



# IPRO 308: Developing an Artificial Pancreas

**Design Description:** (Current Semester)

**Mission Statement:** IPRO 308 is dedicated to developing a closed-loop method of addressing type I diabetes involving a fully automated means of measuring glucose levels in the patient, determining the adequate insulin requirement and administering the dose, not only with minimal input and effort from the patient, but completely non-invasively and with no discomfort.

- Ultrasound emitter upsets lipid bilayer of stratum corneum and breaks membrane enlarging microchannels
- Microchannels allow for the passage of interstitial fluid (ISF)
- Applied iontophoresis increases flow rate of extraction, reverse iontophoresis increases administration
- Vacuum applied to the area pulls the ISF from the microchannels and collects into a trap
- Impedance of the collected ISF is calculated through a sensor and concentration determined
- Administration of Insulin would use pressure and reverse iontophoresis

## Background

**Diabetes (Diabetes Mellitus or Diabetes Insipidus):** a disease in which the body is unable to produce or respond to insulin hormone in a normal way.

- **Type 1:** Deficient Insulin Production
- **Type 2:** Insulin Resistance
- **Gestational diabetes:** women who have high blood sugar (glucose) levels during pregnancy

21 million Americans are currently battling diabetes and 54 million adults and children in the U.S. are on the verge of being diagnosed with diabetes. The United States spend approximately 132 billion on diabetes-related issues per year. Diabetes alone represents 11% of the U.S. health care expenditure. Fasting Plasma Glucose Test (FPG) or an Oral Glucose Tolerance Test (OGTT) is used to determine diabetes. With the FPG test, a fasting blood glucose level between 100 and 125 mg/dl signals pre-diabetes. A person with a fasting blood glucose level of 126 mg/dl or higher has diabetes.

**Fields of research in diabetes** (by American Diabetes Association):

- invention of the first glucose meter
- invention of the portable insulin pump
- oral diabetes medicines to help control blood sugar levels in type 2 diabetes
- transplantation of new insulin-producing cells from a donor pancreas
- blood glucose control to prevent eye, kidney and nerve disease

**Current research in diabetes:**

- understanding the autoimmune process behind type 1 diabetes in children
- replacement of beta cells for the treatment of type 1 diabetes
- the development of programmable implantable insulin pumps
- the discovery of a protein related to food intake and weight control
- understanding the incidence of ulcers, infections, peripheral vascular disease and amputations in diabetic patients

