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Blood Glucose Levels

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Abstract
The purpose of this study was to establish a mathematical model which can be used to estimate glucose levels in the blood over time. The equations governing this process were manipulated with the use of techniques such as separation of variables and integration of first order differential equations, which resulted in a function that described the glucose concentration in terms of time. This function was then plotted, which allowed us to find when glucose concentration was at its highest. The model was then used to analyze two cases where the maximum glucose level could not exceed a certain level while the amount of carbohydrates and glycemic index were varied, independently.

Keywords
Glucose Levels, Glycemic Index, Carbohydrates

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PROBLEM STATEMENT

The following data for glucose concentration in blood were obtained by a person who monitored his glucose levels after ingesting a meal.

Time (minutes)	Glucose (mg/dL)
0	90
30	151
60	137
90	118
120	105
180	94
240	92
320	91

Table 1: Glucose levels over time measured after a meal.

It is proposed that that the kinetics of the reaction steps are first order, so that

$$\frac{dC}{dt} = -k_1 C \quad (1) \quad \text{and} \quad \frac{dG}{dt} = k_1 C - k_2(G - G_0) \quad (2)$$

where C represents the concentration of carbohydrates in the stomach and G represents the concentration of glucose in the blood. G_0 is the baseline value G at $t = 0$. The initial conditions are $C(0) = A_0$ and $G(0) = G_0$. The rate constant k_1 is related to how quickly the food is digested while the rate constant k_2 is associated with how quickly insulin is released.

I. Solve equation (1) along with its initial condition to obtain an expression for $C(t)$.

II. Substitute the result for $G(t)$ into equation (2) and then solve equation (2), with its initial condition, for $G(t)$.

III. Verify (by plotting G versus t for both model and data) that this model provides a reasonable representation of the above data if

$$G_0 = 90, \qquad A_0 = 121.7, \qquad k_1 = 0.0453, \qquad k_2 = 0.0224.$$

IV. Using your expression for $G(t)$ from part (II), develop an expression for the time t_{max} at which G becomes a maximum. Then use this to develop an expression for G_{max} in terms of only G_0, A_0, k_1 and k_2.

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V. The person who made these measurements would like for his glucose level to not exceed a maximum value of 120mg/dL. Examine two case studies: one in which you find the value of A_0 that will result in a max G level of 120mg/dL (keeping all other parameters constant) and one in which you determine the value of k_1 that will result in a max G level of 120mg/dL (keeping all other parameters constant). Plot G versus t for both cases and compare the data and the model represented by the parameters. Comment on the results.

MOTIVATION

Diabetes is characterized as "a metabolic disorder in which the body is not able to regulate the levels of glucose in the blood"[1] (*Connor and Mottola 33*). The cause for this disorder is the lack of insulin, which is the hormone responsible of regulating the levels of glucose. More specifically, "Insulin enables the body's cells to absorb and use this glucose. Without it, glucose does not enter the body cells and it cannot be used as fuel to support their continued function"[2] *(Petray, Freesemann, and Lavay 45).* Besides this, high concentrations of glucose in the blood have many serious effects such as damaging blood vessels and nerve cells which might eventually lead to damaged eyes and liver.

A healthy person will have a blood glucose level of 70 to 105 mg/dl in a fasting state, and person is considered diabetic if they have a blood glucose level at or above 126 mg/dl in a fasting state.[3] *(Gerich 168)*. However, it is important to keep the blood glucose levels below 120mg/dL because "an excess of glucose in the bloodstream causes various chemical changes that lead to damage to our blood vessels, nerves, and cells"[4] *(Sherwood 247).*

The objective of this project is to find a model that represents how the concentration of glucose in the blood varies as time progresses. Our model is based on variables such as initial concentration of glucose, carbohydrates in a meal, glycemic index and the rate at which insulin is released. Once we have modeled the changes in glucose levels, we use this expression to find the time at which the glucose concentration is at its maximum and compared the results against two case studies.

MATHEMATICAL DESCRIPTION AND SOLUTION APPROACH

PART I: DEVELOPING A THEORETICAL MODEL FOR A HUMAN'S BLOOD GLUCOSE LEVEL

In order to determine the blood glucose level $G(t)$ explicitly, we must first solve the differential equations (1) and obtain an expression for $C(t)$. After we separate the variables in (1) we have,

$$\int \frac{dC}{C} = \int -k_1\, dt \quad \Longrightarrow \quad \ln|C| = -k_1\, t + d \quad \Longrightarrow \quad C(t) = A_0\, e^{-k_1\, t} \tag{3}$$

for some constant d and $A_0 = e^d$.

