Final Report Fall 2006
IPRO 308: Developing an Artificial Pancreas

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Purpose of project:

The objective of this Interprofessional Project is to develop an artificial pancreas, which will not only incorporate a non-invasive blood glucose monitoring technique, but also a non-invasive insulin delivery method. Currently, invasive techniques, such as venepuncture, are used to monitor blood glucose levels and deliver insulin in patients. Unfortunately, because diabetic patients must constantly monitor their blood sugar levels and administer insulin, venepuncture is an undesirable procedure, because it requires multiple needle punctures a day. Not surprisingly, this process is uncomfortable for patients, so there is a need for new technology. Our purpose was to develop a non-invasive method that both measures glucose level and uses an automated system to deliver the appropriate amount of insulin, non-invasively. The three main features of a desirable artificial pancreas that the team focused on this semester were to make it non-invasive, automated and user-friendly so as to give diabetic patients more flexibility and freedom.

Project background:

Diabetes mellitus is a group of devastating metabolic diseases caused by insufficient insulin synthesis, increased insulin destruction or ineffective insulin action. Its metabolic effects are due to increased blood glucose levels. The metabolic imbalances that occur have serious, if not life-threatening, consequences. In insulin-dependent diabetes mellitus (IDDM), also called type 1 diabetes, low amounts (if any) of insulin are secreted, because the beta-cells of the pancreas have been destroyed (endocrine disease). Because IDDM usually occurs before the age of 20, it has been referred to as juvenile-onset diabetes. Non-insulin-dependent diabetes mellitus (NIDDM), also called type 2 or adult-onset diabetes, is caused by the insensitivity of target tissues to insulin (metabolic disease). Digestion of food begins in the mouth and continues in stomach. The food then travels to the intestines, where the glucose from the food is absorbed into the bloodstream. Depending on food content, the amount of glucose in the bloodstream varies. This raised blood glucose level stimulates the pancreas to secrete a specific amount of insulin and other hormones to maintain a normal glucose level.

Overview of design:

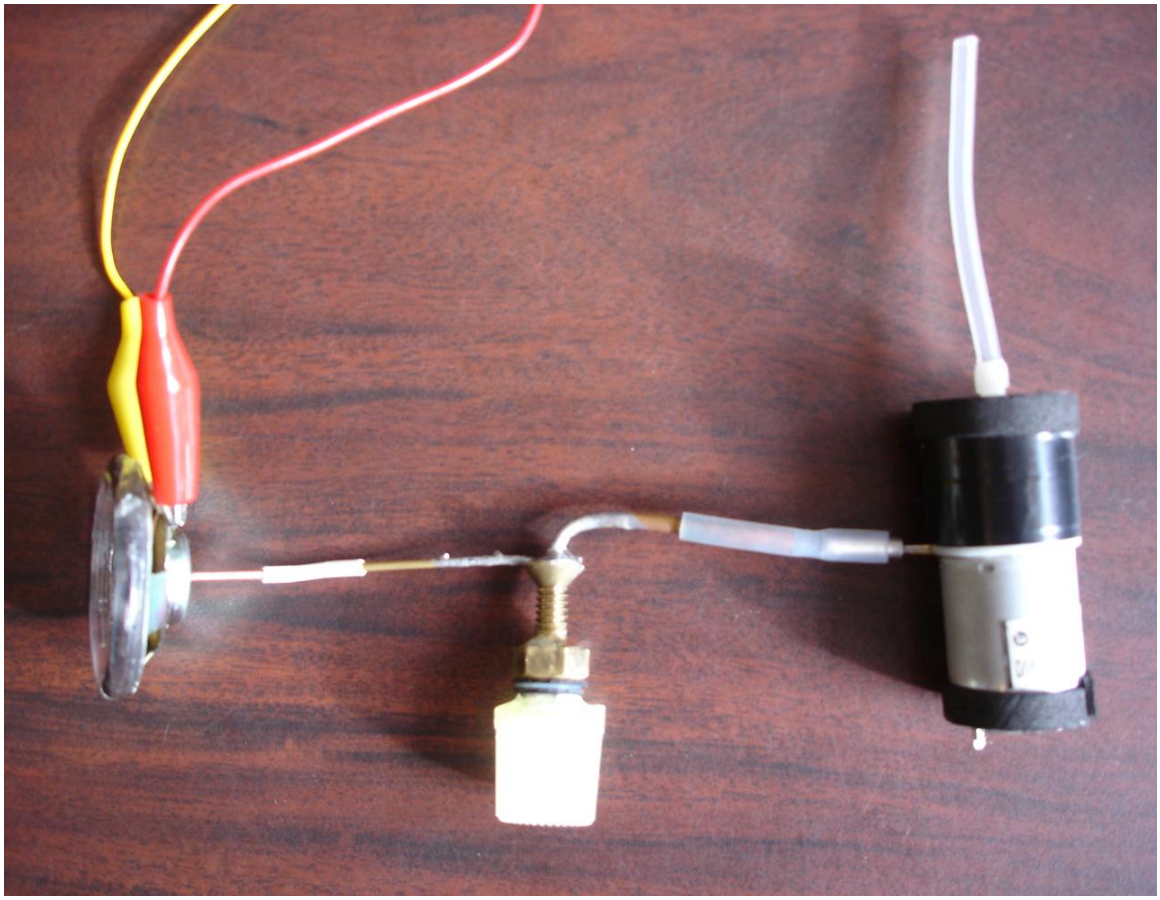

Image 1: Prototype Developed

Extraction:

The first step to developing the device is extraction of interstitial fluid to test the bloodglucose level. The project team reviewed the non-invasive blood glucose monitor model developed by several previous semesters' IPRO teams and decided to base the artificial pancreas on this model. Several technologies are being incorporated into the device; mainly, iontophoresis and ultrasound. The tube to extract fluid is attached to a speaker, which will produce the ultrasound waves to vibrate the skin and open up the pores. The vacuum will be used simultaneously with iontophoresis to extract the interstitial fluid. For iontophoresis the speaker is coated with a conductive material and a conductive contact is made between the skin and the frame of the speaker. Then an electric potential is applied to both poles. Impedance Spectroscopy will be used in the final product to determine the blood glucose level. Radio wave impedance spectroscopy measures how changes in blood composition affect the impedance pattern of the skin and underlying tissue.

Delivery:

The second part of the artificial pancreas is insulin delivery, which is also non-invasive. The main idea behind delivery of insulin into the body is to reverse the extraction method so it moves the fluid in the opposite direction. Instead of a vacuum, pressure will be applied for delivery via the same pump through the pressure port. The speaker is still used to create ultrasound in order to open up the pores in the skin. The charges on the speaker are reversed to produce iontophoresis in the opposite direction and accelerate the diffusion of insulin into the body. A pseudo code has been developed that will allow to control the amount and frequency of insulin injections depending glucose measurements. By frequent blood glucose measurements, the insulin pump will provide the necessary amount of insulin on-demand and keep the blood glucose levels close to normal.

Findings:

It has been shown by the prototype group of the IPRO team that ultrasound and vacuum are capable of extracting interstitial fluid. Since iontophoresis has not been included in the model yet, it cannot be tested. Also, the presence of ultrasound has been confirmed by detecting a magnetic field with the help of an oscilloscope. The delivery of insulin has not been tested so no validations have been obtained on the design, except for research found in literature. Work was also done on the aesthetics of the design and a tentative model as shown in image 2 was created.

Image 2: The Artificial Pancreas

Research methodology:

