Design and Construction of a Quad Rat Vitals Monitor

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Abstract

The design and construction of a rat vitals monitoring device is essential for easily monitoring multiple rats simultaneously. The design team's client currently runs positron emission tomography (PET) scans on four rats simultaneously, and the scans can last up to two hours. During the two hour scans, the rats are under anesthesia and doses of the anesthesia medications must be adjusted based on the rats' vitals. The client desires to have an accurate, reliable, and easy to use rat vital monitoring device to aid in this process. The current design for this monitoring device includes force sensing resistors for monitoring breathing rate, thermistors to monitor rectal temperatures, and pulse oximeters to monitor blood oxygen (SpO_2) levels and heart rates. The design also includes an easy-to-use graphical user interface that displays running averages of the four vitals, the histories of four vitals, and live traces of heart rate and breathing rate. All information will be presented on a single screen, and data from each trial will be stored for further analysis. Current areas of focus in the design and construction of a prototype include programming the graphical user interface and fabricating a pulse oximeter probe. The previously constructed breathing rate monitor must also be modified to improve data collection and the LabVIEW program must be modified in how it interprets the raw data.

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Introduction

Background

The design team's client currently runs positron emission tomography (PET) scans on rats to monitor the location of positron-emitting radionuclides (tracers) within the rats' brains. These scans can last up to two hours, and during the scans the rats are under anesthesia (Figure 1). The client and his assistant must monitor the vitals of the rats during these scans to ensure that they endure no harm while under anesthesia. Currently, the client monitors the rats qualitatively. The skin color of the rats is observed and recorded to ensure that the rats are receiving enough oxygen. The rats' breathing rates are monitored simply by observation, and body temperature is monitored by touch. Currently, heart rate is not monitored. The client would like to be able to obtain quantitative measurements of multiple vitals of each rat during the PET scans.

Figure 1: This picture shows four rats in the PET scanner at the client's laboratory. The rats are orientated in a two by two square. Picture taken from last semester's design team's final paper.

Since the PET scanner is designed for monkeys instead of rats, it is large enough to simultaneously scan up to four rats at a time. The client always scans four rats at a time to keep costs down, because the radioactive tracers used in the rats are expensive to produce. Therefore, the vital monitoring device must be able to monitor four rats simultaneously. While under anesthesia, the rats are wrapped in bubble wrap to keep them warm, because the PET scanner is located in a cold room.

Existing Devices

There is currently one device on the market that is capable of measuring the desired vitals of rats and mice. This is a pulse oximeter designed specifically for rats and mice, called MouseOx, produced by Starr Life Sciences (Figure 2). This device is not capable of monitoring four rats simultaneously, and is priced at $7000 for one device. This is not what the client is looking for because of the high cost and the inability of the device to monitor multiple rats. A different pulse oximeter, produced by Nellcor (the Nellcor N-100), was tested for oxygen saturation (SpO_2) level accuracy when attached to a rat's tail. When SpO_2 levels were between 75% and 95%, this particular pulse oximeter was capable of measuring SpO_2 levels relatively accurately. When compared to the blood sample analysis, the N-100 measured SpO_2 levels with a standard deviation of ±5.7% (Decker).

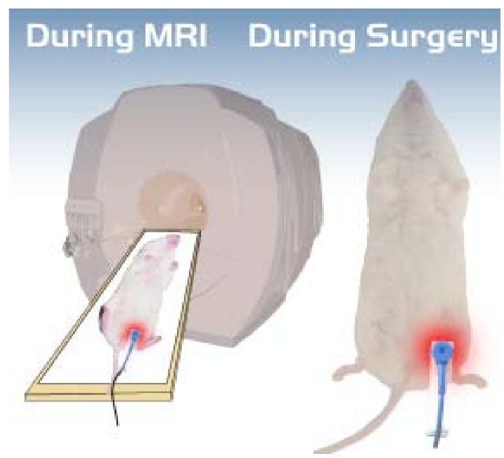

Figure 2: Pulse oximeter produce by Starr Life Sciences capable of measuring heart rate, breathing rate, and SpO_2 levels. Starr Life Sciences™ Corp. ©2009

The client occasionally uses a pulse oximeter designed for small animals, specifically monkeys and dogs, but is unable to consistently obtain accurate data. This is because of the high heart rate and low blood volume of rats. The heart rates of these rats can rise above 300 beats per minute, and this pulse oximeter was not designed with a high enough sampling frequency to measure these pulses or the corresponding oxygen saturation. Therefore, the monitoring device must be able to measure vitals outside the normal ranges of small animals or humans.

Client Requirements

The vitals monitor must be able to simultaneously monitor SpO_2 levels, heart rates, respiratory rates, and rectal temperatures of four rats simultaneously. SpO_2 levels must be monitored with an accuracy of ±2%. Heart rates of up to 500 beats per minute and respiratory rates of up to 30 breaths per minute must also be monitored. Rectal temperatures of 93 to 100 degrees Fahrenheit are to be monitored as well. All four vitals of all four rats must be simultaneously displayed in a user-friendly graphical user interface (GUI) on one screen. All probes used to monitor rat vitals must be non-invasive and cause no harm to the rats. Finally, no component of the device can pass the anterior end of the sternum, because the PET scans are focused around the cranial region of the rats.