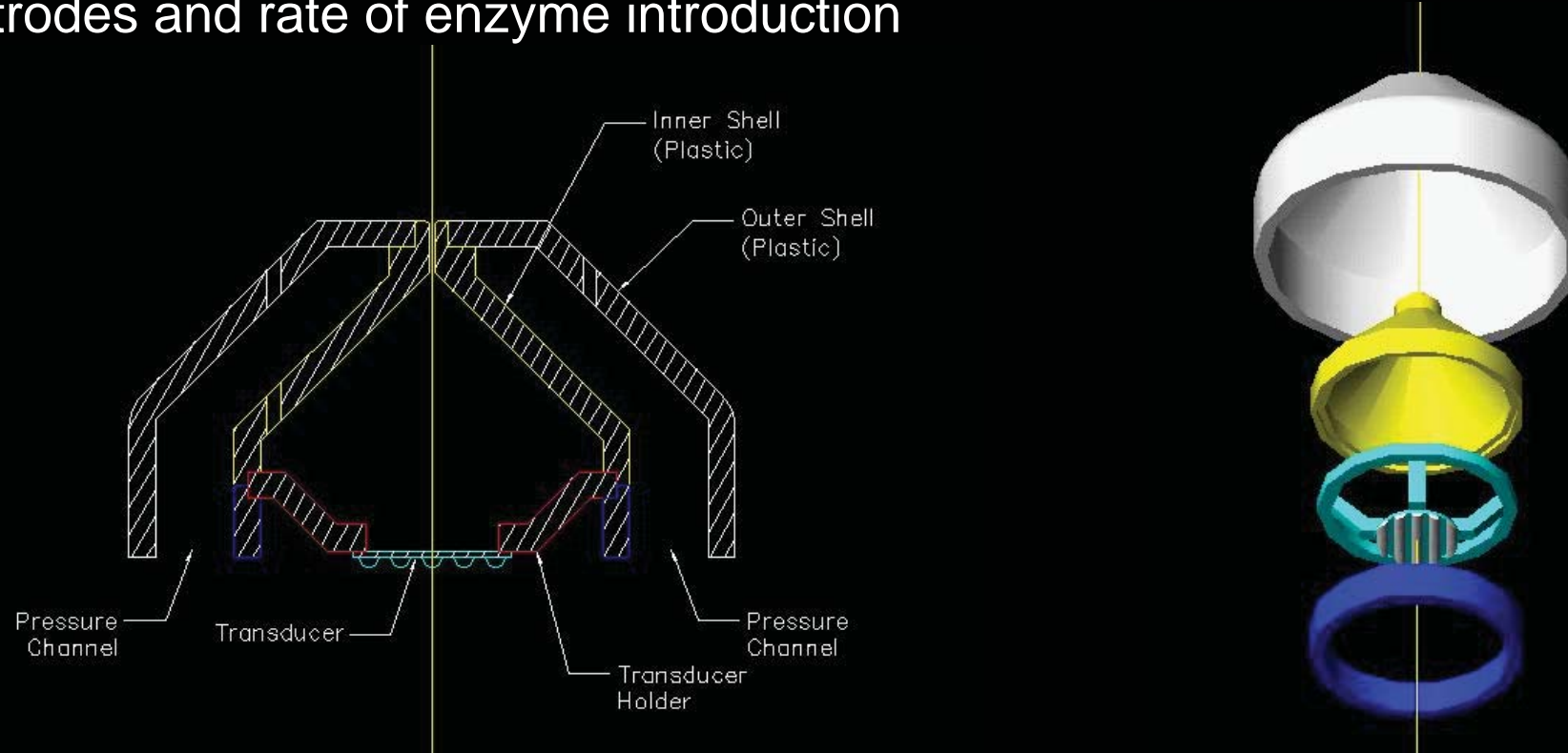
## What Did We Learn From The Previous Semester?

**Closed Loop subgroup**

Used prototype designed by Fall 2007 team, performed experiments on porcine skin, unable to extract any fluid, had tried to perform sonophoresis with vacuum, proposed a new model for Fall 2008 with enhancements

**Measurement subgroup**

Used Electrical Impedance, capacitor with interstitial fluid as dielectric, reliable impedance measurements impossible as solution got ionized, try experiment after plating capacitor with a non-ionizing agent, used Electrochemical sensory, used glucose oxidase to convert glucose to H<sub>2</sub>O<sub>2</sub>, measure the voltage spike induced by the current, no positive correlation between glucose concentration and the voltage spikes, integrate newer technologies to decrease variance caused by separation of electrodes and rate of enzyme introduction



## Closed-Loop Technologies

**Approach:**

Design separate devices for the two main functions during extraction process

- Low frequency ultrasound device (for pore enlargement)
- Vacuum pressure device (for extraction of interstitial fluid)

Verify previous group's result by testing the effect of vacuum pressure, with and without low frequency ultrasound, on pigskin during the extraction process.

Design a working prototype that incorporates both functions.

