosen due to some group member's familiarity with the program and the ease of making a clear Graphical User Interface (GUI) for researchers to understand without previous knowledge of the device or the program.

For temperature the LV program took the voltage and converted it to temperature using the constants found during testing. The current temperature of the rat was then displayed on the GUI for each rat, and the temperature data was stored in an array and saved upon stopping of the program.

For respiratory rate the LV program took the output voltage and stores it in an array. After each new point was added a long average (about 10 sec) and a short average (about a third of a second) were calculated. These two averages are then compared. If the short average drops below the long average, and the time point immediately before was above the long average the program recognizes that as a breath and stores the time (which was previously recorded as soon as the data is brought into LV). An array stores the time each breath is recognized and is used to calculate the respiratory rate through simple arithmetic. The respiratory rate for each rat is displayed on the GUI and the raw incoming data and array of detected breaths is stored upon ending the program.

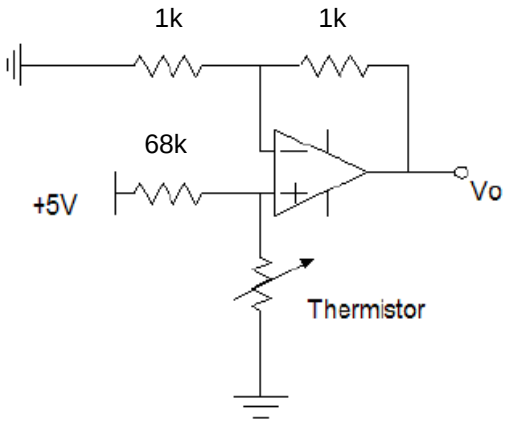

Figure 3. Circuit diagram for the thermistor.

C. Temperature Sensors

Digital oral human thermometers were purchased from Walgreen's and the thermistors were taken out and incorporated into our circuit. The tip and casing were left intact to keep the probe interface identical to what our client currently uses.

D. Force Sensing Resistors (breathing rate)

A force sensing resistor was used to measure the force exerted to the sensor when the rat breaths. The resistor is placed right beneath the abdomen of the rat. When the abdomen expands, it exerts force to the resistor and the resistance changes. Applying a simple voltage divider would allow us to get the fluctuation in resistance in terms of voltage. From the pattern, we can then calculate the breathing rate. The advantage for this design is a simple circuit and that the resistor is always fixed in place (beneath the abdomen), as well as being relatively cheap.

Once the sensor had been built, we wrote a LabVIEW (LV) program that was designed to calculate the breathing rate. As a first attempt, we took a length of time (10 sec during first testing) and calculated the average voltage during that time frame. Once the LV program knew the average it compared the incoming raw data to that and was alerted when one point was below the average and the data point before was above the average. When this occured the program recorded the time to an array (time was actually taken immediately after the data was first recorded).

To calculate the breaths per minute the program took the last eleven time points and found the total time between those points. Then, that time was divided in ten, so as to represent the average time between breaths over the last ten breath intervals. This time was manipulated to account for the change from milliseconds to minutes and was then displayed to the user.

E. Heart Rate and SpO_2

We need to have two waveforms, one red and one infrared, to calculate the SpO_2. Usually in a commercial unit, the red LED and IR LED turns on and off alternatively, with timing circuit built in, so we can get two waveforms and find the ratio between the peak and the baseline and then compare it to a table and get the SpO_2 value. However, originally, we only got one waveform, and that was not sufficient to find SpO_2. As we have been solely using positive DC as our LED source, we guessed that if reversed the polarity and a negative DC source was sent in, we could turn on the infrared LED. It had been tested that when a negative DC signal was feed to the LED, we still got a very nice and clean signal just as when we fed in a positive signal, only a difference in magnitude, which proved our assumption was right.

To find SpO_2, we need to determine when the red LED is on and measure it. Alternatively, determine when IR is on and measure that, and take corresponding readings. That is why the signal polarity frequency needs to be carefully considered. But since our output is still from one channel (having only one photodiode), we have to split it into two sets of data, correspond to the polarity of the input signal. This might be done in LabVIEW. The timing pattern was suggested 480 Hz in Prof. Webster's book [2].