Motivation

Our client's research on rats requires him to monitor the four vital signs of heart rate, breathing rate, blood SpO_2 level, and temperature in each individual rat. Because the rats are under anesthesia, which requires manual adjustment by the laboratory assistants, development of a system that readily displays the current values of each vital sign along with the option to bring up the history of each vital is important. The laboratory assistants must be informed in a timely manner if any of the four vital signs enter critical ranges, in order that proper adjustments to the anesthesia can be made.

Currently there is no accurate, cost-effective method to monitor and display all four vital signs simultaneously. Since our client's research is based off of a four-rat setup, the existing devices previously mentioned will not suffice. Furthermore, the GUI that is to display the four vital traces must be specifically engineered according to the type of data it will be receiving from the circuit elements and corresponding probes designed to monitor each vital sign. Therefore it is our goal to design an inexpensive, easily operable prototype that incorporates both circuit based monitoring systems along with a LabVIEW GUI to display the signals received from each monitoring system.

Previous Semester's Work

The BME 402 design team that began work on this project during the 2008-2009 school year was able to engineer methods for calculating breathing rate and rectal temperature. The method for calculating breathing rate is dependent on a force plate, shown in Figure 3, which contains a force sensing resistor (FSR) that is placed underneath the rat just below the sternum. As the rat breathes, pressure is exerted on the plate, causing the variable resistance of the resistor to change. Applying a five volt voltage dividing circuit across the FSR allows this fluctuation in resistance to be converted to a voltage,

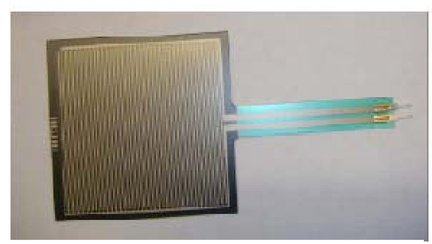

Figure 3: Force plate containing force sensing resistor. Picture taken from last semester's design team's final paper.

which can then be sent to LabVIEW where the digital voltage readings are displayed graphically as a breathing rate (breaths/min).

The method for calculating rectal temperature uses the circuit layout seen in Figure 4. Digital human thermometers purchased from Walgreen's possess an internal resistance that changes along with temperature and thus causes the voltage across it to change, much like the FSR described above changes with pressure. The thermometers are connected to the positive input of a non-inverting amplifier to amplify the voltage signal, which is then sent to LabVIEW where the digital voltage readings can be displayed graphically.

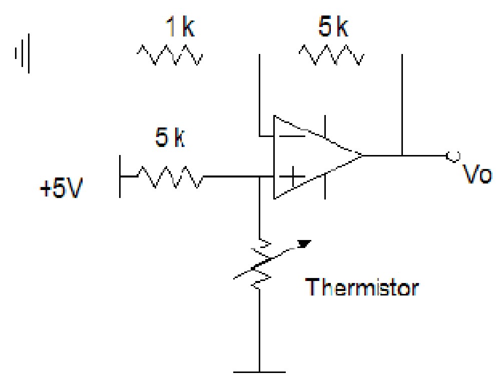

Figure 4: Circuit diagram for temperature sensing thermistors. Diagram taken from last semester's design team's final paper.

After the circuit elements for detecting breathing rate and sensing rectal temperature had been designed, the design group wrote a LabVIEW program for receiving the digital signals from each circuit via an analog to digital converter. LabVIEW calculates the average voltage received from the FSR circuit for the most recent 10 seconds of data, and then compares the incoming raw data to that average value. When two sequential time points fall above and below the average value for the past 10 seconds, the time is recorded and stored in an array. From there, breathing rate is calculated by finding the total time between the past 11 time points stored in the array, and dividing by 10 to give the time between breaths. Lastly, the time calculated between breaths is converted from milliseconds to minutes in order to give a value in breaths per minute to be displayed to the user.

For the temperature sensing circuit, the previous design group ran voltage calibration tests and concluded with an R^2 value of over 0.99 that the voltage versus temperature relationship for the store bought thermistors behaves linearly in the temperature range required by our client. Results can be seen above in Figure 5. This linear relationship is programmed into the LabVIEW GUI to convert the incoming voltage data into a live temperature displayed to the user.

