Type 1 Diabetes Mellitus Mobile Application with Blood Glucose Simulation

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Abstract: *There are many mobile applications for diabetes currently in the market which try to help people with diabetes better manage their condition. Common features are the ability to log in user meal intake, amount of carbohydrates, insulin, physical activity and etc. and present the data back to them in a more organize manner such as in charts so that they can learn their blood glucose trend. However, few are trying to simulate their blood glucose level which might help them understand better the effect of these input to their blood glucose. In this paper, a mobile application is presented which can predict the trend of glucose from the meal and insulin intake of diabetes patient. The application used a glucose-insulin dynamics mathematical model to simulate the changes of blood glucose level over time for the user. Data of a clinical patient was used as input to the developed application to study its performance. It was found out that the accuracy of the application made the application to not be 100% reliable as predictor of blood glucose but a good educational tool for diabetes patient as it can simulate the glucose response from carbohydrate and insulin intake. A more accurate and complex mathematical model needs to be use for future development as the current linear and relatively simple model may not be accurate enough for the application.*

Keywords: *Application, Diabetes, Glucose, Insulin, Mobile, Simulation, T1DM,*

I. INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is a type of diabetes with little to no insulin secreted by the pancreas resulting in the inability of the patient's body to control their blood glucose level [1]. This form of diabetes is also known as insulin-dependent diabetes where patients are reliant on insulin to regulate their blood glucose. The cause of T1DM is still unknown but is believed to be cause by genetic and environmental factor. Beta cells in the pancreas undergo autoimmune destruction,[2]a process where the body immune system attack its own healthy cells and tissue [3].

There is no known cure for T1DM and it is not currently preventable [4]. There are many diabetes applications and design studies previously done by others. The common features that are supported by these applications are the abilities to log in values of blood glucose measurement, meal or carbohydrate, and insulin intake amounts [5][6]. Current method of managing blood glucose level with the aid of the application is by having the application acting as a tool to record patients' history of meal and insulin intake and relay it back to the user in a more appealing form such as in graph or charts so that patients can learn from their history to better plan their future meal intake. These features have been tested and reviewed in other studies and it has been observed that the usage of these application does have an impact in lowering the Hb1Ac level of diabetes patients [7][8][9]. One of the earliest study on designing diabetes mobile application was carried out by Mougiakakouis et al. [10] which presented a prototype of mobile application to improve blood glucose management of T1DM patients. The application provides the interface to record blood glucose measurement, blood pressure measurement, insulin dosage, food intake and a way to keep note and send an emergency call in case of emergency. These are the common features in the existing diabetes mobile application. Another study that tries to design a self-management diabetes mobile application is by Årsand et al. in 2010 [11]. An application called the Few Touch was developed where it integrated the use of off the shelf blood glucose meter, a step counter and the capability to record food habits and provides feedback to the user. The application was tested on a group of Type 2 Diabetes Mellitus (T2DM) and was demonstrated to have a motivational effect on the intervention group.

Another study was carried out by Harris et al. [12] where they designed a mobile support called HealthReachMobile for their existing web-base diabetes program. Their mobile application supports wireless glucose meter uploads with graphical and tabular data feedback. They also have an automated messaging feedback system which received mixed reviews from their participant although they however see value in the system. All of these applications have similar feature where it provided a way for user to record their blood glucose measurement, food and insulin intake and present it back to them to analyze and manage their glucose. However, one feature that seems to be lacking in these studies is the feature to simulate or predict future glucose level trend from patients' input data. We believe that the inclusion of such feature can further improve and help T1DM patient in managing their blood glucose.

Type 1 Diabetes Mellitus Mobile Application with Blood Glucose Simulation

In this study, an application with the said feature was developed and proposed as an improvement to the current standard feature of diabetes mobile application. The simulation from the application was analyze to study their reliability as a tool to predict blood glucose level and subsequently help T1DM patients better managed their condition.

