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Smart Artificial Pancreas with Diet Recommender System for Elderly Diabetes

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Abstract: This investigation presents a smart artificial pancreas (AP) for treating Type 1 Diabetes Mellitus (T1DM) in elderly which simultaneously automates the insulin administration but also diet recommender system using implicit carbohydrate (CHO) measurements. Three main components of the AP are: *(i)* long-term model of physiological dynamics, *(ii)* model predictive controller and *(iii)* a diet recommender algorithm which uses implicit CHO measurements. We first show that long-term dynamics are important for capturing the food influences on blood glucose levels and to maintain within admissive bands. The diet recommender algorithm fuses the insulin infusion information of the MPC, long-term model, average CHO and its variations to recommend diet and its pattern. The proposed artificial pancreas with diet recommender system is illustrated using studies conducted on elderly patients with T1DM based on clinical trials conducted at Jothydev's Diabetes Research Centre, Trivandrum, India. Our studies shows that the proposed AP not only automates the insulin infusion but also provides a recommender system for diet.

Keywords: Artificial Pancreas, insulin administration, food dynamics, carbohydrate (CHO), recommender algorithm.

1. INTRODUCTION

Diabetes is emerging as an epidemic in India and the reason for most of the cardio-vascular diseases related deaths Mohan et al. (2007). The vast majority of patients have type 2 diabetes (T2DM), which has a complex etiology primarily driven by insulin resistance and progressive decline in insulin secretory capacity. Type 1 diabetes (T1DM) which accounts to 4-5% of the total cases, results from absolute insulin deficiency and can set in at any age group with majority affected being children Pickup and Keen (2002),With increasing life expectancy in diabetes, subjects with T2DM on multiple oral therapies after 1 to 2 decades might behave very similar to those with T1DM that is, profound glycemic variability and significant hypoglycemic and hyperglycemic excursions. Therefore such patients are completely dependent on insulin administration for maintaining their blood glucose level (BGL) and closed-loop insulin pumps called artificial pancreas are becoming popular Katsarou et al. (2017). In elderly patients with long standing T2DM and with T1DM, the BGL will be highly fluctuating from hyper to hypo due to multiple factors such as co-morbidity, poly pharmacy, hormonal variations altered pharmacokinetic and pharmacodynamic properties, changes in vital signs due to ageing etc.Few of these factors have short-term effects and could be detected using BGL measurements, others have long-term effects e.g., multiple drug intake with insulin. Therefore, to automate insulin administration, multiple factors leading to poor glycemic control should be considered. Furthermore, diet influences the elderly patients. The quality of diet, quantity of diet and timing has significant influence on BGL control. Typically in clinical practice, a dietician in a diabetes team provides advices on food choices. However, there is an unmet demand for an AP which could combine a recommender system in an AP.

The available literature in AP could be broadly discerned into two broad categories: *(i)* physiological models and *(ii)* control algorithms. The models are categorized as linear or non-linear. Similarly, they could describe short-term or long-term behaviours of the glucose dynamics. Widely

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used physiological models are proposed by Bergman et al. (1981),Bergmans' model uses minimum model parameters and is called the *minimum model* Cobelli et al. (1986) proposed a modified minimal model which separated glucose generation from its utilization and Hovorka et al. (2002); Cobelli et al. (2009), the models are non-linear. A non-linear delay differential model was proposed in De Gaetano and Arino (2000) which provides a comprehensive dynamics of the physiological models. A model for meal dynamics and a simulator (UVa/PADOVA Type 1 Diabetes Simulator) was proposed in Dalla Man et al. (2007) . Roy and Parker (2007) proposed a model based on Bergman minimal model which incorporates exercise effects on plasma glucose and insulin level. In Kanderian et al. (2009) a model was proposed that captured the effect of insulin on the blood glucose concentration in T1DM patients with appearance rate in food. Similarly, linear models based on postprandial breakfast excursions of T1DM was proposed in Kirchsteiger et al. (2011). In Magdelaine et al. (2015) a linear and long-term model was proposed which could capture the variations over 48 hours. This model is very useful for capturing long-term deviations and constant basal insulin rate which is dependent on BGL within a target range.