Note that the equation (2) is a first order linear differential equation of the form:

$$\frac{d\, y(t)}{dt} + p(t)\, y(t) = q(t) \tag{4}$$

It is straightforward to verify that

$$y = e^{-\int p(t)dt}\left[\int q(t) e^{\int p(t)dt} dt + c\right] \tag{5}$$

is a solution to (4) where c is constant. As the first step of solving equation (2), we substitute for $C(t)$ and obtained linear first order differential equation:

$$\frac{dG(t)}{dt} + k_2 G(t) = k_1\, (A_0\, e^{-\, k_1\, t}) + k_2\, G_0 \tag{6}$$

which has solution

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$$G(t) = e^{-\int k_2\,dt}\left[\int (k_1\, A_0\, e^{-k_1\, t} + k_2\, G_0) e^{\int k_2\,dt} dt + c\right]$$

$$= A_0 \frac{k_1}{(k_2 - k_1)} (e^{-k_1 t} - e^{-k_2 t}) + G_0. \quad (7)$$

The parameters

$$A_0 = 121.7,\ G_0 = 90.0,\ \ k_1 = 0.0453, \text{ and } k_2 = 0.0224 \quad (8)$$

best fit the data in Table 1 which can be seen graphically in Figure 2. This simplifies (7) to

$$G(t) = 90 - 240.7428\,(e^{-0.0453t} - e^{-0.0224t})\,. \quad (9)$$

It can be seen clearly from Figure 2 that the graphs for the theoretical model and experimental data are almost identical.

Time (minutes)	**Blood Glucose Levels**	
	Experimental Data	Theoretical Model
0	90	90
30	151	151.09
60	137	136.89
90	118	117.98
120	105	105.33
180	94	94.2
240	92	91.1
320	91	90.8

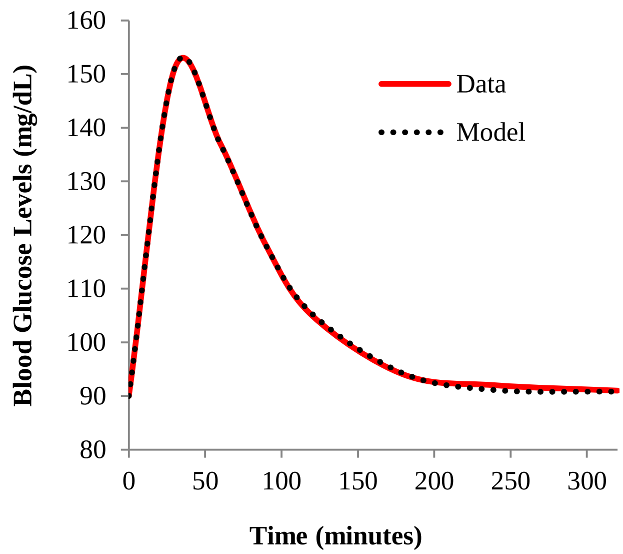

Figure 2: Blood glucose levels for the experiment data of Table 1 and the theoretical model in equation (9).

According to the theoretical model (7), $G(t)$ is maximized when

$$G'(t) = A_0 \frac{k_1}{(k_2 - k_1)} (k_2 e^{-k_2 t} - k_1 e^{-k_1 t}) = 0 \quad (10)$$

which occurs at

$$t_{max} = \frac{\ln k_1 - \ln k_2}{k_1 - k_2} \approx \ 30.75 \text{ min} \tag{11}$$

when the values for $A_0,\ k_1$, and k_2 in (8) are used. From (9) and (11), the maximum glucose level is therefore

$$G_{max} = \frac{A_0\, k_1}{k_2 - k_1}\left[\exp\left\{-k_1\left(\frac{\ln k_1 - \ln k_2}{k_1 - k_2}\right)\right\} - \exp\left(-k_2\left\{\frac{\ln k_1 - \ln k_2}{k_1 - k_2}\right\}\right)\right] + G_0$$

$$\approx 151.11 \text{ mg/dL} \ . \tag{12}$$

<u>PART II</u>: TWO CASE STUDIES

We do not want the blood glucose level to exceed a maximum value of 120mg/dL and consider the following two cases:

I. Finding the value of $C_0 = A_0$ that will result in a max G level of 120mg/dL:

Note that t_{max} from (11) does not depend on A_0, so fixing $k_1 = 0.0453$, $k_2 = 0.0224$, $G_0 = 90.0$ gives $t_{max} \approx 30.75$. Since we constructed $G(t_{max}) = 120$, we get

$$G_{max} = A_0(0.502143) + 90 = 120 \tag{13}$$

which implies that $C_{0(max)} = A_0 = 59.74$.