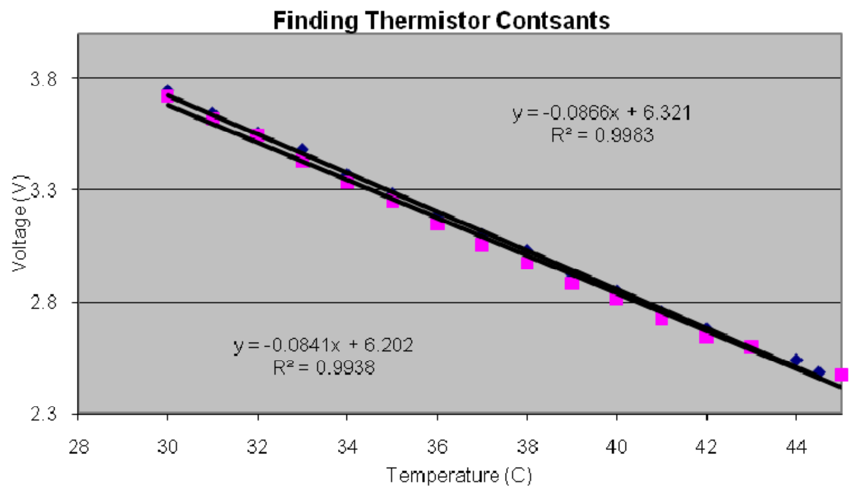

Figure 5: Test data showing the linear relationship between voltage and temperature. Diagram taken from last semester's design team's final paper.

A simple LabVIEW GUI was designed by the previous team to receive the signals from the FSR and thermistors circuits. This GUI, which can be seen in Figure 6 (next page), is far from the final product our client has requested for the final prototype. Nonetheless, the current GUI is able to receive the FSR and temperature signals and display a live trace of voltage from the

FSR circuit, which is used to determine when a breath has taken place, and also display a temperature reading from the thermistors. This GUI layout does not currently possess the

Figure 6: Final graphical user interface from last semester.

capabilities of receiving data from a pulse oximeter circuit nor can it integrate that data to display live traces of blood SpO_2 and heart rate. Expanding this GUI is a priority for this semester, and three design options for doing so are highlighted in the following section.

Pulse Oximeter Probe

Pulse oximetry is based off of Beer's Law. It compares the absorbance of two different wavelengths of light (red and infrared) after the light has passed through tissue. The difference in absorbance is used to generate SpO_2 values. Then, by using peak-to-peak measures of the SpO_2 waveform, heart rate can be inferred. Following several probe design requirements, such as reusability and the ability to adjust to various size rats, the first major component of this design project was initiated.

Foot Clip

The foot clip probe (Figure 7) is loosely based off of existing human pulse oximeter probes. Essentially it works like a clothespin, where the hind paw of the rat is placed between the top and bottom halves of the clip. On the inside surfaces of the two halves are mounted LEDs and a photodiode. The LEDs and photodiodes are positioned across from one another, so that only light passing through the tissue is registered by the photodiode. This design is similar to current devices used by the client, so implementing it into their laboratory would be easy. Although the ability to reposition the probe contributes to its attractiveness, the opportunity for undesired displacement is also possible. Another detriment of this design is the potential for the clip, if poorly manufactured, to apply too much pressure to the hind paw of the rat, altering arterial blood flow. Any disruption in arterial blood flow will result in inaccurate SpO_2 data.

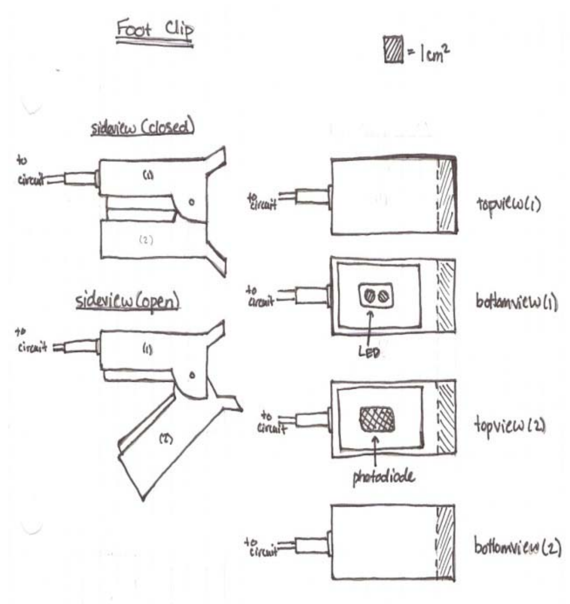

Figure 7: Design of *Foot Clip*

Foot Wrap

The second probe design (Figure 8) is a system of symmetrical hinged plates held in position by a Velcro strap. As before, the LEDs and the photodiode are mounted on opposite plates. The rat's hind paw is placed between the two plates and then held in position once the probe is attached. One of the main benefits of this design would be the immobility of the probe after attachment. Once fixed in place, there is little opportunity for the probe, and therefore LED-photodiode alignment, to be displaced. Although successful in eliminating displacement concerns, this design does not allow for easy readjustment. If any problems arise with probe placement throughout testing, adjustability of the probe is vital to the maintenance of accurate data acquisition.