II. MATHEMATICAL MODEL

The applicationadopted the glucose-insulin dynamics mathematical model from Lehmann and Deutsch [13] which is given as:-

$$\frac{dG}{dt} = \frac{G_{in}(t) + NHGB(t) - G_{out}(t) - G_{ren}(t)}{V_G} \tag{1}$$

Where

$$G_{out}(G, I_{eq}^*) = \frac{G(c.S_p.I_{eq}^* + G_1)(K_m + G_X)}{G_X.(K_m + G)} \tag{2}$$

$$G_{in} = k_{gabs} \cdot G_{gut} \tag{3}$$

While G_{ren} is given as

$$G_{ren} = GFR(G - RTG) \qquad \text{if } G > RTG \tag{4}$$

$$G_{ren} = 0 \qquad \text{elsewhere} \tag{5}$$

The rate of change of glucose in the gut is given as

$$\frac{dG_{gut}}{dt} = G_{empt} - k_{gabs} \cdot G_{gut} \tag{6}$$

With G_{empt} given as the following step functions

$$G_{empt} = \left(\frac{Vmax_{ge}}{Tasc_{ge}}\right)t \qquad t < Tasc_{ge} \tag{7}$$

$$G_{empt} = Vmax_{ge} \qquad \begin{array}{l} Tasc_{ge} < t \\ \leq Tasc_{ge} \\ + Tmax_{ge} \end{array} \tag{8}$$

$$G_{empt} = Vmax_{ge} - \left(\frac{Vmax_{ge}}{Tdesc_{ge}}\right)(t - Tasc_{ge} - Tmax_{ge}) \qquad \begin{array}{l} Tasc_{ge} + Tmax_{ge} \leq t \\ < Tasc_{ge} + Tmax_{ge} \\ + Tdesc_{ge} \end{array} \tag{9}$$

Where $Tmax_{ge}, Tasc_{ge}$ and $Tdesc_{ge}$

$$Tmax_{ge} = \frac{Ch - \frac{1}{2}Vmax_{ge} \cdot 2(Tasc_{ge} + Tdes_{ge})}{Vmax_{ge}} \tag{10}$$

with $Tasc_{ge}$ and $Tdesc_{ge}$ is equal to 30 min (0.5h), however for small quantities of carbohydrate approximately below 10g, such values cannot be used and instead defined as follow

$$Tasc_{ge} = Tdesc_{ge} = \frac{2Ch}{Vmax_{ge}} \tag{11}$$

To determine whether the above equation will be used, a critical carbohydrate ingested value is defined as follow where the above equation will only be used when amount of carbohydrate is lower than Ch_{crit}.

$$Ch_{crit} = \frac{(Tasc_{ge} + Tdesc_{ge})Vmax_{ge}}{2} \tag{12}$$

For insulin, the change in plasma insulin concentration, I is given by the following

$$\frac{dI}{dt} = \frac{I_{abs}}{V_i} - k_e \cdot I \tag{13}$$

The rate of active insulin pool, I_a

$$\frac{dI_a}{dt} = k_1.I - k_2.I_a \tag{14}$$

with k_1 and k_2 are first order rate constant which serve to describe the delay in insulin action. The rate of insulin absorption is modeled according to Berger and Rodbard[14].

$$I_{abs}(t) = \frac{s.t^s.T_{50}^s.D}{t[T_{50}^s + t^s]^2} \tag{15}$$

$$T_{50}^s = a.D + b \tag{16}$$

where a and b are the preparation-specific parameters.

The steady-state of insulin profile, I_{ss} is computed as follow using the superposition principle.

$$I_{ss}(t) = I(t) + I(t + 24) + I(t + 48) \tag{17}$$

$$I_{a,ss}(t) = I_a(t) + I_a(t + 24) + I_a(t + 48) \tag{18}$$

from here the I_{eq}^* which is the insulin level in equilibrium with $I_{a,ss}(t)$ is computed as

$$I_{eq}^* = k_2 . \frac{I_{a,ss}(t)}{k_1} \qquad (19)$$

which is then used to calculate value of $G_{out}(G, I_{eq}^*)$ at that particular time.