II. Determining the value of k_1 that will result in a max G level of 120mg/dL:

Fixing $A_0 = 121.7$, $k_2 = 0.0224$, $G_0 = 90.0$ and using Wolfram Alpha, we find the largest value for k_1 that will result in a max blood glucose level of 120mg/dL is $k_1 = 0.01094$. In this calculation, we relied upon the facts that

$$G(t) = \frac{C_0\, k_1}{(k_2 - k_1)}\left(\mathrm{e}^{-k_1 t} - \mathrm{e}^{-k_2 t}\right) + G_0 = 120, \quad \text{and} \tag{14}$$

$$G'(t) = \frac{C_0\, k_1}{(k_2 - k_1)}\left(k_2 \mathrm{e}^{-k_2 t} - k_1 \mathrm{e}^{-k_1 t}\right) = 0. \tag{15}$$

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These maximum values, $C_{0(\text{max})}$ and $k_{1(\text{max})}$ were then used to calculate the blood glucose level using the theoretical model (Table 3 & Table 4) and plotted against time (Figure 4 and Figure 5). Both graphs seem to follow similar patterns but with some differences on the rate at which the glucose concentration raises and decreases as the food is digested.

Figure 4 clearly shows a steeper pattern before and after t_{max}. The change of glucose in blood seems to be very drastic from $t = 0$ to $t = 35$ and from $t = 45$ to $t = 90$. After these time intervals of far-reaching glucose change the graph seems to set off on to a steady concentration.

On the other hand, Figure 5 shows a much steadier change of glucose concentration. A t_{max} can still be clearly identified but the change of glucose in blood is not as strong as the one shown in the other case.

Both case studies prove that the glucose level can be kept below 120mg/dL if the amount of carbohydrate in the meal (C_0) does not exceed 59.74 or the amount of glycemic index the food contains (k_1) is below 0.01095 (see Figure 3).

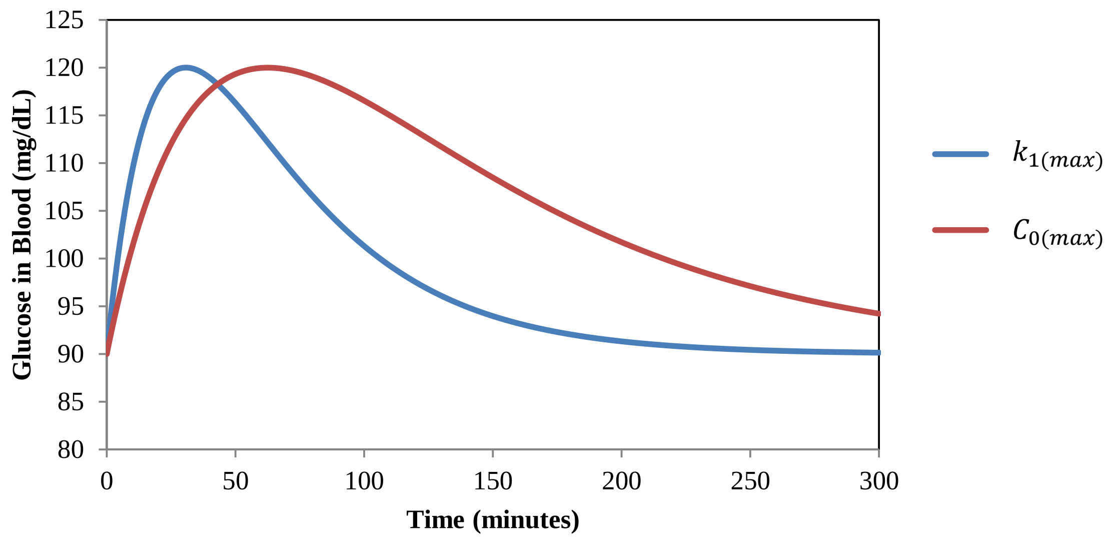

Figure 3: Plots of glucose levels over time such that the glycemic index (k_1) and the amount of carbohydrates consumed (C_0) are maximized while keeping the overall glucose levels below 120 mg/dL.