III. Testing

A. Temperature

The design of the thermistor was tested using a thermometer as a reference. Based on the specification (accurately measuring a temperature range between 32-42 °C), the thermistor and the thermometer were placed in water. The water was then heated to above 45°C and slowly cooled to 30°F. During this process, an analog voltage signal was recorded with measurements from the thermometer. This procedure was repeated twice to ensure accuracy of the thermistor. Data was plotted measuring the analog voltage output versus temperature (Fig. 4). A linear function was chosen to calculate the relationship between output voltage and temperature because the thermistor displayed linear

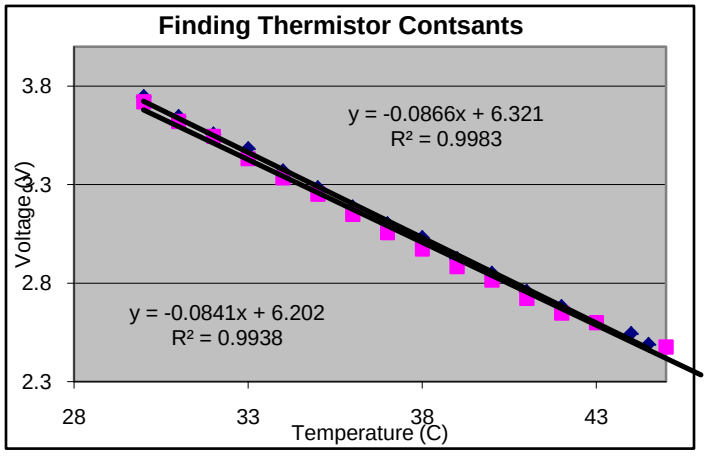

Figure 4. Voltage vs. Temperature. After testing of the thermistor, we found that within our design specification range (~32-42 ˚C) the correlation between temperature and output voltage was very near linear with a R^2 greater than 0.99.

performance through this temperature region. The first trial showed an R square value of 0.9983, while the second trial yielded an R square value of 0.9938. Both R square values are quite high, and repetition of the procedure further improved the R square value (showing increased skill in performing this procedure).

After several tests on rats, our device showed the ability to effectively monitor the temperatures of all four rats simultaneously, as well as store the data digitally on the computer operating LabVIEW.

B. Breathing Rate

During testing with the LV program described in the design section, the program worked well only for exceptionally clean data (Fig. 5). Some data looked clean, but because the average favored the baseline it would occasionally be set off by noise (Fig. 6). It was clear that a better method of peak detection would be needed to calculate breaths per minute for average, and not just exceptionally good data. Our first idea was to use the same block of previous data, and simply find the minimum and maximum data points. This method favors outliers and so puts the comparison line towards the middle of the waveform and can easily detect breaths for good (Fig. 5) and average (Fig. 6) data.

However, neither method works for bad, noisy data. (Fig. 7) shows our first attempt at trying to place our device under a rat and get the breathing rate. If the researcher knows where to place the FSR they should never get data as messy as this, but you shouldn't have to be familiar with our device to be able to use it the first time. Our method to detect breaths mathematically in this mess was to first calculate a shorter moving average which works as a filters to smooth out the noise and react to large peaks. This moving average was compared to another average that takes ten times the data points, this second average works as a DC offset. (Fig. 8) displays the raw data in the background with the DC offset average v. the filtering average. Using this method will greatly improve our devices ability to detect peaks in even the noisiest of waveforms.

C. Pulse Oximeter (heart rate and SpO_2)

The modified pulse oximeter with the circuit discussed in the final design demonstrated a clear output analog signal (Fig. 9). Each heart beat created two peaks (first a larger peak followed by a smaller peak), and the signal was successfully compared by placing existing pulse oximeter on the same finger on the opposite hand. While we were able to obtain a signal from a human, we were unable to obtain any workable signal from a rat. Through testing we discovered that the signal was too small in comparison to the noise. The small signal is due to there being much less blood being pumped through paw of the rat than compared to the blood pumped through the finger of a human during each pulse. Since the signal is so much smaller, the signal to noise ratio increases dramatically. We tried to modify the pulse ox circuit to try to get a better signal. The anode from the probe is forced to ground and then the signal from the cathode is fed to a series of circuits. The first stage is a voltage follower

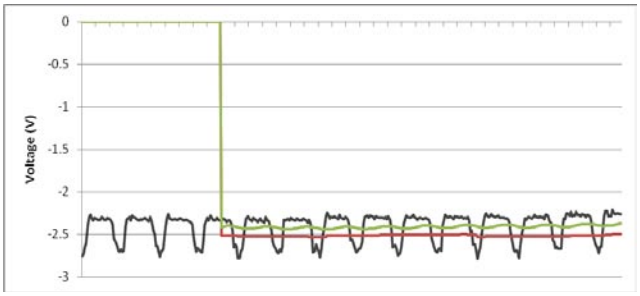

Figure 5. This is exceptionally clean data we acquired after some practice at placing the FSR under the rats. The green line shows the average from a specified amount of time and the red line is the min/max from that same time period. Both of these methods work well for this graph.