As for controllers, Proportional-Integral-Derivative (PID) controller is the simple approach which was used in Medtronic 670G Chee et al. (2003); Marchetti et al. (2008); Ly et al. (2017); Ginsberg and Mauseth (2019). The limitation in this control technique is disturbance handling and information incorporation. This issue can be solved by using fuzzy technique, the decision making feature of fuzzy logic helps to handle insulin infusion decisions based on patient conditions was studied in Atlas et al. (2010) and was used in MD-logic AP. However, these control methods were primitive and were not able to embed available information in terms of food dynamics. More recently, model predictive control (MPC) has emerged as a promising technique due to its ability to fuse information with model and make predictive decision which can automate insulin administration, Non-linear MPC was proposed for the Hovorka model in Hovorka et al. (2004). These results illustrated that the MPC could help smartly automate insulin administration to patients by fusing information (e.g., food intake). However, their complexity increases with non-linear models. The MPC relying on linear models and convex mathematical programming techniques have been studied in Ginsberg and Mauseth (2019); Bequette (2013); Zavitsanou et al. (2015); Gondhalekar et al. (2016). Therefore, MPC design on linear models and capturing long-term impact of insulin administration and food on elderly patients with T1DM is required. Even though, existing APs can automate/control insulin infusion there is no control technique for insulin administration with diet recommendations. To our best knowledge an AP which can automate insulin infusion and also provide diet recommendations for diabetes in the elderly patients has not been proposed in the literature. Our objective in this paper is to develop one such controller. The main contributions of the paper are:

(1) An AP which simultaneously performs insulin administration and diet recommendation for T1DM in elderly patients.
(2) A diet recommender algorithm which provides inputs to diet and its pattern.
(3) Clinical studies showing effectiveness of the AP and recommender system.

The paper is organized as follows: section 2 describes about the problem formulation along with motivation. Section 3 discuss more into AP with diet recommendation algorithm. Results of MPC and diet patterns are shown in section 4. In section 5 conclusions are discussed.

2. PROBLEM FORMULATION

2.1 Motivating Example

Consider the clinical data shown in Fig. 1 for an elderly diabetes patient in a restricted environment at Jothydev's Diabetes Research Center (JDC), Trivandrum, India. The patient has co-morbid conditions and multiple drug intake whose physiological influences are complex to model. The food dynamics adds another complex dimension to the problem. Consequently, one can see that the BGL fluctuates from being hyper to hypo and vice-versa. For example, a food consumption at 8:00 pm causes the BGL to raise at around 12:30 am for which an insulin is administered and this causes a hypoglycemic condition around 5:00 am and remains there for quite sometime, if external intervention is not made. Therefore, understanding long-term effects of food and insulin is essential for avoiding hyper and hypo -glycemic levels.

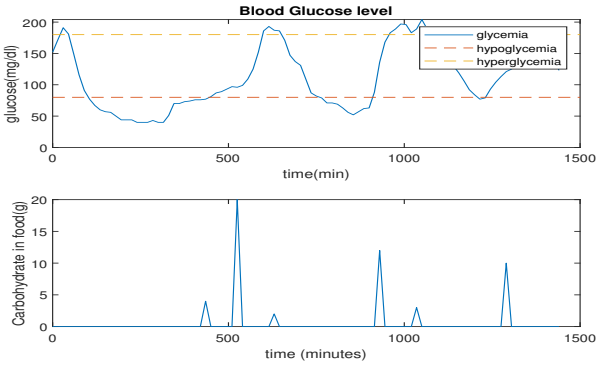

Fig. 1. Glycemia dynamics with food intake

Suppose that there is an automatic insulin administration using AP which uses a short-term model and MPC. Now consider that we start the experiment with a BGL of 200 and insulin bolus is given to reduce it. However, over long time duration say 12 hours, one can see that the BGL increases which cannot be predicted by short-term models which are myopic to long-term impacts of the drug intake and food dynamics. One can conclude from this example that a MPC with long-term impact is required for understanding food intake effects. Similarly, a recommender system for diet and its pattern is highly desired.

2.2 Problem Statement

The problem considered in this paper is the design of AP with a diet recommender system. However, the following challenges need to be handled:

(C1) Understanding impact of food with co-morbid and multiple intake requires understanding long-term behaviours of the physiological model.
(C2) Designing an AP which can perform both insulin administration and diet recommender system is a challenging task as food influences depend on aspects such as preparation, recipe etc.
(C3) