Glucostasis Simulator: An Educational Tool for Visualizing Glucose-Insulin Feedback Using the Clinically Accepted Hovorka Model

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Effective diabetes management requires a fundamental understanding of glucose-insulin dynamics and their regulation through physiological feedback systems. This paper presents an interactive simulation tool, developed in MATLAB App Designer and grounded in the clinically validated Hovorka model, to visualize these complex mechanisms. The simulator was tested across key clinical scenarios including baseline, hyperglycemia, and insulin dosing errors, with results demonstrating physiologically accurate glucose and insulin trajectories that confirm the model's successful implementation. To enhance its educational utility, the tool incorporates myth versus fact flashcards and dynamic visual aids. By bridging theoretical knowledge and practical insight, this work provides a foundational platform for exploring physiological control systems, with potential to inform the future development of personalized diabetes management strategies.

Keywords: Hovorka model, Glucose-insulin dynamics, Diabetes, Feedback Control, Glucostasis

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1. Introduction

Diabetes mellitus constitutes a group of metabolic disorders characterized by persistent elevations in blood glucose concentration. The pathogenesis centers on the hormone insulin, secreted by pancreatic islet cells, which is the primary regulator of glycemic control (Huising, 2020). The condition manifests as either an absolute insulin deficiency, characteristic of Type 1 diabetes, or as a combination of insulin resistance and a compensatory secretory failure in Type 2 diabetes. These impairments disrupt normal glucose metabolism, leading to its accumulation in the bloodstream and a concomitant failure of cellular energy production. If unmanaged, this state progresses to serious complications across multiple organ systems.

According to the latest IDF Diabetes Atlas (2025), diabetes prevalence has reached a critical level, affecting approximately 11.1% of the global adult population (20-79 years), equating to one in every nine adults. Alarmingly, over 40% of these individuals are undiagnosed. Projections indicate a substantial rise, with prevalence expected to increase by 46% by 2050, at which point an estimated one in eight adults could be living with this condition (Manne-Goehler et al., 2019) .

Following meal ingestion, enteral glucose is detected by intestinal cells, which initiate a signaling cascade to the brain. This, in turn, stimulates the pancreas to secrete insulin, the hormone responsible for facilitating cellular glucose uptake and metabolism (Dimitriadis et al., 2021). In Type 1 diabetes (T1D), an autoimmune pathogenesis leads to the destruction of pancreatic β-cells, resulting in an absolute insulin deficiency (Eizirik et al., 2023; Tomita, 2017). Consequently, lifelong exogenous insulin replacement therapy becomes imperative for survival. Insulin is unequivocally a life-saving intervention for individuals with T1D, and its

meticulous management is of critical importance (Subramanian S & Baidal D, 2021). This underscores the necessity of a robust understanding of glucose-insulin dynamics, which forms the foundational principle for emerging medical technologies such as the Artificial Pancreas System (APS). An APS is a closed-loop system that integrates a continuous glucose monitor, an insulin infusion pump, and a control algorithm to automate insulin delivery in response to real-time glycemic levels (Cobelli et al., 2011) .

The quantitative study of these dynamics has been a long-standing research focus, particularly through mathematical modeling. A primary objective has been the artificial replication of endogenous insulin production using closed-loop control, which aims to mimic the body's natural negative feedback mechanism. Consequently, numerous models describing the insulin-glucose regulatory system have been developed (Kang et al., 2022; Palumbo et al., 2013; Shi et al., 2019). The Minimal Model, pioneered by Bergman et al., represented a seminal contribution to the field of diabetes modeling, though it possesses limitations in real-world clinical applicability (Bergman et al., 1979; Gallardo-Hernández et al., 2022) . Hovorka's model subsequently addressed several of these shortcomings through the introduction of a more sophisticated compartmental structure, enhancing its physiological fidelity (Hovorka et al., 2004). However, a translational gap persists between these sophisticated modeling efforts and their accessibility for educational purposes. While physiologically-grounded models like Hovorka's are instrumental in advancing therapeutic technologies, their inherent complexity often renders them unsuitable for direct pedagogical application. This has resulted in a shortage of tools capable of bridging this divide by translating advanced computational models into intuitive learning experiences for students, healthcare professionals, and patients. Many existing educational resources, while valuable, often lack both the rigorous physiological foundation of contemporary models and the interactive components necessary to visualize and experiment with the core principles, such as feedback control that underpin modern diabetes technology.

