Spring 2007
IPRO 308 Midterm Report

Developing an Artificial Pancreas

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1.0 Current and Revised Objectives

The objective of this IPRO is to assess the practicality of the of the different components of the prototype conceived in the last semester. In particular, the current IPRO team is to determine the reliability of interstitial fluid extraction from pig's skin using a vacuum device system following application of ultrasound to the skin. The team desires also to assess the measurement of glucose levels in the interstitial fluid using both electrical impedance and light transmittance measurement. These tasks are expected to advance the aim of the IPRO to come up with a working prototype. The team will also review existing patents dealing non-invasive blood glucose measurements in order to explore the patentability of the technology being developed in this IPRO.

In addition to the previous objectives stated, the revised objectives included looking into additional methods for the measurement of glucose aside from Impedance Spectroscopy. These methods include Nuclear Magnetic Resonance (NMR) and Absorbance measurement using a UV-Visible Spectrophotometer. The possibilities of these techniques to be used in the prototype added new tasks for the prototype group. More information was sought out on NMR and experiments were done to test absorbance using water and glucose as well as glucose dissolved in the physiologic fluid called Krebs-Ringer bicarbonate buffer so as to simulate the measurement of glucose levels in the interstitial fluid..

2.0. Results to Date

The IPRO has completed several of its tasks. The development of a pseudo code has just begun. The long halt was due to the prototype team. The code could not be prepared because the prototype team was unable to estimate the product delivery time. Additionally, there is very little time for the IPRO team to construct a circuit.The patent search has yielded about 20 patents which are now being reviewed to determine if there are any obstacles to an eventual patent application for the technology developed in the IPROThe team in charge of patents is focusing on patents describing glucose measurement in interstial fluid after extraction and if the measurements involve impedance spectroscopy or other technologies being considered as analytical tools for glucose measurement in our technology.

. Most of the work is geared towards having a working prototype. As for using spectrophotometry for glucose measurements, the results are coming along. Approximately fifteen trials have been run to test the validity of the experiment. The results are fairly consistent. A value for proportionality constant is found for absorbance vs. glucose concentration. The team is waiting for additional supplies to test the idea on a biofluid (Ringer's Solution). Another set of experiment is expected to be performed using the biofluid as the solvent for glucose. For the prototype groups, two prototypes for interstitial fluid extraction will be tested. One prototype was developed last semester and the second prototype is a modification of the original prototype, which is being

developed by the current team. . On March 8, 2007, the prototype group ran two trials using the old prototype. The first trial was on pigskin. No interstitial fluid was extracted from the pigskin. The second trial was on a human subject, Alok Patel. Once again, no interstitial fluid was extracted. The team has identified several reasons for the device not working.

The first problem identified by the prototype is that the suction is very low from the vacuum pump used. This problem would be solved by using a stronger vacuum (part is waiting for delivery). Another problem that exists is leak of air between tube junctions. This problem is going to be solved by using single tube rather than multiple small tubes (Tubes have arrived and need to be connected). Furthermore, the gasketwhich is used to hold the vacuum inside the speaker, is too ridged. This problem is going to be solved by using either silicon or polyethylene tubes as gaskets (tubes need to be picked up from lab). One final problem that was noted is that the function generator does not send a constant signal. A DC function generator needs to be bought.

3.0. Revised Task / Event Schedule

The IPRO team was initial split into two major groups following the development of a prototype and a smaller group dedicated to further research and development of aspects of the prototype that were fully researched and thus cannot be implemented into the prototype. Materials and safety research are largely pending upon the development of the prototype group whereupon the assessment of each of these items will proceed. Research into the measurement of glucose and the development of a biosensor is proceeding concurrently with the development of the prototype. Another group was formed to research patentability and patent applications for the device.