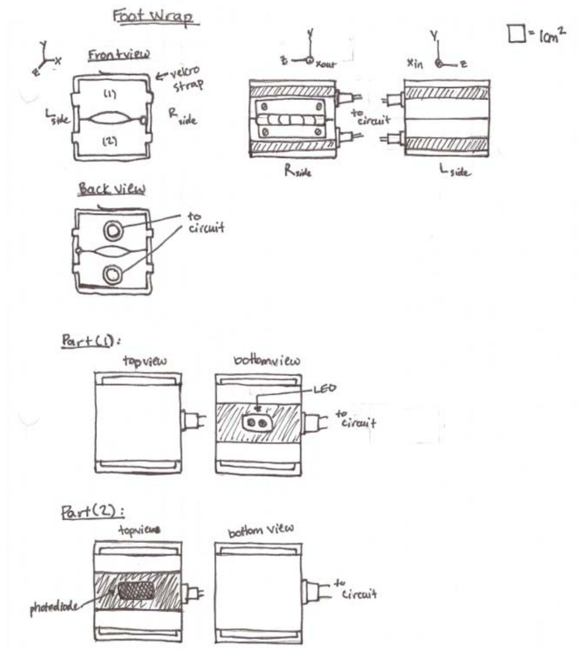

Figure 8: Design of *Foot Wrap*

Tail Clip

The final probe design is very similar to that of the foot clip. It again behaves as a clothespin would, trapping the tail between the two halves of the clip. For this design, the rat's tail is positioned so that it rests within the groove machined into the opposing halves of the tail clip. As in the case of all the probe designs thus far, the LEDs are mounted on one side of the clip with the photodiode mounted on the other. However, this design specifically restricts the LEDs and photodiode to the groove in their respective clip half. Similarly to the foot clip, the tail clip is easy to attach as well as adjust. Along with the dangers of applying excessive pressure on the arteries within the tail, this probe design also has the potential to interfere with or damage the catheter located below the tail during the course of the experiment.

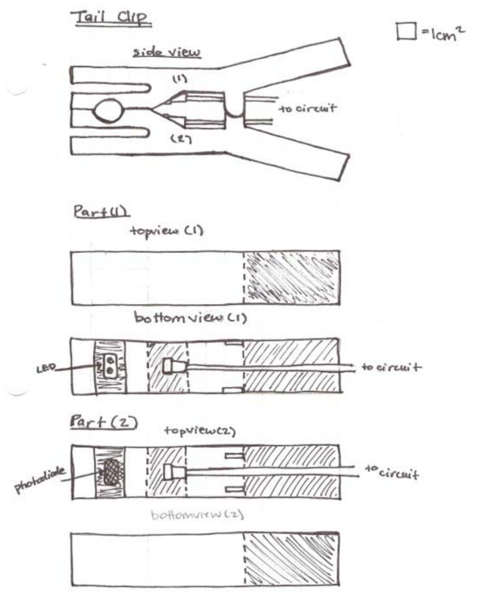

Figure 9: Design of *Tail Clip*

Pulse Oximeter Probe Design Matrix

The pulse oximeter probe design matrix (Table 1) was used to evaluate the various probe designs and to determine which design best fit the client's needs. For ergonomics, the foot clip scored the highest because of its ease of use and adjustability. The cost for each probe was relatively the same for each case, and therefore did not heavily influence the final probe decision. The accuracy of the tail clip was rated significantly lower than the other two designs due to the denser skin properties of the tail, as well as the location of the catheter in close proximity to the tail. The flow of blood through the tail is also less than that of the foot, so the tail clip may have difficulty collecting data. As for safety, all three designs were rated relatively the same; none of the probe designs put the long term health of the rats in danger. Although it was mentioned that the foot and tail clips may exert excessive pressure on their relative body parts, with proper manufacturing, this can be avoided. The durability of the foot wrap was rated low because of the potential for the Velcro strap to wear out over time. For the amount of times these probes will be used, durability is vital for extended use. Just as in cost and safety, feasibility is relatively the same for each probe. With help from graduate students on the wiring and circuitry, making the physical clips to mount the LEDs and photodiode on, is easily achievable in each case.

Table 1 - Design Matrix: Pulse Oximeter Probe			
Criteria (Weight)	Foot Clip	Foot Wrap	Tail Clip
Ergonomics (20)	18	12	14
Cost (5)	4	5	4
Accuracy (50)	46	46	35
Safety (10)	8	9	8
Durability (10)	9	6	9
Feasibility (5)	4	5	4
Total (100)	**89**	**83**	**74**

Graphical User Interface

The second major component of this design project is to display the collected data to the user in an easy-to-use fashion. The decision was made last semester to utilize National Instrument's LabVIEW software package not only for data acquisition, but to generate a GUI. This semester's team fully intends to go forward with that decision. LabVIEW, in deviation from normal programming languages, is a graphical-based programming language that allows the programmer to wire connections between functions provided by LabVIEW. These functions include, but are not limited to, math functions, tools to acquire signals from devices, and displaying data on graphs.