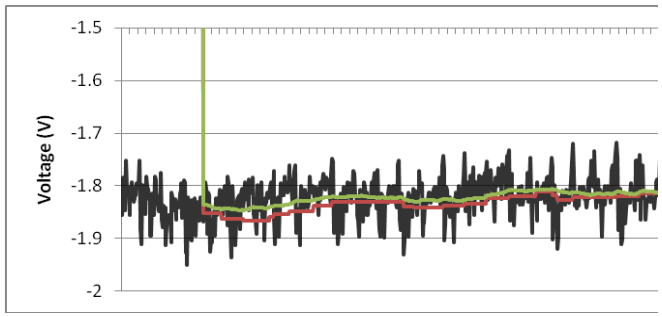

Figure 7. The first data we took using the FSR. The sensor was placed in a very bad spot and was being handled at the same time. Both the long average and the min/max comparison lines would not effectively measure the breathing rate.

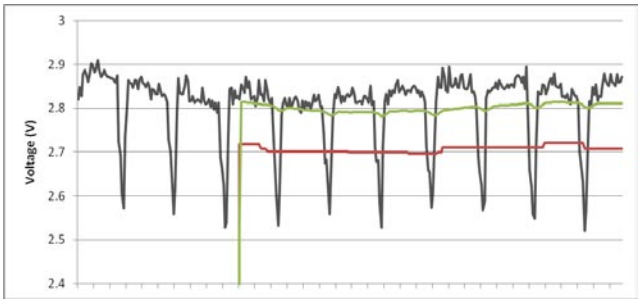

Figure 6. This is some average looking data from our testing. The green line shows a long moving average. That method for breath detection favors the baseline and so some of the noise on the baseline sets off the computer that a breath is taking place. The red line shows a min/max average of the data, this proves to be a much more effective method of breath detection on this data.

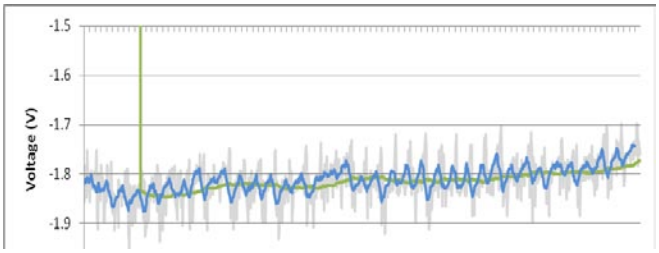

Figure 8. The raw data from a very noisy and misplaced trial is displayed in the background. The blue line is the short average (filtering average) and the green line is the long average (offset). Comparing the blue and green lines will get a reasonably accurate breaths per minute with even the worst data.

to ensure the signal is not affected by additional resistance. The second stage is a non inverting amplifier, with varying gain using a potentiometer. The third stage is filtering. We chose a low pass four pole Butterworth filter with a cutoff frequency of 20 Hz. Corner frequency of 10 Hz, 15 Hz were tested but the amplitude of the waveform is lower and it is more harder to distinguish the pulse (See Appendix for reference to filtering data). Even though the signal is filtered, there still is a lot of noise that makes a pulse hard to distinguish. The signal is analyzed with frequency analyzer and there is a peak at 60 Hz even after filtering, signifying that most of the signal is still noise. So despite developing filters using active and cascading low-pass filters, we were still unable to filter out enough of the noise in order to obtain a workable signal. In consequence, software/digital filtering may be the solution to this problem.

IV. Conclusion

For the final integration of all the sensing components, a printed circuit board was purchased to condense the circuitry and minimize the size of the device (see Appendix for schematic and picture). Four thermistor circuits and four FSR circuits were constructed and connected to the DaQ box, in which the signal was then sent to LabVIEW on the laptop computer.

A completed fully functioning prototype for temperature and breathing rate has been tested on the rats and the results show that the device is capable of accurately monitoring the vitals. A GUI has been made that also incorporates heart rate and plethysmograph display for future completion of the pulse ox sensor (Fig. 10).

While we were unable to finish the development of the heart rate monitor, our device allows our client to now monitor the temperatures of all four rats without having to probe the rats one by one, as well as store the recorded data digitally. Furthermore, it allows him to monitor the breathing rates of the rats, something that he has never been able to do before.