In this work, we present a simulation-based educational tool designed to illustrate the application of feedback control in glucose regulation, utilizing the Hovorka model as its physiological basis. The tool provides dynamic visualizations of glucose-insulin kinetics through interactive plots and incorporates an educational component that dispels common misconceptions via a myth versus fact module. The primary objective of this initiative is to offer an accessible educational platform to facilitate foundational understanding of glucose-insulin homeostasis.

2. Method

Simulation Objective

The primary objective of this work was to develop an interactive, simulation-based educational tool to facilitate the understanding of physiological control systems, with a specific focus on Glucostasis. The tool was designed to demystify the concept of negative feedback in glucose homeostasis and illustrate its critical relevance to diabetes management. The simulation demonstrates glucostasis in the human body through real-time graphs of glucose levels and corresponding insulin infusion. Its core function is to illustrate the role of negative feedback in blood glucose regulation, contextualized within diabetes management, using a dedicated control model (Ponsiglione et al., 2023).

Modeling Approach

This tool utilizes the Hovorka model to simulate glucose-insulin dynamics, leveraging its multi-compartmental framework for enhanced physiological fidelity (Hovorka et al., 2004). The core computational engine involves the numerical integration of a system of ten coupled differential equations. User-provided inputs for meal carbohydrates and insulin doses are processed by this model, with solutions being computed via the ode45 solver in MATLAB.

The following system of equations, adapted from the Hovorka model (Hovorka et al., 2004) , forms the mathematical foundation of our simulation:

$$dQ_1/dt = -F_{01} + k_{12}\cdot Q_2 - x_1\cdot Q_1 + Ra - EGP_0\cdot(1 - x_3) \quad (1)$$

$$dQ_2/dt = x_1\cdot Q_1 - k_{12}\cdot Q_2 - x_2\cdot Q_2 \quad (2)$$

$$dI_p/dt = U_2 / (t_{max}I\cdot VI) - k_e\cdot I_p \quad (3)$$

$$dx_1/dt = -k_{a1}\cdot x_1 + S_1\cdot I_p \quad (4)$$

$$dx_2/dt = -k_{a2}\cdot x_2 + S_2\cdot I_p \quad (5)$$

$$dx_3/dt = -k_{a3}\cdot x_3 + S_3\cdot I_p \quad (6)$$

$$dU_1/dt = -U_1 / t_{max}I + u(t) \quad (7)$$

$$dU_2/dt = (U_1 - U_2) / t_{max}I \quad (8)$$

$$dD_1/dt = -D_1 / t_{max}G + Ra(t) \quad (9)$$

$$dD_2/dt = (D_1 - D_2) / t_{max}G \quad (10)$$

The mathematical model is partitioned into three distinct subsystems to represent key physiological processes. Glucose dynamics, including appearance, distribution, and endogenous production, are modeled by the Glucose Subsystem (Eq. 1-2) using compartment variables Q_1,Q_2,D_1, and D_2. Subsequently, the Insulin Subsystem (Eq. 3-8) describes the absorption of subcutaneously administered insulin (U_1,U_2), its concentration in plasma (I_p), and its dynamic action on glucose metabolism (x^1,x^2,x^3), parameterized by specific rate constants (k_a^1,k_a^2,k_a^3) and sensitivities (S_1,S_2,S_3). The Gut Absorption Subsystem (Eq. 9-10) completes the model by simulating the transit of glucose from the gut into the systemic circulation, where t_{max} is a key time constant calibrated for a standard 70 kg adult.