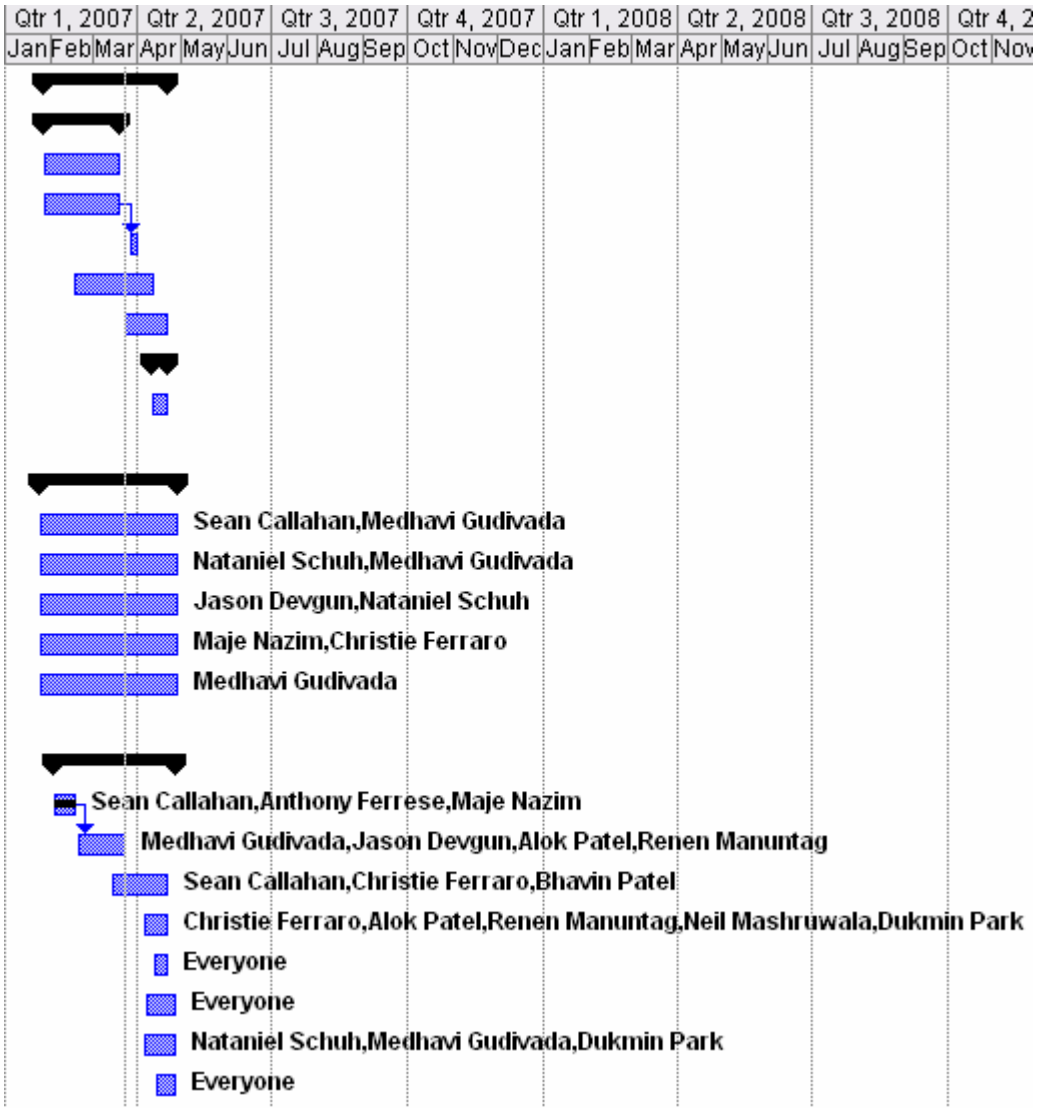
The last IPRO team did not perform any extensive research into the feasibility of using impedance spectroscopy in this device. Additionally, because there is not much professional academic literature on the subject matter the IPRO group has encountered an obstacle in both procuring the materials necessary to implement impedance spectroscopy as a biosensor to measure glucose concentration as well as getting professional assistance from someone with an electrical engineering background to assist in this matter. Thus, the timeline on implementing impedance spectroscopy as a biosensor to measure glucose concentration will be delayed until these obstacles are overcame.

In addition to impedance spectroscopy, research into an optical biosensor has also been included in the project timeline. Progress has been made by this subgroup in the team to identify a characteristic absorbent frequency of glucose in saline and eventually Ringer's solution (which will accurately simulate the composition of interstitial fluid). The current timeline has been set to include research in this area until mid-April, however, reliable results have been obtained in saline solution. With the promise of near infrared spectroscopy as a reliable method to measure glucose concentrations some inquiry has also been made into the materials required to complete this task. The materials research subgroup will likely employ this task later in the semester upon the delivery of the optical research group.

Within the prototype group a number of subtasks were completed by ad hoc groups that form based upon tasks that arise as obstacles are identified, or new developments from the research group. A second prototype is being built by the current team is yet to be completed, but will be very shortly as the prototype group has been waiting on key parts to arrive. Furthermore, members of the prototype group will complete the test of the first prototype built from last semester in its abilities to extract interstitial fluid the week of the 19th. The assessment of the vacuum system will also occur concurrently with this task. The assessment of the second prototype's vacuum will occur shortly thereafter. Upon the successful implementation of the vacuum system and extraction of interstitial fluid the prototype group will begin testing of insulin delivery via reverse iontophoresis.