DISCUSSION

The first objective of the project was to exhibit an equation that took into account the initial conditions stated in the problem. They are important because these are the constants which influence the person's body that have an effect on the glucose levels. This was done using separation of variables on the two initial equations (conditions) in order to integrate them in terms of time.

The second objective of the project was to solve Equation (2), provided by in the problem statement, using the integration factor as a tool. This provided a mathematical expression that would allow the person to determine how the glucose level in the blood varies as time progresses, taking into account the initial conditions calculated previously for carbohydrate concentration. This expression takes into account the baseline value of glucose in the blood (G_0), the amount of carbohydrates consumed by the person (A_0), the rate at which the person digests food (k_1) and the rate at which insulin is released (k_2).

The third objective of the project was to compare the model with the actual values given by the problem. As the values were tabulated it was shown that the model was very consistent with the levels of glucose in the blood measured by the person. This proves that the calculated expression appropriately represents how the glucose levels in the blood vary with time.

The fourth objective of the project was to develop an expression for the time at which the concentration of glucose in the blood is at its maximum (t_{max}). This value was then plugged into the theoretical model to obtain an expression for the amount of glucose in the blood at t_{max}.

The final objective of the project was to study two case studies. First we considered the maximum value of carbohydrate intake per meal (C_0) that would not cause the person to have

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more than 120mg/dL of glucose in the blood. Then we found the largest amount of glycemic index (k_1) that would not allow the concentration of glucose in the blood to exceed 120mg/dL. This turned out to be a complex equation that required the use of a computational mathematics program (Wolfram Alpha).

CONCLUSION AND RECOMMENDATIONS

The simulated values of blood glucose were very close to the actual values measured in the subject. To be precise, the margin of error between the values calculated and the values given was of 0.2mg/dL. This shows that the model took into account all of the necessary constants and that it is an instrument that the person can use to keep track of his glucose levels in the blood.

Besides this, it was also shown that glucose levels peaked 30.75 minutes after the carbohydrates were consumed. This was observed both numerically and graphically.

After analyzing the two case studies it is shown that the person may keep his glucose in blood concentration in a safe range (below $120\ \text{mg/dL}$) if he/she lowers the amount of carbohydrates in a meal or controls the glycemic index of the food contains. By keeping carbohydrates below 59.67 and their glycemic index below 0.0109 the person will not exceed glucose in blood concentration of 120mg/dL.

The progression of glucose levels in blood over time had a similar pattern in each case, varying only in rate of increase, peak, and rate of decrease. If the person controls their carbohydrates in a meal, the rate at which their glucose peaks, then drops, faster than if the person controls their glycemic index.

This project showcases how mathematical expressions can be used to predict biological processes like the amount of glucose in the blood as it varies over time based on food intake. Our model also illustrates how glucose levels may vary from person to person. For instance, the rate at which insulin is released might change according to the metabolism of each person. Further, the case studies provide two distinct ways of controlling the levels of glucose in blood, and also highlight that glucose levels are individualized. One model with fixed parameters will not work for everybody. A personalized expression must be developed for each individual according to their metabolism.

Accurate models of glucose levels allow people to predict their concentration of blood glucose without having to monitor it mechanically and allow them to stay at safe levels by controlling the amount and types of food they consume.

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NOMENCLATURE

Symbol	Definition
G	Glucose level in the blood
G_0	Baseline value of glucose in blood
C	Concentration of carbohydrates in stomach
C_0	Amount of carbohydrates in the meal
k_1	Glycemic index
k_2	Rate at which insulin is released
t	Time

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APPENDIX – WOLFRAM ALPHA CODE

CODE 1

Code used to calculate the largest A_0 for which the maximum of $G(t)$ is 120.

Input:

```
Maximize[{a,90-1.9781*a*(E^(-0.0453*t)-E^(-0.0224*t))==
120,t>=0,a>=0},{a,t}]
```

Result:

59.7459 at $(a, t) \approx (59.7459, 30.7531)$

CODE 2:

Code used to calculate the largest k_1 for which the maximum of $G(t)$ is 120.

Input:

```
Maximize[{k,90+121.7*k*(E^(-k*t)-E^(-0.0224*t))/(0.0224-
k)== 120,121.7*k*(0.0224*E^(-0.0224t)-k*E^(-k*t))/(0.0224-
k)==0,t>=0},{k,t}]
```

Result:

0.0109469 at $(k, t) \approx (0.0109469, 62.5159)$

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