Four Corners with Buttons

The first design idea divides the user's screen into four sections; each rat is designated a section, as seen below in Figure 10. Within each section, the user is presented with a live trace of breathing and heart rate. Below the live traces, the numerical values of the vitals can be found. Buttons are available for the user to view a graph of the history of a vital over the

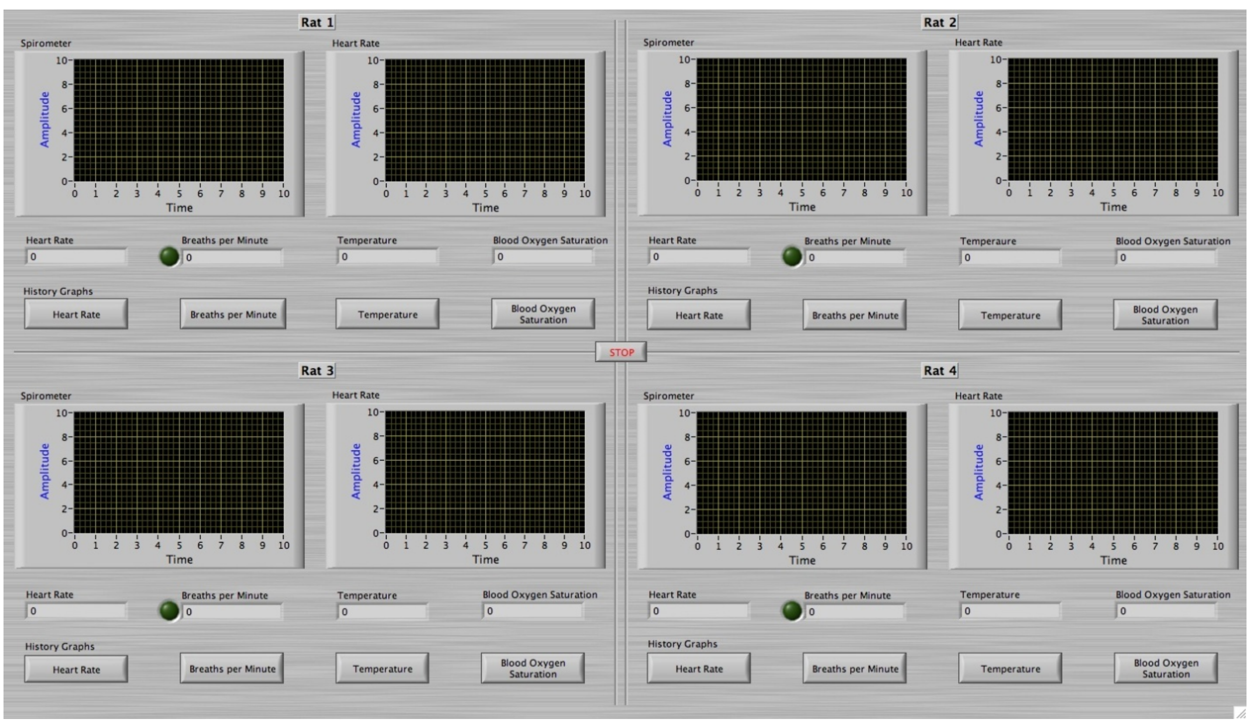

Figure 10: Design of *Four Corners with Buttons* interface

course of the experiment or a user-specified amount of time. This design allows the user to quickly glance at the screen to view the current status of a rat and compare it to the other rats. It is attractive and would work well on many different sized screens. However, because the user must click a button to view the history graph, it may become cumbersome for the user to view the history of a vital and compare it to others because of the extra clicking involved. Additionally, because of the clicking involved, this may detract from the researcher's experiment because it is another task they must be concerned about. Additionally, this option requires much more programming in order to code the individual buttons for their functionality, but it is not beyond this team's abilities to do so. Overall, this design idea would result in a clean, easy-to-use interface.

Tabbed

The second design idea is a departure from the first. Each rat is designated a tab, and within each rat tab, two more tabs are present: one for live data and one for histories. This tabbed organization is visible in Figure 11 (next page). The live data tab displays the same two live traces as the first: breathing rate and heart rate. The values of the vitals being gathered are displayed underneath the live traces. The history tab displays the four history graphs over the course of the entire experiment or over a user-specified amount of time. This interface is even cleaner and with a few clicks, the user can quickly navigate to the data they wish to view. Because of the nature of this design, the user cannot compare the available data, live or history, between any of the rats simultaneously. Additionally, similar to the first design idea, this would require extra clicking on the user's part. However, using the tools LabVIEW provides, the