Another team has expressed interest in finishing the development of the heart rate monitor as well as further developing it into a fully functioning pulse oximeter over the coming summer. Apart from finishing the monitoring capabilities of the device, we hope that in the future our device may be integrated with a computer program that would be capable of automating the anesthesia system as well, removing the need for constant human observation.

If there are further inquiries or comments, please contact us at *RatMonitor@gmail.com*.

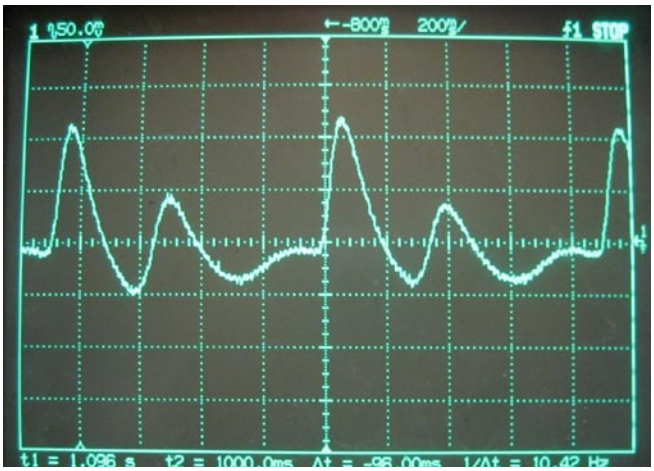

Figure 9. Oscilloscope screen shot. Shows the clean signal obtained from our pulse oximeter circuit. We believe the two peaks are red and infrared transmission of each pulse.

