Insulin Optimization: Sustaining Production and Chemical Balance

Surya Reddy

March 2024

1 Introduction

Insulin, a vital chemical in the human body, plays a crucial role in regulating blood sugar levels essential for energy production and overall well-being. Its primary function involves facilitating the movement of glucose from the bloodstream into the body's cells, where it can be utilized for energy. Without sufficient insulin, glucose accumulates in the bloodstream, leading to a condition known as hyperglycemia. For individuals diagnosed with diabetes, administering insulin injections becomes pivotal in managing blood sugar levels effectively, allowing them to lead a healthy and stress-free lifestyle. Insulin deficiency or ineffective use can result in diabetes-related complications, emphasizing the importance of proper insulin regulation for overall health.

Scientists have engineered bacteria to produce insulin through genetic manipulation, enabling accurate replication of human insulin. However, the process poses challenges as insulin, while beneficial for humans, inhibits bacterial growth, necessitating regular harvesting to prevent harm to the bacteria. Understanding the optimal insulin removal rate becomes essential for maximizing insulin yield in bacterial strains with known growth patterns, insulin-induced death rates, and insulin production rates. This inquiry aims to address the question: What insulin removal rate optimizes insulin harvesting efficiency for a given bacterial strain with known growth, insulin-induced death, and insulin production rates, ensuring maximum insulin yield?

2 Model

We introduce a mathematical model aimed at elucidating the interaction between bacteria and the insulin they produce, alongside insulin harvest. Our goal is to understand how different factors influence insulin production and harvesting efficiency over time. The model comprises three differential equations: one governing bacterial growth (dN/dt), another for insulin production (dI/dt), and a third representing insulin removal (dE/dt).

$$\frac{dN}{dt} = \alpha \cdot N \cdot \left(1 - \frac{N}{K}\right) - \beta \cdot I \cdot N \tag{1}$$

$$\frac{dI}{dt} = \frac{N}{C} - \lambda \cdot \delta(t - n \cdot \Delta t) \tag{2}$$

$$\frac{dE}{dt} = \lambda \cdot \delta(t - n \cdot \Delta t) \tag{3}$$

In the equation for $\frac{dN}{dt}$, α represents the growth rate of bacteria, reflecting how quickly bacterial populations increase over time. The term $\frac{N}{K}$ signifies a logistic growth pattern, indicating that bacterial growth initially rises until reaching a carrying capacity (K), beyond which it becomes limited. This parameter K denotes the maximum population size of bacteria in the absence of limiting factors, such as space or nutrients, ensuring the model captures realistic growth dynamics.

The term βIN in the $\frac{dN}{dt}$ equation accounts for the impact of insulin on bacterial death, where β represents the rate of insulin-induced death for bacteria. Higher insulin levels lead to faster bacterial demise, shaping the dynamics of bacterial populations in response to insulin concentrations.

Moving to the $\frac{dI}{dt}$ equation, $\frac{N}{C}$ reflects the insulin production time scale being proportional to bacterial population size (N), with C representing a constant. This parameter C signifies the time scale for insulin production by bacteria, ensuring that the model accurately captures the dynamics of insulin synthesis over time in response to bacterial growth.

Additionally, the $\frac{dI}{dt}$ equation incorporates insulin harvesting through the Dirac delta function, represented by λ, which acts as a pulse at specific time intervals. This parameter λ denotes the amount of insulin removed every 10 minutes, influencing the rate at which insulin is extracted from the system.

To assess insulin harvesting efficiency, we will compute $E(t)$ to determine the total amount of insulin extracted over time for each value of λ. These values were derived from experimental data where bacteria and insulin growth were modeled, and the parameters were adjusted to best fit the dataset. The time intervals at which insulin is extracted (Δt) were chosen based on practical considerations to ensure consistent and reliable data collection throughout the study, facilitating accurate assessment of insulin removal dynamics.

2.1 Constants

The values for K, C, α, and β were derived from an experiment run in which we modeled bacteria and insulin's relationship using a provided data gathered by scientists. The dataset ran three experiments while genetically modifying bacteria. The scientists recorded the amount of bacteria and insulin at each time step. We were able to form logistic equations to create the model, to find the appropriate constants that best fit our data set for this experiment.