This simulation models glucose absorption from meal intake to plasma appearance. To enhance realism and prevent non-physiological outcomes, the model incorporates a non-linear ramp function. This function dynamically adjusts the glucose decay rate as concentrations approach and fall below the baseline level, thereby ensuring stable and biologically credible simulation behavior.

System Structure

The system architecture is designed around an interactive simulation workflow. The user inputs values for meal carbohydrate content (grams) and insulin dosage (units). Upon initiating the simulation, these parameters are integrated into the system of differential equations derived from the Hovorka model. MATLAB's ode45 solver computes the numerical solution, simulating the resulting glucose-insulin dynamics. The output is visualized graphically, demonstrating the principle of glucoregulation in response to user-defined inputs, thereby rendering these complex physiological concepts more accessible for educational purposes. The logical workflow of the system, encompassing user input, simulation processing, and result visualization, is depicted in Figure 1.

Figure 1. Block Diagram of the glucose-insulin simulation process using the Hovorka model

GUI Design In MATLAB App Designer

A graphical user interface (GUI) was developed using MATLAB's App Designer, as shown in Figure 2.

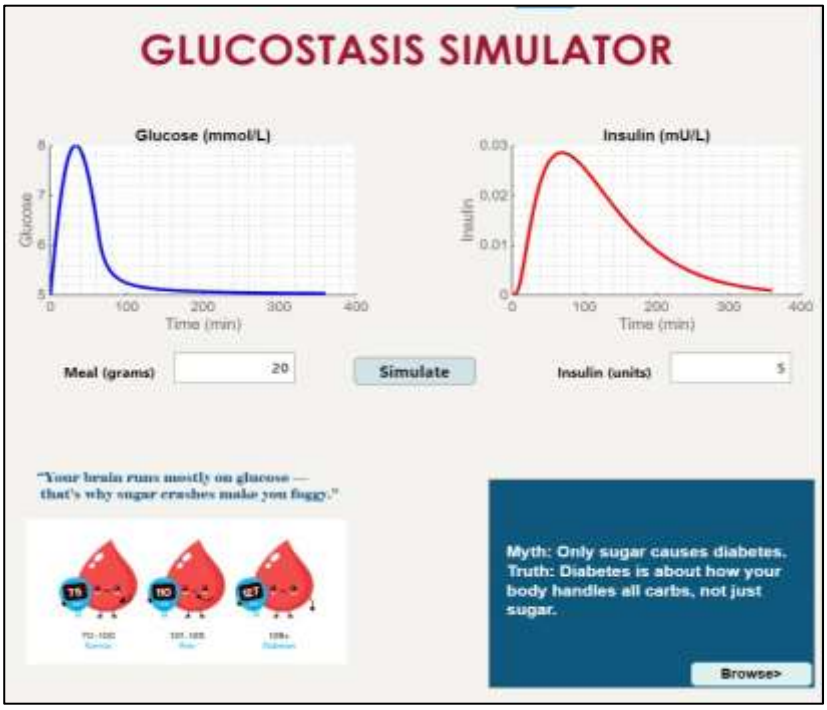

Figure 2. Graphical user interface of simulation tool designed using MATLAB app designer

The interface features two primary axes for plotting real-time graphs of plasma glucose concentration and compartmental insulin action. Users can input specific values for meal carbohydrates and insulin dosage, enabling them to visualize the resulting metabolic dynamics under various conditions. Execution is initiated by a 'Simulate' button, which triggers the model to generate the corresponding graphs. To provide educational context, the interface also includes a reference panel displaying normal blood glucose ranges and an interactive Myth vs. Truth section, where users can browse common societal misconceptions about diabetes alongside evidence based clarifications.

App Features

The application's features were designed to prioritize interactivity and user engagement. Key functional and educational components include:

a. Dynamic visualization of glucose concentration and insulin infusion profiles.
b. Adjustable input parameters for exploring diverse physiological scenarios.
c. Integrated labels and annotations to improve interface usability.
d. An interactive splash screen that provides immediate educational context upon launch.
e. A flashcard module dedicated to addressing and correcting common diabetes misconceptions
f. Contextual display of normative glucose ranges for user reference.