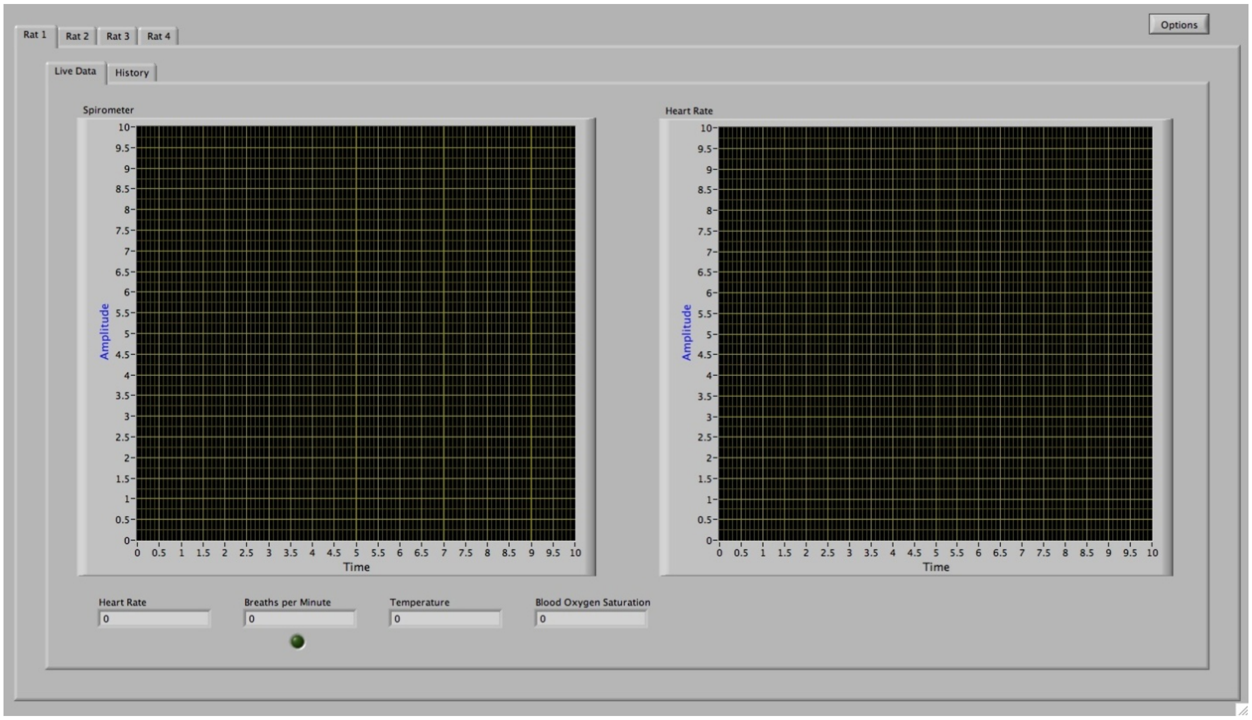

Figure 11: Design of *Tabbed* interface

tabs are very easy to program. This design is an acceptable contender, but its positives must be completely evaluated against its deficits.

Four Corners with Histories

The third proposed design is similar to the first in that it divides the screen into four sections. This design can be seen in Figure 12 (next page). Within each section, all the data that is available for rat is displayed. There are two live traces of breathing and heart rate and the values of the vitals are displayed. But in departure from either of the first or second design ideas, the four history graphs are also displayed. By displaying the history graphs on the same screen as the other data, the screen appears cluttered, but this is an acceptable tradeoff for the least amount of user interaction required. As matter of fact, the only user interaction required with this design is to start the data collection, adjust options as necessary (such as the time

