Control Algorithm and Thread-Based Sensors for the Artificial Pancreas

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Introduction

Abstract: Diabetes is a growing disease that affects 415 million people worldwide and can cause lifelong concern. The disease results from a lack of insulin-producing beta-cells, due to autoimmune destruction (type 1), or by lack of sensitivity to insulin and insulin deficiency (type 2).[1] While there is currently no cure, existing treatments prove to be physically invasive and require attention and regulation by the patient. Recent breakthroughs in stem-cell engineering are working towards a solution that would provide patients with a more autonomous approach to their glucose regulation. This project focuses on two components within the automatization process, including a control algorithm for insulin secretion regulation and thread-based sensors for glucose measurements. Thread-based sensors harbor many of the desired qualities for a glucose measurement tool. The thread design allows for flexibility and high surface area which improves signal strength. Their production is inexpensive and allows for point-of-care measurements with quick and accurate results. Each with the goal of allowing for the regulation of blood glucose with minimal attention from the patient.

Objectives:

- Using MATLAB, explore and develop a control algorithm (PID) for the regulation of insulin secretion in response to blood glucose levels.
- Develop a flexible and accurate measurement tool to be used for determining interstitial fluid glucose levels.

Methods: Control Algorithm

Background:

- Goal: Determine the correct amount of insulin to deliver to a patient for a given blood glucose level.
- Using a PID (proportional - integral - derivative) feedback design, the control algorithm uses an initial glucose level as input, to then calculate its output value (secretion rate of insulin).
  - The frequency of the glucose measurement can be set which will affect how many times the algorithm iterates
- The algorithm implements a series of 6 differential equations upgraded from Bergman's minimal model.[2]
- The first three account for glucose kinetics, insulin in plasma and insulin in intercellular space. The remaining three are associated with certain delays of the insulin effect on the hepatic glucose production.[3]
- With inputs from the user such as time span, basal glucose, and meal ingestion, these equations govern the behavior of the glucose-insulin system The control loop used in this project is implemented in MATLAB.[4]

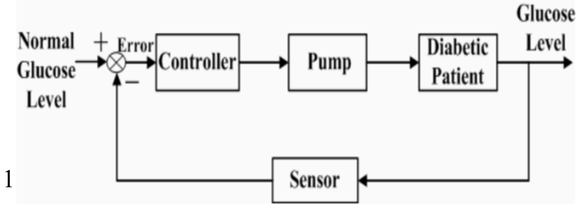


Figure 1

Results: Control Algorithm

Figure 2 shows the stimulation output from a trial run using the control algorithm. The top chart displays blood glucose level, interstitial fluid level and a baseline reference. The middle chart shows active insulin effect representing the insulin held in a remote compartment to account for time delay associated with insulin absorption. The bottom chart is the blood insulin level.

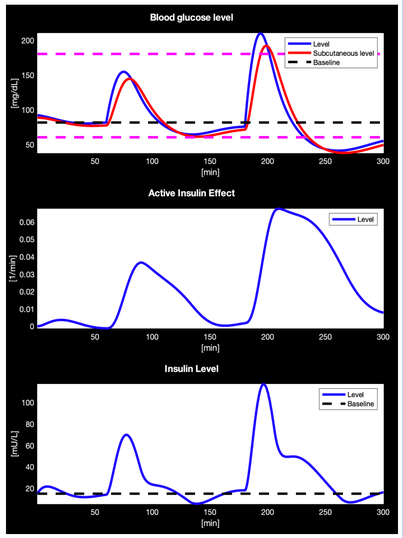


Figure 2

- The graphs display successful control of the glucose level within a virtual type 1 patient.
- The matching spikes in insulin level in sync with rising glucose levels show that with increasing glucose, the necessary amount of insulin was distributed.
- The accurate automatic control of glucose levels allows for minimal interaction from the patient.

Methods: Thread-Based Glucose Sensor

Background: Thread-based sensors for this project work off of a 3-electrode system shown in figure 3. During electrochemical glucose sensing, glucose is decomposed catalytically and the H_2O_2 generated is oxidized at the electrode surface, providing a measurable current. This current is what is is seen in figure 7.

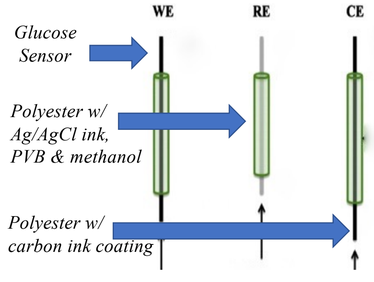
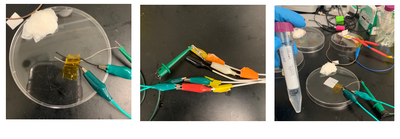


Figure 3 [5]

Experimental Procedure:

1. Prepare glucose sensor (detailed procedure available).
2. Set up glucose sensor with 3 electrodes (cannot be touching each other) each connected to potentiostat for measurements (Figures 4 and 5).
3. Deposit 100 µl of desired glucose solution onto filter paper covering sensor (Figure 6).
4. Calibrate sensor allowing filter paper with solution to sit for 30 minutes before first reading. From then on, allow 2 minutes of calibration between measurements.
5. Observe final current reading from potentiostat ~ 200 seconds (Figure 7).



From left to right: Figures 4-7

Results: Thread-Based Glucose Sensor

Five different glucose solutions were tested, varying in concentration from 2mM/L to 10mM/L. Each concentration was tested twice as shown in the graph to the right.

- Results exhibited a linear trend, showing increasing current with glucose concentration, which was the desired output.
- Concentrations of micro-molar were tested and similar results occurred.
- With a linear trend glucose concentrations can be confidently measured.
- Each sensor can have a two point calibration before use to account for inconsistencies in fabrication.

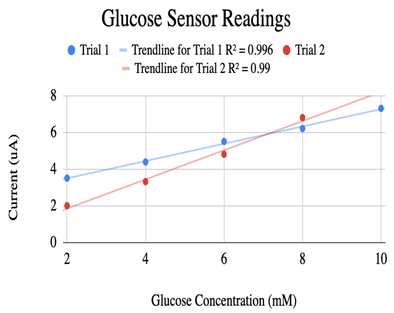


Figure 8

Conclusions

Conclusion: The use of a control algorithm has shown to be successful in being able to control glucose levels by calculating the correct rate of insulin infusion. Most importantly it has proven to be versatile through rapid glucose level changes caused by meal intake, and work towards automatized control of blood glucose. The thread-based sensors displayed their ability to not only have flexibility for medical application, but also give accurate glucose readings across concentrations even to the micro-molar.

Future Work: With regards to this project, the next steps include testing the glucose sensor in the interstitial fluid of mice and connecting it to the control algorithm to asses real-time performance. If successful, the control algorithm and thread-based glucose sensor form two important components of a possible fully automated diabetes treatment. Optically controlled beta-cells have been engineered to produce insulin upon light stimulation and could be used in sync to lead the path to a functioning alternative to current diabetes treatments.

Acknowledgements

A special thanks to Professor Tzanakakis, Professor Lee, Professor Ryder and PhD candidate Rachel Owyeung for their guidance. This project was supported by the NSF and Tufts Chemical and Biological engineering department.

NSF 1560388

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