Enzymatic Batteries for Implantable Medical Devices: Focus on Glucose Monitoring

[1]D. Galindo, [1]N. Gebriel, [1]N. Kao, [1]H. Saluja, [1]D. Strangman

Abstract— **With medical device innovation being ever so prominent than ever, the need for small form factor power supplies increases. Beyond the lithium-ion battery, new battery models have been made to provide an alternative for situations where lithium-ion batteries are too large to have within the device and to provide a more eco-friendly alternative. Some recent technologies, such as the bio battery, provide a means to create electrical power at a micro scale using organic compounds such as carbohydrates. The sugar battery, for example, breaks down units of glucose at the anode of the device and produces electrical flow through a substrate to the cathode. To quantify the glucose flow of the system in accordance with the regulation of glucose in the body, an ODE model based on chemical kinetics for the battery consumption of glucose was made and tested to determine a necessary feedback system to keep stable voltage at varying blood sugar levels. By implementing this fluctuation in the Simulink model, it was possible to determine the needs of glucose in the system and to test for its viability to rely on the body's sugar levels. Glucose testing showed that it is possible to run batteries off of the sugar alone but needs further analysis to make it efficient enough to perform in trials without detriment to patients.**

I. Introduction

One of the most prominent features in medical devices is the need for reliable and long-lasting power sources that need minimal maintenance. While traditional alkaline and lithium-ion batteries have been used for medical devices, they pose challenges and limitations in terms of reliability and long-term utilization [1]. Traditional alkaline batteries tend to need recharging or replacement after a short duration of use, and have a negative environmental impact. Additionally, traditional batteries are often large in size, and can pose as a significant design constraint in the development of implantable medical devices. Similarly, while lithium ion batteries are a better alternative, they also tend to lose their energy capacity overtime resulting in a gradual decline in performance. As a result, this project will analyze the ODE model to explore bio-batteries as a viable alternative power source for implantable medical devices, especially with varying glucose concentrations occurring as a natural process in the body.

II. Background

The industry of creating enzymatic sugar batteries was catalyzed in 2007 with Sony for their prototype sugar battery that proved to effectively be powered by a renewable energy source of glucose[2]. Compared to lithium -ion and alkaline batteries, sugar enzymatic batteries act as a more reliable and efficient energy source by using the release of electrons from naturally occurring chemical reactions in the body to produce energy[1],[3],[4]. the process of generating electricity from sugar batteries is through the oxidation of sugar molecules(in most cases glucose) to gluconic acid to release electrons. From this point, studies typically diverge in creating further pathways to create recycling mechanics in the battery or to further cascade oxidative pathways[1],[3], [4]. The oxidations release electrons in the membrane of the battery that flow from anode to cathode and drive an electrical potential that can power devices. Due to the field being young, there has not been many applications of the sugar battery beyond ideal conditions of an outside fuel source. Therefore, testing within the confines of bodily conditions has not been explored enough to make it a viable option. In the scope of this project, the bio-batteries would use the consistent flow of electrons from organic compounds to create a self-sustaining power source. This would be a cyclic process and thus having continuous monitoring of glucose levels allows for real time data to be provided to the user.

III. Control System Model

A. Assumptions

This model will be based off of a patient within the typical glycemic ranges for initial testing. This battery will be assumed to be able to fit within the body and so has a small volume of $6cm^3$. The rate at which glucose flows into the battery is dominated by the influx system that will be created rather than the natural flow rate from non-convective diffusion. It is also assumed that the oxygen in the system is constant in the system due to the small amount of oxygen required for oxidation and the supply of oxygen that can be injected into the membrane and supplied by the body as well.

B. System Boundaries

The system will be primarily based within the battery itself, with only the glucose flowing in from the body and the outflow of voltage being the externals of the system. However, both the glucose and the voltage do not inherently alter when they enter or leave the system so we can determine the system as closed from outside perturbations.

C. Operational Constraints

The operational configuration of the proposed system is primarily encapsulated within the battery, where glucose serves as the input from the body, and voltage constitutes the output. The system provides a controlled environment, which facilitates the analysis between glucose consumption and voltage generation.

[1]. Department of Bioengineering, Jacobs School of Engineering, UC San Diego, La Jolla, CA 92093, USA.

D. Goals

The main goal of this system is to create a dynamic response mechanism for a sugar battery to increase glucose flow as a response to lack of voltage. Sugar batteries rely on constant supplies of glucose or the natural diffusion of glucose into the battery so this model intends to force glucose flow into the battery as a function of voltage error. This will be done by measuring voltage generated as a function of glucose influx into the battery against a target voltage. This model also furthers the ideas of using bio batteries for implants by interpreting glucose flow into the battery and how much glucose is required to reach target voltage value, implying a possibility of having the bio-batteries being fueled by glucose in the blood. Therefore, the global goal of this study is to comprehensively analyze a bio-battery that not only converts glucose into electrical energy but also optimally adjusts its glucose intake to maintain or attain specific voltage levels that are dependent on the required power.

IV. Mathematical model

A. Equations

The basis of the battery voltage generation originates from the chemical reactions of glucose to gluconolactone to produce electrons. Therefore, the battery model is centered around the kinetics of this particular redox reaction. Electron generation is measured as a function of gluconolactone by converting the concentration of gluconolactone as molecules of electrons. This system is modeled from Eq. 1 and the model response can be seen in Eq. 2-4 with parameters of the system listed in table 1[5]. G is the concentration of glucose in the system and P is the concentration of gluconolactone.

$$2C_6H_{12}O_6 + O_2 \leftrightarrow 2C_6H_{12}O_7 + 2e^- \quad \text{(Eq. 1)}$$

$$\frac{dG}{dt} = \frac{1}{K}f(t) - 2k_1[O_2][G]^2 + 2k_2[P]^2 \quad \text{(Eq. 2)}$$

$$\frac{dP}{dt} = -2k_2[P]^2 + 2k_1[O_2][G]^2 \quad \text{(Eq. 3)}$$

$$V(t) = K * [P] \quad \text{(Eq. 4)}$$

$$f(t) = (T - K * V(t)) \quad \text{(Eq. 5)}$$

Where *V(t)* represents the voltage created from the flow of electrons, and *f(t)* represents the forcing function of glucose flow from the difference between the target voltage *(T)* and the measured voltage. Our target voltage was chosen from comparison to other batteries in the market for implants[6]. As glucose enters the system it is simultaneously oxidized to produce gluconolactone and two electrons. However, the oxidation can be reversed so considering the reverse reaction playing a role in voltage development is crucial. The model is nonlinear due to the coefficients of the reagents and products so it is necessary to linearize around the steady-state points of both glucose and gluconolactone. Below shows the linearization of the rates equations.

$$\frac{d\widehat{G}}{dt} = \frac{1}{K}\widehat{f}(t) - \alpha[\widehat{G}] + \beta[\widehat{P}] \quad \text{(Eq. 6)}$$

$$\frac{d\widehat{P}}{dt} = \alpha[\widehat{G}] - \beta[\widehat{P}] \quad \text{(Eq. 7)}$$

$$\alpha = 4k_1[O_2][G_{ss}] \quad \text{(Eq. 8)}$$

$$\beta = 4k_2[P_{ss}] \quad \text{(Eq. 9)}$$

Eq.4 and Eq.5 do not need to be linearized directly as they are linear when Eq. 6 and Eq. 7 are used in the system. Steady state for both substances were determined by assuming the steady state of glucose[G_{ss}] approaching the blood sugar level and using the system of equations to determine a steady-state for gluconate[P_{ss}][7].

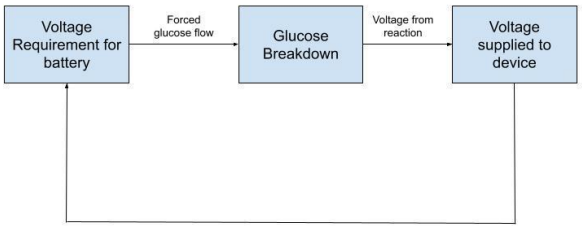


Figure 1: Block diagram of the glucose-voltage system

Parameter	Description	Value
k_1	Forward reaction rate (s^{-1})	0.00116
k_2	Reverse reaction rate (s^{-1})	0.0003
$[O_2]$	Oxygen concentration in battery(M)	0.0355
T	Target voltage (V)	1.5
K	conversion factor for gluconate to voltage equivalent($\frac{V}{M}$)	1.16e3
$[G_{ss}]$	steady-state glucose(M)	0.00475
$[P_{ss}]$	Steady-state gluconolactone(M)	0.00176
α	lumped constant of linearized forward kinetics	2.89e-6
β	lumped constant of linearized reverse kinetics	7.82e-7

Table 1: All parameters pertaining to the linearized glucose response model

B. *Simulink Model*

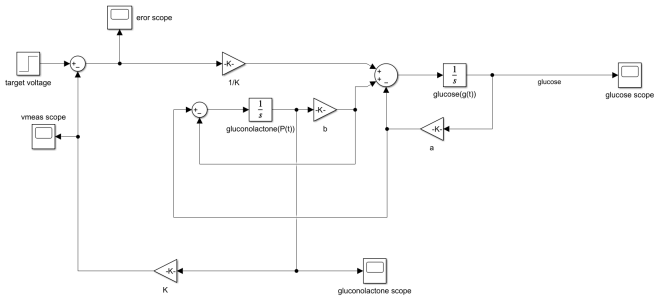


Figure 2: Simulink model of the glucose battery system response

C. *Overall Transfer Function*

To measure the capabilities of this battery influx system, we can measure the voltage $V(t)$ as a function of glucose influx $f(t)$. Below are the Laplacian equations of Eq. 4-7

$$\widehat{V}(s) = K * \widehat{P}(s) \quad \text{(Eq. 10)}$$

$$\widehat{f}(s) = T - K * \widehat{V}(s) \quad \text{(Eq. 11)}$$

$$s\widehat{G}(s) - G_0 = \frac{1}{K}\widehat{f}(s) - \alpha\widehat{G}(s) + \beta\widehat{P}(s) \quad \text{(Eq. 12)}$$

$$s\widehat{P}(s) - P_0 = \alpha\widehat{G}(s) - \beta\widehat{P}(s) \quad \text{(Eq. 13)}$$

Combining these equations and inputting our parameters allows us to model the following transfer function.

$$H(s) = \frac{7.824e{-}7}{s^3 + 5.006e{-}6s^2 + 7.824e{-}7 + 1.6523e{-}12} \quad \text{(Eq. 14)}$$

This transfer function expands the voltage V to glucose flow f to approach the target voltage. Due to glucose flow in our system relying on driven target voltages, we can use it as our input and is justified as it will dominate the other glucose rate components in Eq. 6. Figure 2 depicts the bode plot of this system. The system appears to have significant underdamping issues as seen by the magnitude blow up towards the end of the plot. This underdamping is parallel to what is expected of a glucose battery as the glucose flow response is limited to non convective diffusion into the battery. To counteract this, PID control can be instated to negate the underdamping components of our system and stimulate a forced glucose flow into the battery.

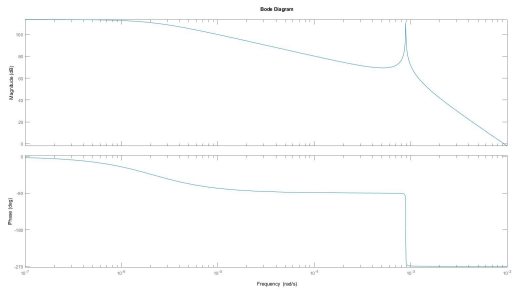


Figure 3: Bode plot of the unaffected battery model.

Poles were determined using matlab and subsequently PID parameters were determined to eliminate the underdamping nature of the system from two imaginary poles. This imaginary component can be seen in the bode plot where the magnitude spike occurs. Our overall system then takes error in correspondence to the voltage driven and the target voltage, drives this difference through the PID controller, and glucose flow is then altered to reach the set point. This simplification of the model can be seen in figure 4.

Parameter	Value
k_p	1000
k_i	7.235e-4
k_d	3.455e8

Table 2: parameters for the PID controls

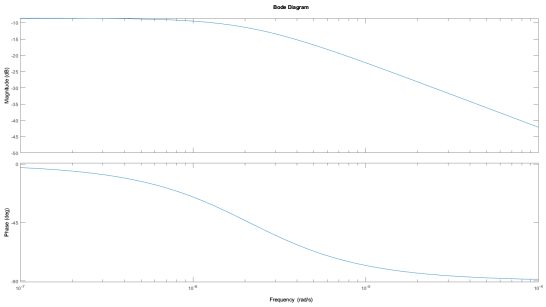


Figure 4: Bode plot of our battery model following PID control. It is evident that there is a much smaller phase change and higher magnitude since the function used is in relation to each glucose molecule.

Figure 5: Simplified system of our PID controlled glucose battery

Now the Bode plot shows a low pass effect on glucose release by having the highest magnitude being at the beginning of the frequencies and immediately dropping, instigating a instantaneous change in voltage from a glucose flow spike.

We can compare the natural setting of the glucose secretion and the PID glucose secretion by evaluating the glucose and voltage values of both systems. Figure 5 depicts this comparison and shows that the voltage value for the non-PID system does not reach target voltage within an appropriate time range while the PID system does. Glucose also spikes in the PID system to drive voltage quickly while the non-PID system has a slowly increasing glucose value. The nature of the non-controlled system aligns with the bode plot depicted from the transfer function as they both show underdamping characteristics. Overall, the PID system

successfully drives the glucose concentration to reach operational voltages.

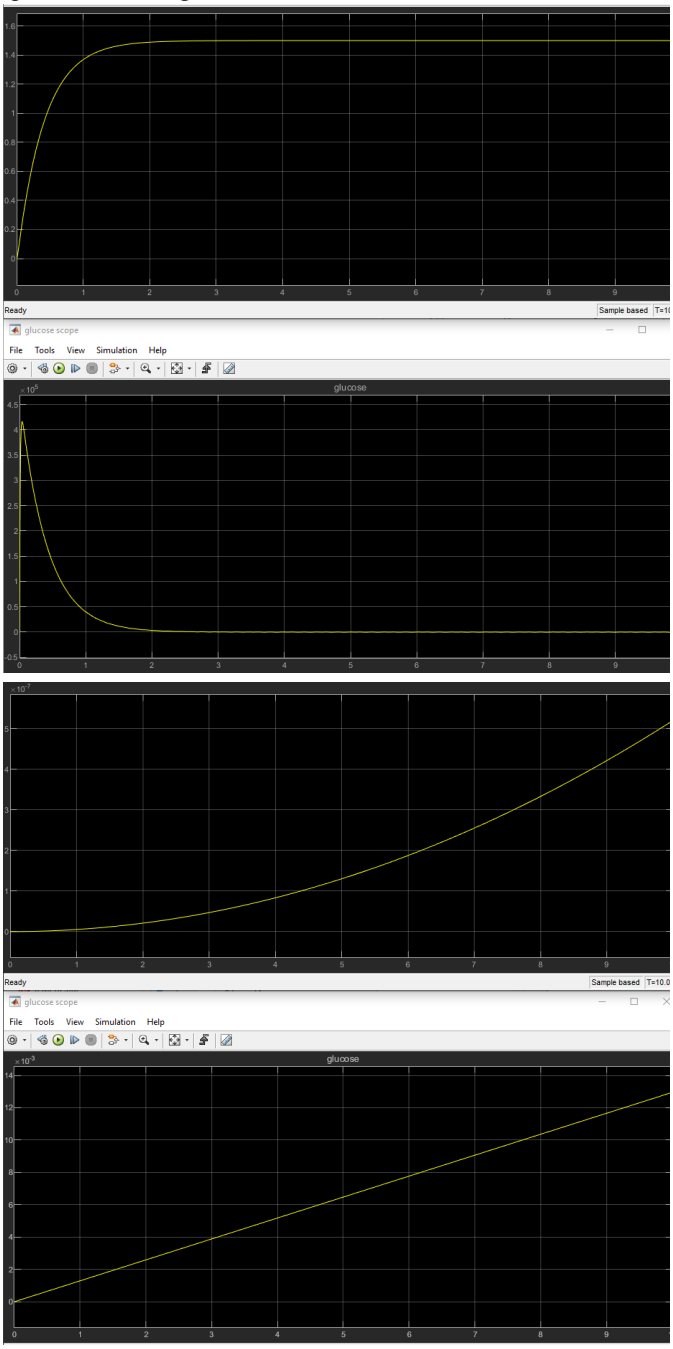
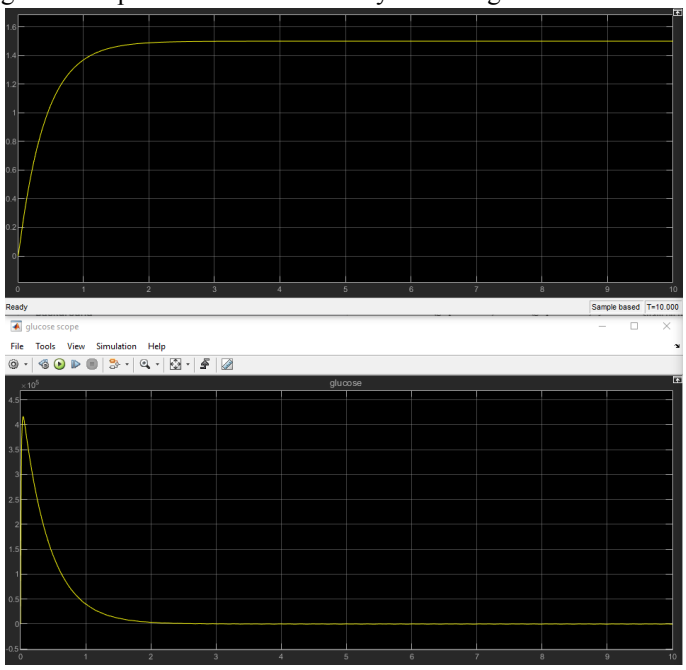


Figure 6: Comparison of glucose and voltage for the non-PID (graphs 1 and 2) and PID (graphs 3 and 4) system

V. Clinical Syndrome Perturbations

One key factor that could play into disrupting the model would be abnormal glycemic conditions. The two most applicable glucose conditions to our model are hypoglycemia, blood sugar levels below 70 milligrams per deciliter, and hyperglycemia, blood sugar levels above 125 milligrams per deciliter [8],[9]. Extracting glucose from the body with hypoglycemic issues could be detrimental to the user as the battery could pull excessive amounts of sugar from the blood especially in high voltage situations. Hyperglycemia should also be monitored to determine if extraction of glucose also could be detrimental to their body as well, but it may prove to be an indirect way to reduce glucose levels in patients with hyperglycemia due to diabetes.

To model these two conditions the system was remade with new steady state glucose values of 0.0029M for hypoglycemia and 0.0069M for hyperglycemia. Running the same model with the new values for steady-state and applying the initial conditions of the blood sugar to the glucose inside the battery it was shown that the conditions do not change from the varying blood sugars. However, the modeling shows high glucose flow from the body indicating possible issues with putting this battery model into trials due to metabolic disruption. Iit may be possible to outweigh the rate at which the battery pulls glucose from the blood by consuming high amounts of glucose based foods (ie maltodextrin supplementation). Overall, the battery does not change drastically in reaching voltage from varying sugar levels, but it would be more important to evaluate the glucose of patients to ensure healthy blood sugar levels.