Test working Prototype on live rat

**Results:**

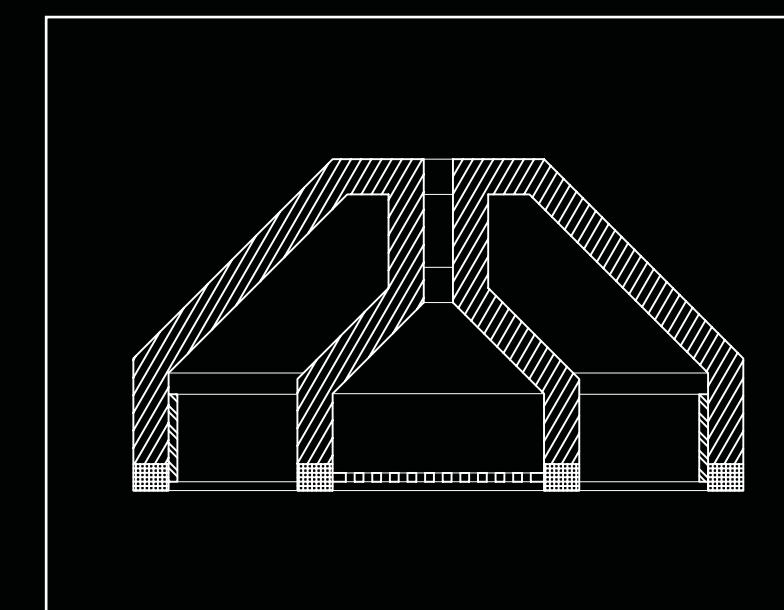
Early experiments showed promise:

Green spots seen on the surface of the skin after application of ultrasound and vacuum. Increasing time of exposure to ultrasound and vacuum seemed to increase the amount of coloration seen on the surface of the skin.

**Further investigation and testing proved our results to be inaccurate:**

Because the test tissue was no longer attached to its donor organism, the tissue became dry with increased exposure to atmospheric conditions. This caused the tissue to become translucent which gave the appearance that with increased testing time, greater amounts of fluid were being drawn to the surface. In fact fluid was being viewed through the surface of the tissue.

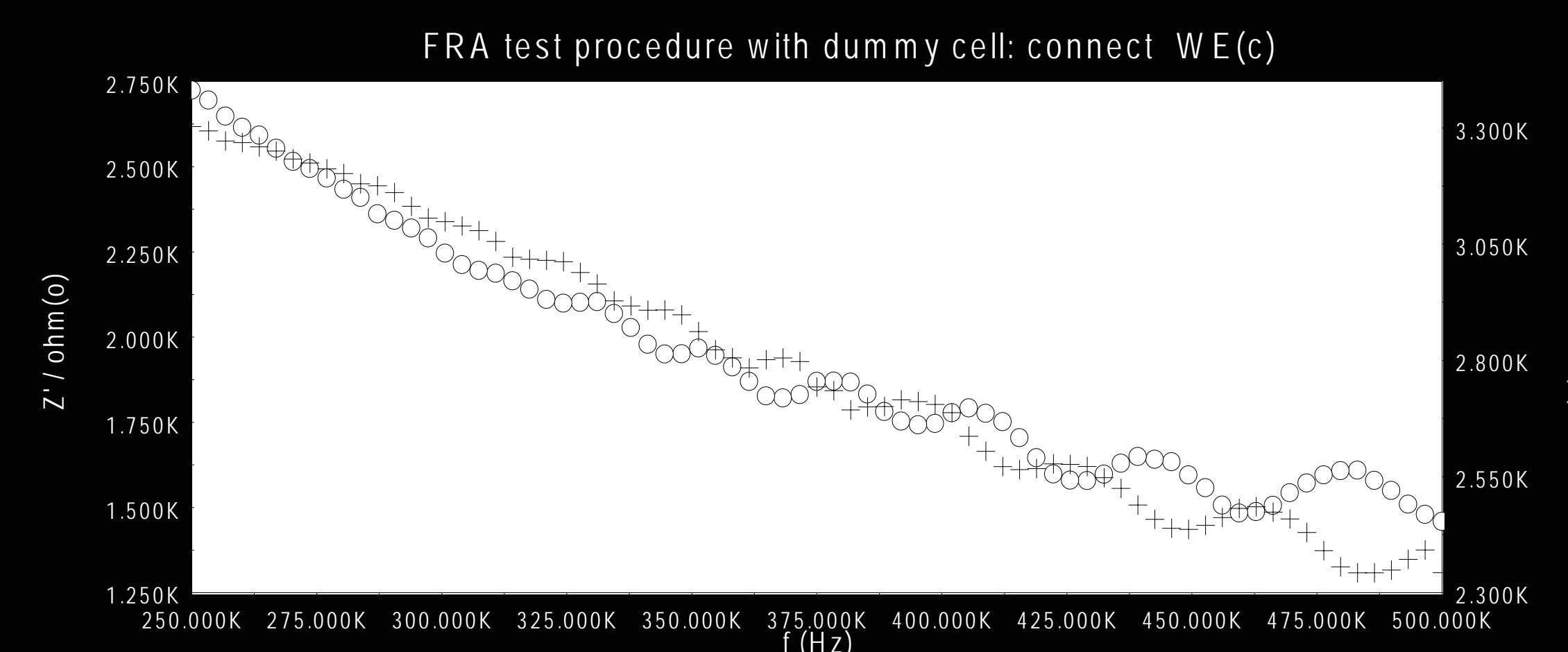
Variations in the test procedures also uncovered that results varied based on which vacuum prototype we used and were a direct result of ultrasound application