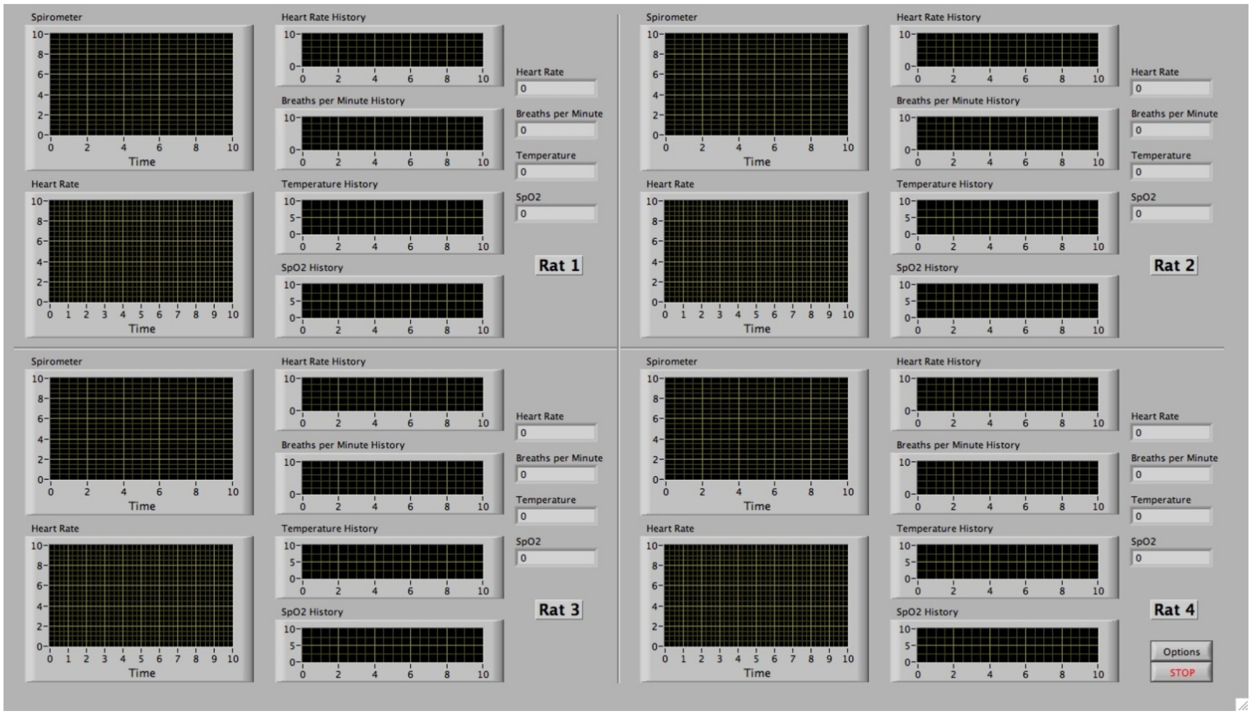

Figure 12: Design of *Four Corners with Histories* interface

interval of history graphs) and to stop the data collection. A glance at the screen by the user is all that is necessary to check the status of a rat. Because the history graphs are all on the same time interval, it is easy for the user to correlate trends not only among one rat, but also among all the rats. This option is doable well within the programming expertise of the group. However, because of the large amount of data on the screen, this display may become small and hard to read on smaller screens. It is also unknown how the performance of this design will keep up with a massive amount of data due to LabVIEW's need to process all the data before it can be displayed every time the history graphs update. This design has many positive points and meets all of the client's requirements, but some further investigation is required.

GUI Design Matrix

The graphical user interface design matrix (Table 2) was used to evaluate the three design ideas on the basis of ergonomics (45), programming feasibility (35), and aesthetics (20). For the purposes of this matrix, ergonomics refers to the ease of use for the user and weighed the highest because of the client's need for an easy-to-use and view interface. The four corners with histories option scored the highest on ergonomics because of the least amount of user interaction required to view the data. However, because of the cluttered interface, this option also scored the lowest in aesthetics. This option did not score as well in programming feasibility as the tabbed interface due to the amount of precise measurements and resizing of elements required to make the interface appear uniform and have even spacing. However, this was a minor tradeoff for a gain in ergonomics.

Table 2 - Design Matrix: Graphical User Interface

Criteria (Weight)	Four Corners with Buttons	Tabs	Four Corners with Histories
Ergonomics (45)	38	25	44
Programming Feasibility (35)	26	32	30
Aesthetics (20)	15	18	14
Total (100)	**79**	**75**	**88**

Testing

Preliminary testing was conducted on a single anesthized rat at the Wisconsin Institute for Medical Research (WIMR) with the assistance of Elizabeth Ahlers. The goal of this preliminary testing was to confirm that each FSR and temperature probe was functioning properly. Also, an analysis of the signal received by LabVIEW would allow for confirmation that the prototype breadboard circuits for the breathing rate and temperature monitoring systems are functioning properly, and therefore are ready to be printed to actual circuit boards. However, preliminary testing yielded very poor results. Only three of the four FSRs were producing a voltage signal, and zero of the four temperature probes were producing accurate temperature readings (even room temperature was unable to be recorded). The three FSRs that were properly functioning produced extremely noisy data at uneven intervals, and required constant manipulation of the force plate underneath the abdomen of the rat to obtain a constant signal. Such poor results are most likely due to excessive sensitivity of the FSR in combination with the delocalized force applied by the abdomen of the rat. The reason for the failure of the temperature probes to accurately monitor temperature remains unknown and will require future testing and calibration.

Future Work

The four primary goals to be accomplished throughout the rest of the semester are to: 1) Finalize the LabVIEW GUI and integrate it with the signal received from the Pulse Oximeter circuit being designed by Biomedical Engineering graduate students, 2) Diagnose the problem causing the current temperature thermistors to not display accurate temperature readings, 3)

Determine a method to obtain optimal signal from the FSR circuit by experimenting with force plate placement, or by engineering an impedance strain gauge to more effectively measure the breathing rate of the rats, and 4) Design the pulse oximeter probe described above in Design Option #1 and properly connect it with the circuit being designed by Biomedical Engineering graduate students. If time permits, the circuit board prototypes will be printed through the company Express PCB. Once printed circuit boards are obtained, the entire prototype needs to be organized with all circuitry and wiring housed in a box-like apparatus, made of either acrylic or Plexiglas. This will function to significantly reduce clutter.