Feedback Simulation

The graphical user interface (GUI) implements a closed-loop feedback system based on the Hovorka model. Within this system, the simulated plasma glucose concentration serves as the input signal. The controller responds to deviations from the target glycemic range by modulating the insulin infusion rate, which is proportional to the magnitude of the deviation. This insulin action enhances glucose utilization, thereby restoring homeostasis, a process that mimics the body's endogenous negative feedback mechanism.

Mathematically, this is governed by the influence of the insulin action compartments (x_1, x_2, x_3) on the glucose compartments (Q_1, Q_2) within the model's structure.

3. Results And Discussion

To evaluate the simulation's performance, we input and analyzed a range of values corresponding to distinct physiological scenarios. This was designed to assess the model's demonstration of glucoregulation across various glycemic conditions. The system's response was simulated over a 6 hours period, with glucose and insulin action trajectories visualized via dynamic plots. We specifically tested four clinically relevant glycemic states common in diabetes management:

a. Baseline (Euglycemia)
b. Untreated Hyperglycemia
c. Insulin overdose
d. Insulin underdose

Baseline (Euglycemia)

To establish a baseline response, a moderate insulin dose of 6 units was administered in conjunction with a 90-gram glucose challenge. The resulting glucose and insulin dynamics are presented in Figure 3. The simulation showed a plasma glucose peak of approximately 28 mmol/L, coinciding with an insulin concentration peak of 0.035 mU/L. The subsequent return of glucose concentrations toward the baseline range demonstrates the model's capability to correctly simulate glycemic recovery following a meal when an effective insulin dose is delivered.

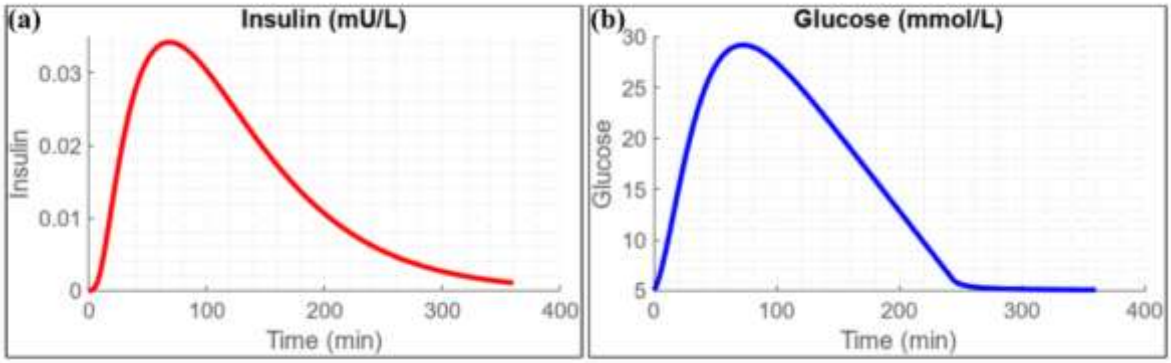

Figure 3. (a) Insulin infusion profile at baseline conditions showing response to meal intake, (b) Plasma glucose concentration dynamics at baseline after meal intake and insulin administration.

Untreated Hyperglycemia

This scenario simulated a Type 1 diabetes patient consuming a large meal of 220 grams of carbohydrates without subsequent insulin administration. The resulting glucose and insulin dynamics are shown in Figure 4. As predicted by the Hovorka model in the absence of insulin-mediated glucose uptake, the plasma glucose concentration rose to a peak of approximately 78 mmol/L. The observed slow decline from this peak is attributable to glucose consumption by insulin-independent tissues, a phenomenon consistent with established physiology (Ahrén & Pacini, 2021).

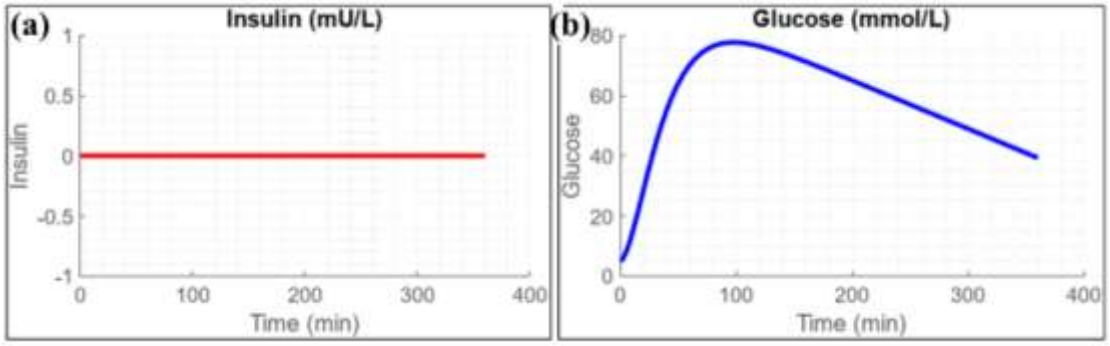

Figure 4. (a) insulin infusion dynamics during untreated hyperglycemia without insulin administration. (b) Glucose concentration curve during untreated hyperglycemia showing peak levels due to absence of insulin

Insulin overdose

This scenario was simulated with a 60-gram carbohydrate meal and a 12-unit insulin dose. As shown in the glucose trajectory (Figure 5 (b)), the concentration increased from a baseline of 5 mmol/L to a peak of 19 mmol/L at approximately 70 minutes, returning to baseline after about 200 minutes. Notably, no hypoglycemic event was observed despite the high insulin dose. This demonstrates the model's ability to maintain system stability and prevent physiologically unrealistic overshooting in response to a significant glucose challenge, as further illustrated by the corresponding insulin action profile in Figure 5 (a).

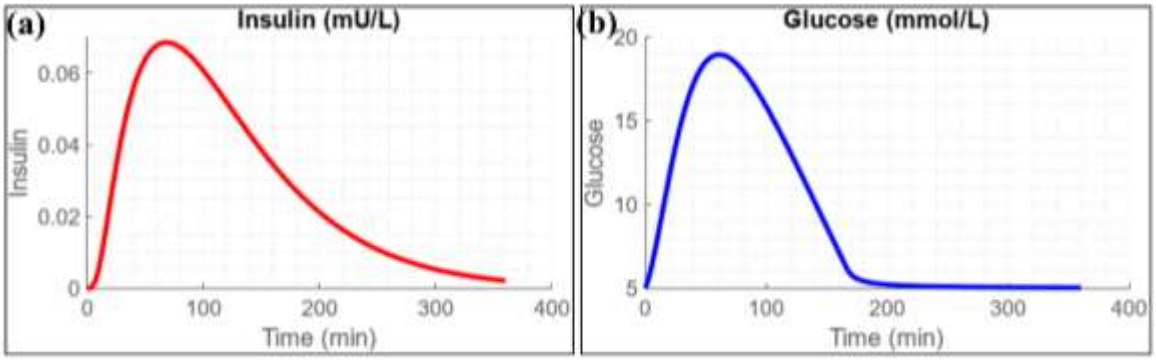

Figure 5. Insulin infusion curve in response to insulin overdose, showing elevated insulin. (b) Glucose concentration curve following insulin overdose, illustrating system recovery

Insulin underdose

In this scenario, a 120-gram carbohydrate meal was administered with a suboptimal insulin dose of 4 units. The simulation results, presented in Figure 6, show a plasma glucose peak of approximately 39.5 mmol/L, coinciding with an insulin concentration peak of 0.022 mU/L. The glucose concentration remained elevated above the baseline for more than 300 minutes, demonstrating a prolonged hyperglycemic state consistent with the delivery of an inadequate insulin dose to clear the glucose load.