## Measurement Group

**Impedance Spectroscopy**

- Using the resonant frequency of glucose, measure the concentration of glucose from the magnitude of the dip in imaginary impedance at the resonant frequency
- Last semester's IPRO scanned from 1-100 KHz (the max output of the machine they used) and did not find a resonant frequency.
- This semester we scanned from 100 KHz to 1MHz. Frequencies larger than 500 KHz produce inconsistent results probably due to changing internal inductance.



The results we have thus far do not indicate a relationship between concentration of glucose and any of the other variables tested including: real, imaginary, and total impedance, phase shift, and locations/magnitudes of peaks.

**Other options**

**Nuclear Magnetic Resonance:**

NMR tests a molecule by using a constant magnetic field and changing the frequencies, or by using an electromagnet and changing the strength of the magnetic field.

1. The accuracy of the NMR technique is proportional to the strength of the magnetic field, and since a very strong magnetic field isn't practical in a mobile glucose monitor, we would need a way to greatly reduce, and ideally eliminate, outside interference during measurement

**Symphony™ tCGM System:**

A system designed for the non-invasive extraction and measurement of glucose. Some of the drawbacks of this system that we would like to avoid are:

1. The sensor they use to measure glucose concentration is "single use." By using either NMR or impedance spectroscopy we would eliminate the need for disposable components.
2. The measurement device would need to be applied to an area after using their ultrasound device on the area; our device would incorporate the two together.

## Research

**Technologies:**

Further research in the field of non-invasive glucose measurement and administration has revealed new technologies that can be tested and used in such a prototype. They are as follows.

**Micro needles** - Create skin pores without causing any pain

**Photo acoustics** - Measurement of glucose using light rays

**Near Infra-red spectroscopy** - Glucose measurement using IR rays

**Electro- enzymatic sensor** - Glucose measurement from tears using contact lens

**Closed Loop Technologies:**

**Mechanical Sieves:**

- Microfiltration used to simulate pore openings.
- Can be purchased in various sizes to account for ranges in ultrasound effectiveness.

**Personal Ultrasound Devices:**

- Hand held devices that can be used to administer ultrasonic vibration.
- Operate at more effective frequencies than standard audio speakers.

**Dual Chamber Vacuum System:**

- Would have an outer ring of constant vacuum. This would act to keep the device on the surface of the skin while Insulin is administered through pressure in the inner circle.

## What Does The Future Hold In Store For This IPRO?

**Closed-Loop Group:**

- Use of mechanical sieves to produce accurate flow rate, sonicated pore diameter and pressure gradient data
- Data to be used to justify rat testing
- Results to come from testing on living being

**Measurement Group:**

- Further investigation into resonant frequency of glucose
- Exploration of other technologies including:
  - Electronic "sniffing"
  - Nuclear Magnetic Resonance
  - Near Infrared Spectroscopy

**Research Group:**

- Continue providing the necessary information requested by the other sub-groups while also providing self-initiated pertinent information