Firstly, $\alpha = 0.035$ represents the growth rate of bacteria. This value was chosen to simulate realistic bacterial growth dynamics observed in laboratory settings and previous studies, ensuring that our model accurately reflects bacterial proliferation over time.

Secondly, $\beta = 1.8$ signifies the rate at which insulin induces death in bacteria. Determined through empirical data and theoretical modeling, this parameter reflects the impact of insulin on bacterial survival, providing insight into how varying insulin levels affect bacterial populations.

The carrying capacity, denoted by $K = 100000$, represents the maximum population size of bacteria that can be sustained in the absence of limiting factors. We selected this value to mirror a realistic upper limit for bacterial growth in our experimental conditions, enabling us to explore how bacterial populations respond to different environmental conditions.

Next, $C = 100000$ reflects the production time scale of insulin by bacteria. This parameter was chosen to align with typical rates of insulin production observed in bacterial cultures, ensuring that our model accurately captures the dynamics of insulin synthesis over time.

Lastly, $\Delta t = 0.3$ represents the time intervals at which insulin is extracted during the experiment. This value was selected based on practical considerations to ensure consistent and reliable data collection throughout the study, facilitating accurate assessment of insulin harvesting efficiency.

By carefully selecting these parameter values, we aim to create a robust model that accurately captures the dynamics of bacterial growth, insulin production, and insulin removal, providing valuable insights into the interplay between bacteria and insulin in our experimental system.

3 Method

Using code in python we solve these ODE's numerically over the specified time interval (100 min), enabling us to obtain the solution. This solution yielded values (N, I, E) containing the populations of bacteria, insulin, and removed insulin over time. To ensure the simulation closely mimicked real-world conditions and to maintain uniformity in our experimental setup, we opted to keep the variables α, β, K, and C constant throughout the experiment. By maintaining these variables constant, we aimed to isolate the effects of insulin removal rate (λ) on insulin harvesting efficiency, enabling a focused investigation into the dynamics of insulin extraction from the system.

We will be conducting 4 different experiments at different values of lambda to see which one optimizes insulin harvesting the best.

- Experiment 0: $\lambda = 0.000$
- Experiment 1: $\lambda = 0.001$
- Experiment 2: $\lambda = 0.0001$
- Experiment 3: $\lambda = 0.00001$

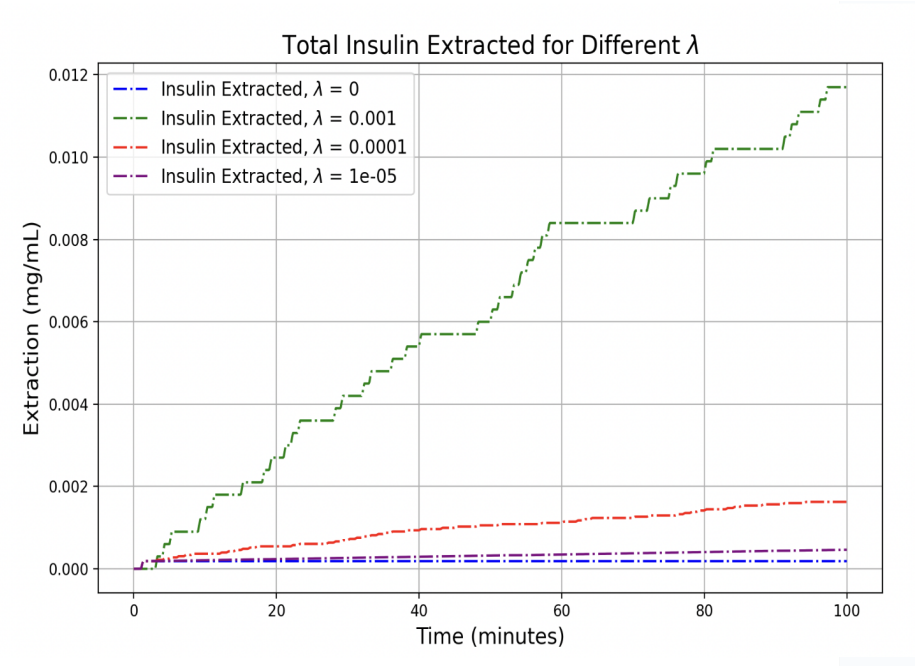

Figure 1: The results for the 4 different levels of lambda (insulin removal rates) are presented in this graph with the amount extracted on the y-axis and the time taken on the x-axis.

4 Results

In Figure 1, we observe the lines on the graph, and the slope of each curve illustrate the rate of insulin growth over time for different experiments. These results arise from the use of different values of λ in each experiment. As λ, or the insulin removal rate, increases, we observe a larger amount of insulin being extracted. For instance, in our base case where $\lambda = 0$ (blue line), no insulin is removed from the system, resulting in a straight horizontal line staying at 0 mg/ml. This implies that the bacteria grow slower or may even die faster. However, in another experiment where we set $\lambda = 0.001$, we extract a larger amount of insulin, as shown by the steeper green line in the figure.

In Experiment 0 ($\lambda = 0.000$), where no insulin was removed from the system, the insulin level remained at 0 mg/ml throughout the experiment. Experiment 1 ($\lambda = 0.0001$) showed a small increase in harvested insulin, reaching around 0.00162 mg/ml, indicating that a slight increase in the insulin removal rate led to a measurable increase in harvested insulin. Experiment 2 ($\lambda = 0.001$) resulted in the highest amount of harvested insulin, at 0.0117 mg/ml, suggesting that a higher insulin removal rate significantly boosted harvesting efficiency. Conversely, Experiment 3 ($\lambda = 0.00001$) yielded the least favorable outcome, with

a minimal amount of insulin produced (0.00042 mg/ml). These findings underscore the importance of a high insulin removal rate in optimizing harvesting efficiency. Balancing this rate with bacterial and insulin population dynamics is crucial for maximizing insulin production.

5 Discussion

The discussion regarding the model's limitations and areas for improvement encompasses several key considerations. Firstly, external factors influencing bacterial populations and insulin production, such as environmental changes or fluctuations, remain unaccounted for in the current model. This oversight raises concerns about the model's applicability in real-world scenarios, where environmental conditions can significantly impact insulin harvesting dynamics.

Moreover, the model's short-term perspective may overlook long-term considerations regarding the sustainability and viability of continuous insulin harvesting practices. While the model demonstrates promise in controlled laboratory settings, its real-world application may face challenges due to the dynamic nature of actual environments and the potential for unforeseen complications.

Another critical aspect is the assumption of a homogeneous bacterial population within the model, which neglects the potential presence of biological diversity. This oversight could have significant implications for insulin production in real-world scenarios, where variations in bacterial populations may affect harvesting outcomes.

To address these limitations and enhance the model's accuracy, several recommendations are proposed. Firstly, validating the model in real-world settings through experiments conducted outside of controlled laboratory conditions would provide valuable insights into its predictive capabilities and potential discrepancies between model predictions and real-world outcomes.

Additionally, integrating environmental factors such as temperature, pH, nutrient availability, and substrate concentration into the model is essential for a comprehensive understanding of insulin harvesting dynamics. Developing a more robust model that incorporates these variables would yield a more accurate representation of insulin production and bacterial growth dynamics.

Furthermore, conducting long-term studies to evaluate the sustainability and viability of continuous insulin harvesting practices is crucial. Assessing the system's performance over extended periods would enable the identification of potential challenges and opportunities for optimization.

The inquiry into optimizing insulin production through bacterial engineering has uncovered the intricate interplay between insulin levels and bacterial growth, essential for medical progress. Manipulating bacterial genetics has identified a delicate balance: elevated insulin levels inhibit bacterial growth, requiring frequent harvesting to sustain stability and enhance insulin yield. Results highlight the critical importance of insulin removal rate, as minor adjustments can significantly enhance insulin harvesting. Experimentation demonstrates a clear correlation between higher insulin removal rates and increased harvesting efficiency,

offering valuable insights into maximizing insulin production while maintaining bacterial stability.