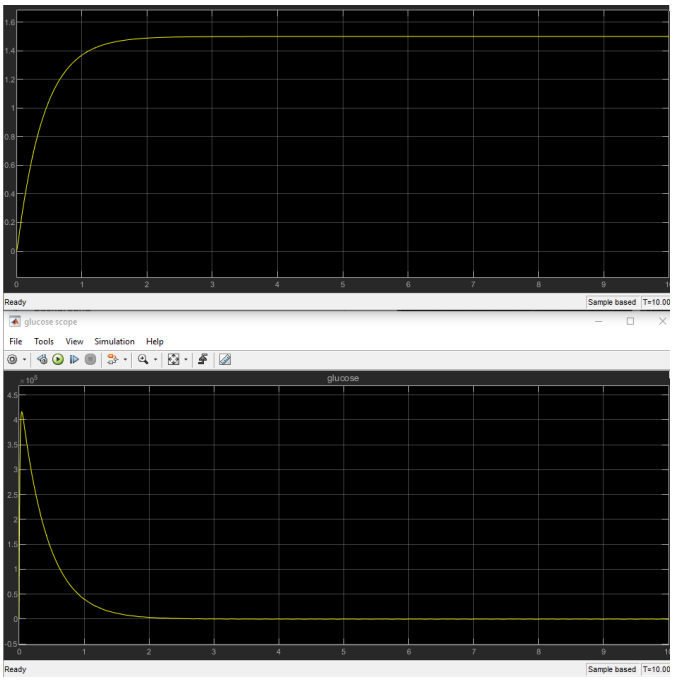


Figure 7: Hypoglycemic and Hyperglycemic glucose (graphs 2 and 4) and voltage model (graphs 1 and 3).

VI. Discussion and Future Applications

Our model was able to successfully drive to the target voltage within an acceptable response time. However, something to note is the high concentration of glucose that is needed to create the voltage. The unrealistic volume of glucose needed to create this voltage is primarily due to our model using one of the least energy efficient models of sugar oxidation to create electrons. While it is the least energy efficient this model relies on the least amount of reagents and enzymes to produce voltage. For instance, a recent study created a synthetic enzymatic pathway that released 24 electrons per sugar molecule[3]. One key component of our model is it is feasible to instigate voltage jumps from glucose spikes. On the other hand, most studies have relied on testing with steady glucose flow concentrations that relied on steady glucose flow and therefore have had low output voltages ranging from 0.5V to 0.7V with some instances of 1.2V being acheived[3],[4]. Metabolic strain on the body proves to be the largest factor in applying bio-batteries to implants due to their reagent requirement and varying blood sugar levels of the person using the battery. Furthermore, our model proves to be effective in establishing glucose requirements and metabolic strain on the body in response to charging the battery.

This study has shown that the battery is operable with specific glucose levels and branches out into a problem of supplying glucose without perturbing bodily functions. Examples of this would be the glucose supplementation as mentioned before or even supplying glucose outside of the body such as a glucose reservoir you can attach to skin that is connected to the battery. Furthermore, the effective voltage control from the glucose battery could prove to expand beyond implants and work in larger industries as an eco-friendly option to other power sources[10].Going beyond the medical field, successful development and implementation of enzymatic batteries for implantable medical devices can be applied to environmental and energy harvesting applications. Enzymatic batteries have potential uses in environmental monitoring devices, outside of the medical domain. Enzymatic batteries could be used to power implantable sensors in ecosystems, gathering information on wildlife behavior, pollution levels, and environmental factors. Enzymatic batteries may also play a role in energy harvesting systems, offering long-term power for remote sensors situated in off-grid areas[11].

The analysis above has effectively illustrated the sugar battery's dynamic response mechanism, highlighting the function of PID control in reducing underdamping problems. To attain the ideal balance between stability and responsiveness, more research and experimentation may be necessary to perfect the PID parameters. Optimizing the control system may lead to improved battery performance and more effective glucose use. In regards to future applications, branching out the battery design to both larger industry power sources and inside implantable medical devices is possible with proper control of the glucose environment fueling the battery and feedback flow to reach operating voltages.

VII. Conclusion

All in all, this project report delves into the idea of using enzymatic batteries as alternative power sources for implantable medical devices. The current market of traditional batteries, including lithium-ion and alkaline, pose obstacles in regards to maintenance, reliability, and size constraints for medical devices. Enzymatic batteries, specifically bio-batteries, utilize the body's inherent chemical reactions to generate an independent power source. In order to ensure a steady flow rate of glucose at different concentrations, an Ordinary Differential Equation (ODE) model was formulated to analyze the glucose consumption and feedback behavior of the system. In order to develop a response system for a sugar battery that boosts glucose flow in reaction to a voltage deficit, operational constraints, parameters, and goals are established. The chemical interactions of glucose to gluconolactone serve as the basis for the control derivations and equations that support the Simulink model. The glucose battery system's dynamics are further demonstrated by the Simulink model, which highlights the technology's potential as an implantable medical device's real-time, self-sustaining power source. With more analysis on the non-linear pathways (especially the synthetic enzyme pathways), it could be possible to create a safe model in the enar future that could prove helpful to test with in trials.

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