Estimated costs for the future work described above are dependent on how much needs to be changed from the previous semester's prototype. If new thermistors need to be purchased, those will cost $11.99 per rat, and if impedance strain gauges need to be designed, total materials required are estimated at less than $100 per rat. Lastly, materials that need to be purchased for designing a pulse oximeter probe will be taken from existing small animal probes, estimated to be $15 per rat (LED's and photodiodes are free through the University). If circuit boards need to be printed this semester, the cost for the two boards that would be printed is estimated to be roughly $300 ($150 per board). Therefore, in a worst case scenario, the total costs for this semester would total $508. Our client's total budget for this project is $4,000.

Ethical Considerations

First and foremost, the goal of this device is to help the experimenter monitor the status of each rat during the course of the experiment. This device, however accurate, cannot prevent the rats' vitals from entering dangerous levels; rather, it will supply the data and the experimenter must utilize the data in order to decide on the proper course of action. This device is not intended to replace any standard laboratory procedures and is only to be used as a diagnostic tool. All government and university regulations regarding animal research are still expected to be observed.

Conclusion

This semester, the design team has greatly improved the GUI for the LabVIEW program. The interface will be able to simultaneously display running averages of the four vitals, the histories of four vitals, and live traces of heart rate and breathing rate. All of this will be displayed on one screen in an easy-to-read format.

A pulse oximeter probe design has also been chosen for fabrication. This design is easy to attach to the rats' hind paw and also easy to reposition. Accuracy is extremely important for the pulse oximeter, so the probe has been designed to block out ambient light to ensure precise readings. Currently, two graduate students are working on producing a pulse oximeter circuit so that SpO_2 levels and heart rate can be obtained using the pulse oximeter probe.

The design team was able to test the prototype produced by the previous semester team. This included testing the force sensing resistors' ability to sense breaths, and LabVIEW's ability to interpret the data to come up with a value for breaths per minute. The breath rate monitor, using force sensing resistors, was unable to accurately sense breaths, so a new component for monitoring breathing rate may need to be incorporated into the design.

References

Decker MJ et al. *Noninvasive oximetry in the rat*. Biomed Instrum Technol. 1989 May-Jun;23(3):222-8.

Product Design Specifications
Rat Quad Vitals Monitor
10/20/09

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Function: A device that is capable of recording and displaying SpO2 levels, heart rate, rectal temperature, and breathing rate of four rats simultaneously. The purpose of this is to help maintain appropriate anesthesia dosage on the four rats.

Client requirements: Accurately record and display SpO2 levels, heart rates, breathing rates, and body (rectal) temperatures of four rats under anesthesia simultaneously.

Design requirements: Build a device that takes and displays the vital readings of four rats under anesthesia. The device must be able to accurately detect heart rates of up to 500 bpm and blood oxygen saturations level accuracy of ±2% so that the anesthesiologist is able to determine the adequate dosage of isoflourine to keep the rats anesthetized. Device will also be designed to monitor respiratory rate (around 20 breaths/min) and rectal temperature (93-100° F).

Physical and Operational Characteristics

1. *Performance requirements:* The device, at minimum, should be able to take the heart rates, breathing rates, and temperatures of four rats simultaneously and display them onscreen. It should also have a running graph showing the levels/rates of each rat for the last five minutes, meaning 16 graphs displayed simultaneously. The software should also record all data to a hard disc as the data is acquired. A history graph of the entire experiment must also be available.
2. *Safety:* The device should be safe for animal use and be consistent with the safety standards of the current rat platform.
3. *Accuracy and Reliability:* The device must be able to accurately detect heart rates of up to 500 bpm, blood oxygen saturations level accuracy of ±2%, respiratory rates of at least 30 breaths/min, and rectal temperatures of 93-100° F.
4. *Life in Service:* The device must be functional for at least 5 years, with calibration as needed.
5. *Shelf Life:* The device should be able to go without use for a semester and be put back into use with normal functionality.
6. *Operating Environment:* Will be used in a laboratory environment.
7. *Ergonomics:* The device should, in the end, comfortably fit onto the hind paw of each rat without affecting the device's performance or accuracy. The graphical user interface must display real-time graphs for each of the four measurements for

all four rats simultaneously, for a total of 16 graphs. It must also be able to easily display the history of data for any one of the four rats on command.

8. *Size:* Clips must be small enough so that it will not interfere with surrounding sensor and/or devices. No sensors should interfere with the PET imaging, keeping any large components inferior to the base of the heart.
9. *Weight:* The sensor system must not have a mass greater than 1 kilogram.
10. *Materials:* Derived oximeter sensors, converted human oral thermometers, and force sensing resistors. All other materials will not be in contact with the rats.
11. *Aesthetics, Appearance, and Finish:* There must be no exposed circuit components.

- **Production Characteristics**
    1. *Quantity:* One.
    2. *Target Product Cost:* under $4,000
- **Miscellaneous**
    1. *Standards and specifications:* N/A
    2. *Customer:* Research organizations working with rats.
    3. *Patient-related concerns:* Currently no patient-related concerns.
    4. *Competition:* MouseOx produced by Starr Life Sciences