III. SIMULATION ALGORITHM

Fig 1 is the simplified algorithm flowchart for blood glucose simulation in the application. It shows the working and the flow of the codes that simulate blood glucose level of a diabetes patient. Each box represents multiple process or lines of codes that achieve their desired purpose.

The process starts by first retrieving required information to simulate blood glucose which is the food, insulin input and the initial state obtained from previous simulation. The initial state is obtained from saved data from previous simulation which include the initial blood glucose, plasma insulin, active insulin level, glucose concentration in the gut, ongoing absorption of insulin and ongoing rate of glucose emptying in the stomach. This would provide a seamless continuation from simulation of the previous day. The input lists are filtered so that only input for the current date are considered. For example, if the application is simulating blood glucose for the 1st of May, only food consumed and insulin injectedon the 1st of May will be stored into a variable during the simulation. This would save processing time and increase the performance of the application. The simulation then entered into the main loop of the numerical calculation using the Runge-Kutta method [15]. This particular method to solve ODE is chosen because it offer the same accuracy with the Taylor series method which is very accurate without requiring to solve the higher order derivatives which can be tedious and repetitive [16]. Hence, this method is chosen because of its practicality while having the same high accuracy as the Taylor series. For each second, the amount of carbohydrate and insulin consumed on that exact time is calculated and added up. If there is a presence of carbohydrate consumption, an instance of *EmptyingSession*, a custom class designed to handle the progress of carbohydrate is created. This is then use to calculate rate of emptying and keep track of its progress on every second of simulation.

Similarly, a class *InsulinSession* is used to calculate and keep track of insulin absorption from every insulin injection taken by patient. The preparation specific parameters a, b and s were retrieved each from their respective function[14]. With this, the concentration of insulin, I and active insulin, I_a in the patient body can be calculated. It then continues to calculate the input rate of glucose into the blood plasma, renal excretion of glucose, output rate of glucose the body and I_{eq} which is the insulin level responsible for the hepatic and peripheral control action. Another term that needs to be calculated is the net hepatic glucose balance, *NHGB* which is obtained by interpolating the table from Lehmann and Deutsch [13]. Finally, plasma glucose level is then calculated using Runge-Kutta numerical method[15] and the result of glucose and insulin level for the current loop instant of time is appended to their respective arrays which is then use to plot the graph.
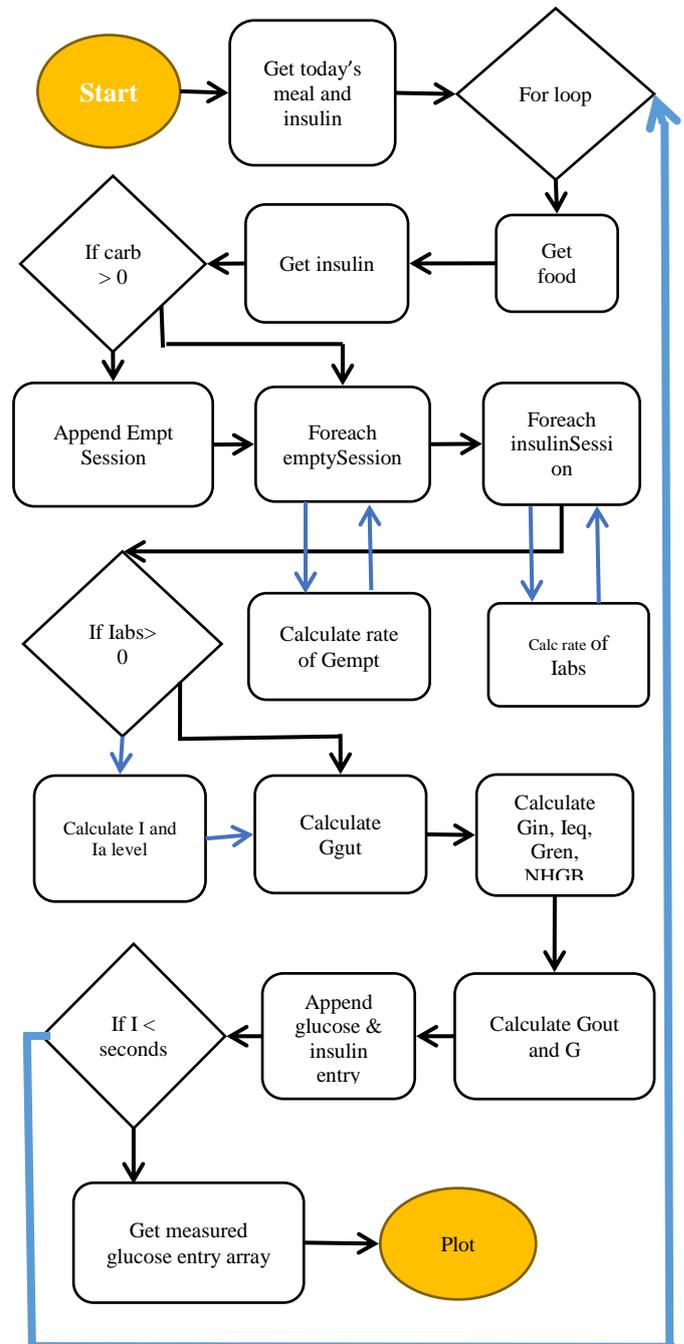