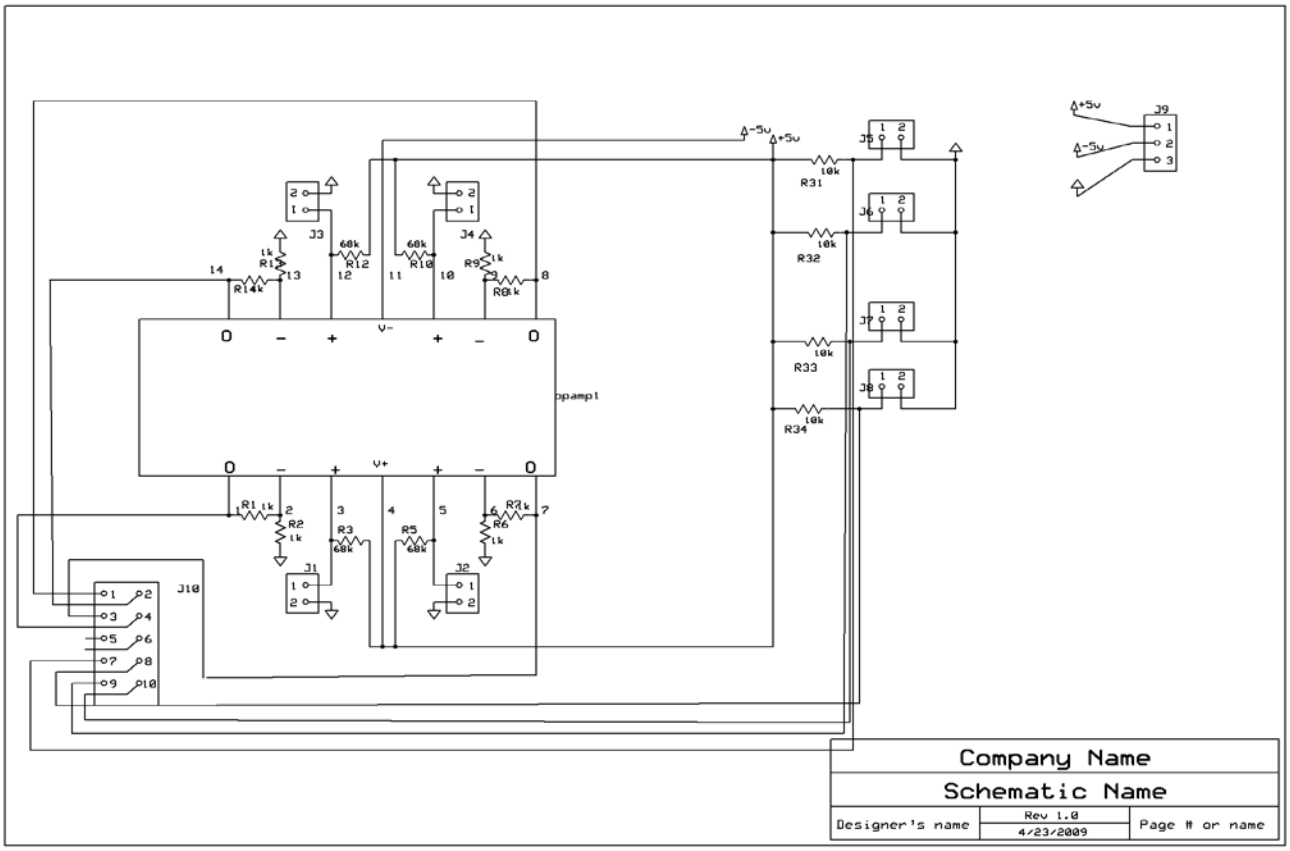

Figure 10. Printed circuit board schematic for the PCB board containing both thermometer and FSR circuit.

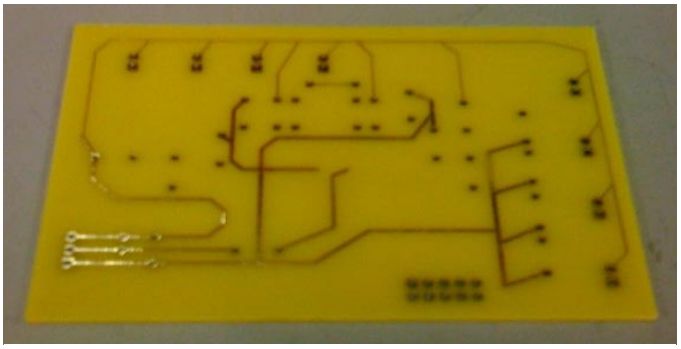

Figure 11. Actual printed circuit board.

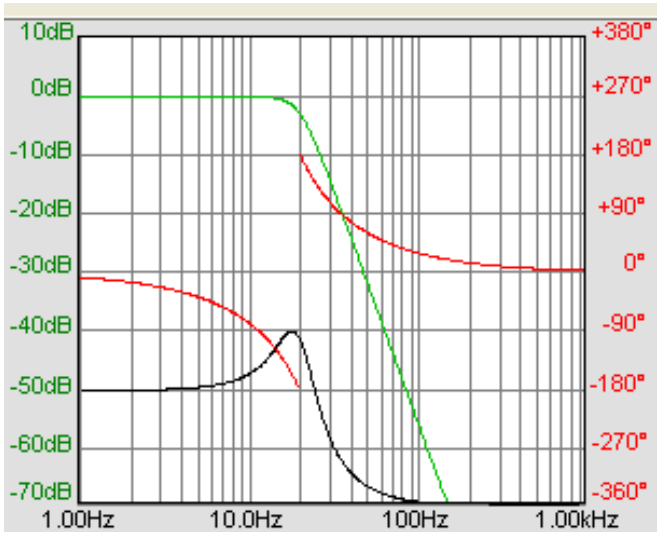

Figure 12. Amplitude response (green), Phase response (red) of the filter

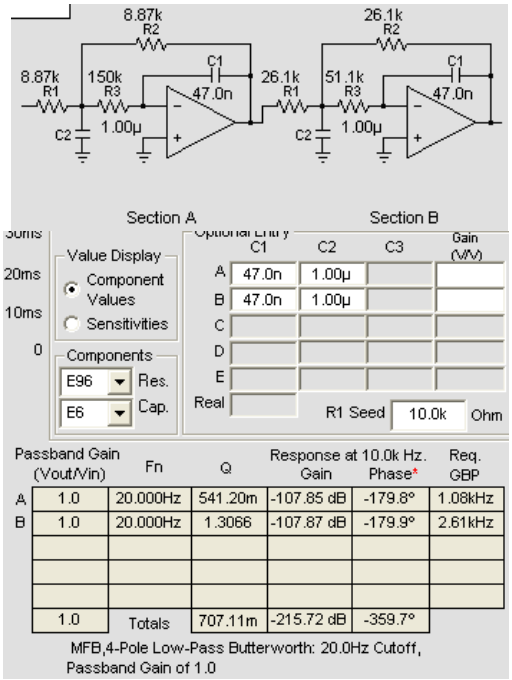

Figure 13. Circuit layout of the 4 pole low-pass filter (stage 3) and corresponding values

APPENDIX

Additional figures of printed circuit board (Fig. 10, 11). Additional figures on low-pass filter used for the detection of blood plethysmograph (Fig. 12,13).

ACKNOWLEDGMENT

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[1] Starr Life Sciences (2008). MouseOx. From http://starrlifesciences.com.

[2] Webster, J. G. (1997), Design of Pulse Oximeters. IOP Publishing Ltd.