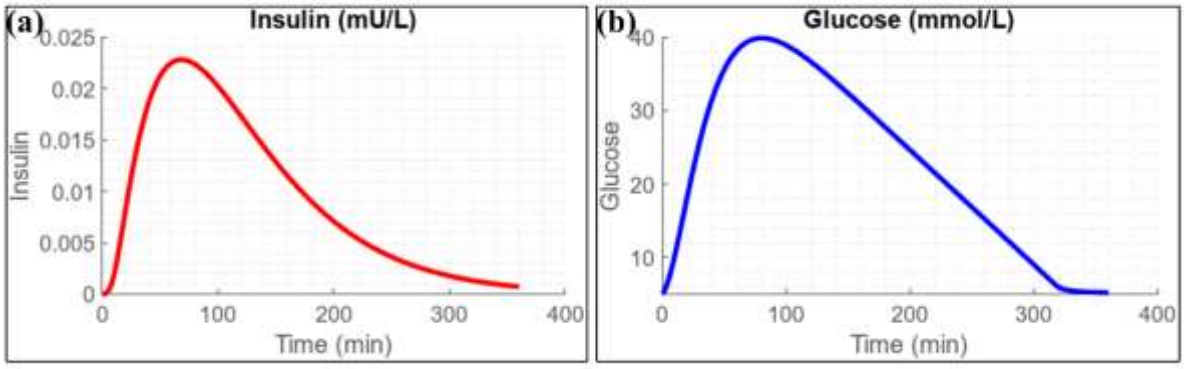

Figure 6 . insulin infusion profile during insulin underdose showing insufficient insulin delivery. (b) Glucose concentration curve during insulin underdose demonstrating prolonged hyperglycemia

The simulation tool demonstrated robust and physiologically consistent responses across a spectrum of clinically relevant scenarios, thereby validating its underlying model and educational utility. In the baseline (euglycemia) scenario, the model accurately replicated the homeostatic response to a meal. The administration of a moderate insulin dose in conjunction with a glucose challenge resulted in a characteristic postprandial glucose excursion. Crucially, the subsequent action of the infused insulin effectively promoted glucose disposal, returning systemic concentrations to the pre-meal euglycemic range and demonstrating a closed-loop negative feedback mechanism. Conversely, scenarios modeling dysregulation produced equally instructive outcomes. Under conditions of untreated hyperglycemia and insulin underdose, the simulation produced a sustained hyperglycemic state. Following the initial peak, glucose concentrations failed to return to baseline, remaining pathologically elevated for the duration of the simulation. This trajectory accurately reflects the impaired glucose clearance observed in uncontrolled diabetes, where the absence or insufficiency of insulin prevents effective utilization of the glucose load.

A critical test of the model's physiological fidelity was its performance in the insulin overdose scenario. Despite a supraphysiological insulin dose, the system demonstrated remarkable stability by avoiding hypoglycemia. This robust behavior is a direct result of the Hovorka model's compartmental architecture, which incorporates insulin-independent glucose uptake by obligate tissues such as the brain and central nervous system. This inherent mechanism, combined with the model's distribution kinetics, imposes a physiological constraint that prevents unrealistic and non-physiological glucose depletion, thereby enhancing the simulation's predictive validity. Collectively, the dynamic trajectories of plasma glucose and insulin infusion, graphically represented in Figures 3 through 10, provide compelling evidence for the simulation's responsiveness and accuracy. The tool not only replicates established metabolic principles but also generates clear, interpretable, and educationally valuable outputs that effectively bridge the gap between abstract mathematical models and tangible physiological concepts.

4. Conclusion

This study presents an interactive simulation tool that implements the Hovorka model to elucidate complex glucoregulatory dynamics. By housing this sophisticated model within an intuitive graphical interface, the tool successfully bridges the gap between theoretical models and practical understanding of glucose-insulin feedback. Validation across diverse clinical scenarios confirmed its ability to generate physiologically plausible outcomes. The tool's primary contribution is its dual utility as an innovative educational resource and a platform for public health advocacy in diabetes management. Furthermore, it establishes a

foundational framework with translational potential, serving as a testbed for prototyping next generation, personalized glucose control systems.

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