Fig 1: Algorithm Flow Chart of the Simulation

IV. RESULT AND DISCUSSION

The application has been successfully built with the following figure showing the main four sections of the application. The user interface was built by employing the concept of familiarity to help user understand the application easier. Buttons have been placed in familiar spots where users are accustomed to from using other famous applications. This is shown in the following figure with the buttons on the bottom of the pages used to travel between the main sections while buttons on top used to trigger other extra functions existed on a section. This practice of providing similar user interface give users familiar experience and remove the learning curve when using the application [17].

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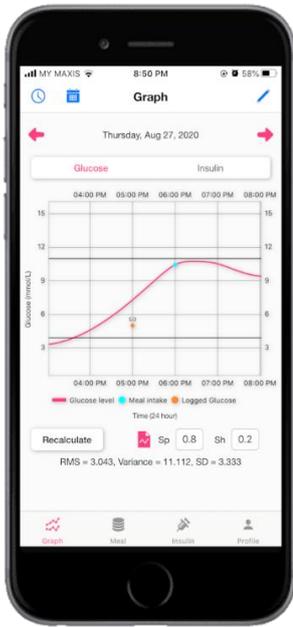
Fig 2: Main section of the application

Fig 2 above shows the main section of the application with its user interface, UI. The main section contains the simulation of blood glucose and plasma insulin level against time. It's is where users can see the results of their input to their simulated blood glucose level. From here, they can navigate to various section of the application such as the input sections using the tab button at the bottom of the screen, or to their previously simulated blood glucose level by changing the date of simulation. Below the graph are two insulin-sensitivity parameters S_p and S_h which are patient-specific and vary from person to person. The application calculated the values of these two parameters by taking their input data and iterate different values of the parameters that best fit their measured glucose values.

The second section is the meal input section where it handles meals to be inserted by users. The third section is the insulin's input section for users to insert their insulin injections details. The last one is a profile section which asks user's information. Each of the section add information needed to simulate glucose and insulin level.

Fig 3 shows the two section for input of meal and insulin respectively for the application. On the left is how the user insert their meal intake while on the right is how they enter their insulin intake.
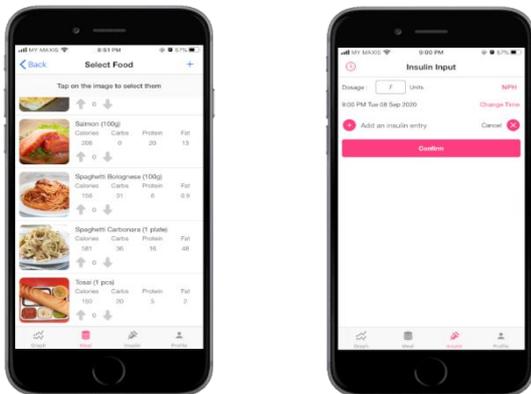