Our main methodology in reaching our goals was based on team-work. In the beginning of the semester we divided ourselves into some groups involving research and some involving incorporating the research in making our prototype. We did this based on the methodology the previous IPROs used in their research on non-invasive glucose monitoring techniques. Each group cooperatively carried on the tasks assigned to them. In this way we obtained all the information that were necessary towards building our prototype. These topics considered for information included the advantages of choosing iontophoresis for our insulin delivery scheme over other noninvasive methods, the extent of skin permeability under ultrasound, ionic properties of glucose, dimers and polymers that insulin naturally converts into, properties of interstitial fluids and how it can be used to determine glucose concentration in blood, as well as using impedance spectroscopy as a methodof measuring glucose concentration in interstitial fluid. After evaluating the advantages and disadvantages of the researched topics, we decided to use ultrasound and a two-way vacuum system to extract interstitial fluid, and impedance spectroscopy to determine blood glucose concentration. In the insulin delivery system, we decided to use iontophoresis in introducing insulin into the blood stream non-invasively. During the process of creating our prototype, we discovered new ways in making our system more unique and at the same time very convenient. We thus, came up with the concept of a continuous insulin delivery system that works solely on the glucose levels just like a real pancreas does without any external monitoring required.

Team organization & Assignments:

Our IPRO group regularly divided itself into different groups based on the needs of the IPRO throughout the course of the semester. There were different groups assigned every time there was a new task at hand. In this way everyone in the class got a chance to get to know all the other students in the IPRO. All the research and the work on the prototype were conducted by the groups individually and subsequently presented in class.

The following is a listing of the general groups our IPRO team was divided into:
Research Group: This group was responsible for gathering as much information as possible on the ways to extract glucose using reverse iontophoresis, the effects of application of ultrasound on the skin, ways to insert insulin into the blood stream using reverse iontophoresis, using impedance spectroscopy to measure glucose concentration in the interstitial fluid, how glucose concentrations in the interstitial fluid corresponds to glucose concentrations in the blood and other such topics which helped put together our prototype.
Market Analysis: This group was responsible for studying the different types of insulin pumps and glucose monitoring systems that are available in the market, which ones are the most successful and why. Based on these results and assessing the advantages and disadvantages of all the pumps, we determined how we could make our artificial pancreas create a revolution in the lives of diabetic patients all over the world.
Device design: This group was responsible for incorporating all the information obtained by the groups doing research and market analysis into novel ways of creating a

continuous all-in-one glucose monitoring and insulin delivery system, which is truly an Artificial Pancreas.

Obstacles and barriers:

As with any new project, our group was faced with a multitude of problems. The first obstacle our group tackled was that of deciding what needed to be researched and how it was going to be divided amongst the members. Many small research groups were formed along with a prototype group. Team members took turns in leadership positions with each group created. New ideas were suggested throughout the research process. Many of these ideas were investigated and depending on how useful or feasible the idea, were integrated into our final product. Funding also posed a major concern. Our research and prototype is limited due to lack of funds and lab space. The final issue the team faced dealt with what could be disclosed during IPRO Day that would not jeopardize a potential patent.

Recommended next steps:

The overall goal of the team is to eventually create a non-invasive artificial pancreas that can be patented, produced, and marketed. To help achieve this goal, our team plans to enter the biomedical engineering innovation contest. Future members of this IPRO will need to complete a working prototype and use lab time for testing. They will also need to apply for a patent in order to protect the current research and ideas. Eventually, if created, the non-invasive insulin pump combined with a non-invasive glucose monitoring system could potentially replace current insulin pumps.

References and Resources:

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Iontophoretic topical and transdermal drug delivery

By, Ajay Banga

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By, Seiji Tokumoto[a, b], Naruhito Higo[b] and Kenji Sugibayashi[a,] (http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T7W-4KC2J8T-6&_coverDate=07%2F08%2F2006&_alid=469391296&_rdoc=1&_fmt=&_orig=search&_qd=1&_cdi=5069&_sort=d&view=c&_acct=C000038758&_version=1&_urlVersion=0&_userid=694905&md5=365a30ea08867a267de55bf65dd5aadf)

Dielectric spectroscopy study of specific glucose influence on human erythrocyte membranes

By, Yoshihito Hayashi1, Leonid Livshits1, Andreas Caduff2 and Yuri Feldman

Transdermal iontophoretic delivery of bovine insulin and monomeric human insulin analogue

By, N. Kanikkannan[*], J. Singh[1] and P. Ramarao[2]

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Analysis of ultrasonically extracted interstitial fluid as a predictor of blood glucose leveles

By, Samir Mitrogi..
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