To date the only deliverable completed has been the project plan. Research into optical and electrical impedance sensors has been conducted in addition to tentative research into materials to build an optical sensor. Work has been done to the previous prototype to make it electrically conductive for iontophoresis and ultrasound. Trials have commenced to test the efficiency of the vacuum system in extracting interstitial fluid from pigskin.

Extract interstitial Fluid from tissue	**Wed 3/7/07**	**Fri 4/20/07**		**Dukmin Park,Anthony Ferrese,Medhavi Gudivada**
Analyze Prototype	**Wed 3/7/07**	**Fri 4/20/07**		
Build a Second Prototype	Wed 3/7/07	Mon 3/19/07		
Assessment of vacuum Syster	Wed 3/7/07	Mon 3/19/07		
Testing and Development	Tue 4/10/07	Fri 4/20/07	4	
Glucose Measurement	**Fri 1/26/07**	**Fri 4/20/07**		**Renen Manuntag,Alok Patel,Dukmin Park**
Research	**Fri 1/26/07**	**Mon 3/19/07**		
Electrical Impedance	Fri 1/26/07	Mon 3/19/07		
Optical Sensor	Fri 1/26/07	Mon 3/19/07		
Testing and Development	Mon 3/26/07	Fri 3/30/07	10	
Optical Sensor	Fri 2/16/07	Tue 4/10/07		
Electrical Impedance	Wed 3/21/07	Fri 4/20/07		
Insulin Delivery	**Tue 4/10/07**	**Fri 4/20/07**		**Bhavin Patel,Alok Patel,Neil Mashruwala**
Testing and Development	Tue 4/10/07	Fri 4/20/07		
Ongoing Tasks	**Wed 1/24/07**	**Fri 4/27/07**		
Materials Research	Wed 1/24/07	Fri 4/27/07		Sean Callahan,Medhavi Gudivada
Safety Research	Wed 1/24/07	Fri 4/27/07		Nataniel Schuh,Medhavi Gudivada
Device Design	Wed 1/24/07	Fri 4/27/07		Jason Devgun,Nataniel Schuh
Getting Patents and Grants	Wed 1/24/07	Fri 4/27/07		Maje Nazim,Christie Ferraro
Minutes	Wed 1/24/07	Fri 4/27/07		Medhavi Gudivada
IPRO Deliverables	**Fri 2/2/07**	**Thu 4/26/07**		
Project Plan	Fri 2/2/07	Fri 2/16/07		Sean Callahan,Anthony Ferrese,Maje Nazim
Midterm Report	Mon 2/19/07	Fri 3/23/07	25	Medhavi Gudivada,Jason Devgun,Alok Patel,Renen Manuntag
Website	Wed 3/14/07	Fri 4/20/07		Sean Callahan,Christie Ferraro,Bhavin Patel
Exhibit/Poster	Wed 4/4/07	Fri 4/20/07		Christie Ferraro,Alok Patel,Renen Manuntag,Neil Mashruwala,Dukmin Park
Abstract	Wed 4/11/07	Fri 4/20/07		Evervone



4.0 Updated Task Assignments and Designation of Roles

The objective of this project was to implement and improve upon the research done by the previous semester group by developing a prototype. The plan for the project involves extracting interstitial fluid from the pigskin using the procedure of vacuum and ultrasound. The process of reverse iontophoresis would aid the extraction process and measure the glucose levels. This process is reversed in order to pump insulin into the body via transdermal infusion. The vacuum and ultrasound will open the pores and iontophoresis would help in pumping insulin inside the body. There has not been any significant change in the plan except for the techniques to be used in determining the glucose levels in the body. The prototype group has been divided into two sub units, with one working on the process of electrical impedance and the other on optical absorbance spectroscopy. Upon testing both the procedures, the decision would be made on the best process in a short period. In addition, the initial testing of extraction was performed on the old prototype in order test the efficiency of the procedure. This would be replicated on a second device, which is being developed by a sub unit of the prototype group. The

organization of the three main sub groups has been listed as under along with the team members responsible for the remaining tasks for the semester.

1) Prototype:

Extraction of interstitial fluid (ISF) (Anthony Ferrese, Dumin Park, Medhavi Gudivada)

- Identify the appropriate gasket required for effective extraction from pig skin by testing
- Test speakers for successful ultrasonic emittance with and without a conductive gasket
- Test the old prototype for extraction of ISF from pig skin

Glucose measurement

Reverse Iontophoresis (Jason Devgun, Nathaniel Schuh)

- Use glucose concentrations (5-10 microliters) in some form of buffer and then measure electrical impedance.
- Use saline solution to test Reverse Iontophoresis.
- Use normal solution of (100mg/dL) ~5.5millimolar for lab testing.
- Pathological level—400mg/dL~22.2mM
- Develop a sensor that measures electrical impedance at a certain resonant frequency

Optical Absorbance Spectroscopy (Neil Mashruwala, Alok Patel)

- Obtain a standard curve for glucose in Krebb's Ringer solution
- Research on how to incorporate miniaturized IR sensors into the device to measure glucose
- Incorporate this sensor into the device

Assembly of a second device [Dukmin Park, Renen Martung, Bhavin Patel]

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- Test the second vacuum system
- Incorporate the new gasket and other supplies into the device

Insulin delivery [Bhavin Patel, Neil Mashruwala, Alok Patel]

- It is similar and reverse to the extraction of ISF, work simultaneously on it.

2) Materials & Research

Materials (Sean Callahan, Medhavi Gudivada)

- Find alternative conducting rings with an equivalent derometer in case the current one does not work
- Research miniaturized IR sensors available in the market

Research (Jason Devgun, Nataniel Schuh)

- Research resonant frequencies listed for interstitial fluid with various concentrations of glucose levels and their corresponding blood glucose levels.
- Research on the NMR process of measurement for glucose

. **Safety** (Nataniel Schuh, Medhavi Gudivada)
- It is being looked upon simultaneously with the techniques and different procedures have different risks associated with it.
- Research optimum ultrasound levels for its application on the skin.

Patent (Christie Ferraro, Maje Nazim, Nathaniel Schuh)
- Identify prospective scientific organizations, start up companies that could fund the project
- . Research private sponsorship

• Research on the feasibility of the current prototype for a patent

IPRO Deliverables

• The tasks have been divided among the members based on their skill sets.

Deliverable	**Responsible Members**
Exhibit/Poster	Christie Ferraro, Alok Patel, Dukmin Park, Renen Martung & Neil Mashruwala
Website	Sean Callahan, Christie Ferraro, Bhavin Patel
Abstract	Everyone
Presentation	Maje Nazim, Jason Devgun, Christie Ferraro, Sean Callahan
Final Report	Nataniel Schuh, Medhavi Gudivada & Dukmin Park

5.0 Barriers and Obstacles

One of the barriers that the IPRO team has encountered was a lack of funds to file a patent proposal. In order to resolve this obstacle, grant proposals would be needed but that served as another obstacle since grant proposals would take too long to obtain. One of the barriers that the team has come by is the time constraint. A project as ambitious as this one would require more than 13 weeks to complete. A way around this is to get as much done in the present semester so that the succeeding semesters will be able to pick where this team has left off and hopefully file a patent. The cost of lab equipment and components for the actual device is a large factor that is hindering this IPRO from making progress. A larger budget is indicated for this IPRO so that efficient equipment can be obtained as well as high-quality parts for the prototype.

The research group for this IPRO encountered obstacles such as a lack of published research on impedence spectroscopy with regards to glucose and measuring glucose concentration. There was also a lack of a sufficient device to measure the

electrical impedance of glucose solutions or simulated interstitial fluid. Despite continued efforts in seeking professional help, another obstacle was a lack of help that could guide us in the implications and feasibility of creating a device to measure the impedance of glucose solutions. Help was sought out in the field of Electrical Engineering, but no solid response was obtained leaving the IPRO research group to seek other resources. The research group also reported that a lack of a Vector Network Analyzer at Argonne Laboratories was an obstacle.

The obstacles that the prototype group encountered were a lack of lab space, obtaining the parts from past IPRO team members and new additional parts for the prototype. The search for EMI conductor rings became a barrier when the company that the prototype group was looking up was only based in the United Kingdom. Distributors based in the Unites States were sought out and eventually found. Direct retrieval of old parts from the previous IPRO was done so that the current prototype group could work on optimizing the device. After contacting the respective people namely Dr. Promila Dhar and Dr. Connie Hall, the prototype group was given access to the Biomedical Engineering lab to test the prototype on pig-skin.