Fig 3: Input section of the application

V. VALIDATION

The task of validating the model used in the application has already been done by Lehmann & Deutsch [13] where they used their model with a clinical patient's data that weigh 70kg, male, insulin dependent diabetes patient and on a three times daily insulin regimen and proved that the model can satisfactorily simulate T1DM patients. In this section, their simulation that was done by computer was replicated by our application on the mobile phone. They however, did not state the exacts input data used in their simulation and there are some information needed that are missing such as the amount of insulin taken the night prior to the day of simulation and the initial state of the simulation such as plasma glucose, plasma insulin level, glucose level in the gut from the day before and etc. As a result, the application was not able to replicate the simulation exactly as in Lehmann and Deutsch [13] paper. Estimated input data was used in the application's simulation. As we can see from the Fig 4, the application's simulation is similar to the one simulated by Lehmann Deutsch with root mean square error, RMSE of 3.043. The biggest difficulty in trying to replicate is probably the absence of initial state data such rate of emptying of stomach and rate of change of plasma insulin. At = 0 h, we can see that the blood glucose from Lehmann & Deutsch was going at a downward slope indicating the presence of insulin action from the night before which is logical since NPH insulin, the one that is used by this patient, is advisable to be taken at bedtime [18]. The amount of insulin and the time at which this insulin was taken however was not mention and hence, an estimated amount of insulin at time t = 0 was used in the application in an effort to replicate the insulin from the night before. Since there will always be a delay in insulin action from the moment it was administered to the moment it starts to reduce the blood glucose level, a slight upward curve can be seen for the application's simulation starting from t = 0 before it goes back downward. This explains the dissimilarity between the two curves. However, the difference between the two curves were not that large for the most part.
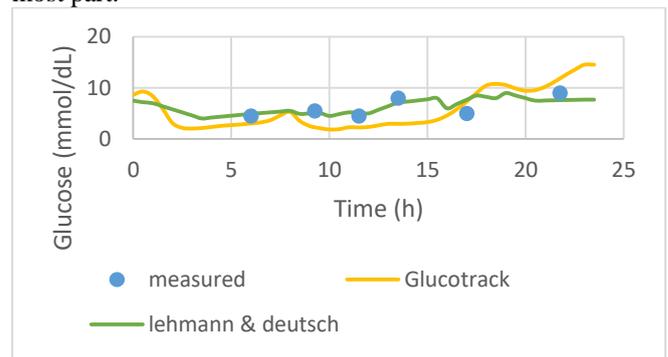

Fig 4: Comparison of glucose level against time

As for the accuracy of the application's prediction compared to measured glucose level of the clinical patient, it can be said that although the simulated glucose level from the application can be close to the measured glucose at times, there are still huge inaccuracy that can be observed along the simulated glucose curve that may indicate some unreliability of the application.

The application however can show the trend and impacts of perturbationslike meal and insulin intake to blood glucose level which is promising as educational tool for T1DM patients. This feature of simulation of estimated future blood glucose can give an added value and provide an additional tool for T1DM patient to use to better manage their blood glucose. Another thing that the application is capable off is to show the impact and the difference of taking insulin at different time relative to meal time have on their blood glucose control. Since every insulin have an onset time, which is the duration between the time when insulin was administered to the time of insulin action, the users can use the simulation feature of the application to educate themselves of taking insulin at different time and also why it is a commonly accepted practice to take regular insulin at 15-30 minutes before a meal [19].

VI. CONCLUSION

The application is able to simulate and predict T1DM patient blood glucose level trend from their carbohydrate and insulin input data. However, the simulation can also be slightly inaccurate at times. The accuracy of simulation is dependent on how accurate the input data of the patient provided and the mathematical model used by the application. Overall, the simulation feature of blood glucose from input data of diabetes user can be a good educational tool and help people with diabetes better manage their condition. Although the simulation feature was developed with the intention to predict future blood glucose of diabetes patient, the current mathematical model used is not able to perfectly predict glucose level from just input data of meal and insulin intake. A more comprehensive, non-linear mathematical model of glucose-insulin dynamics needs to be used for future improvement of the application. The model also needs to consider the impact of physical activity on the blood glucose of T1DM patients.

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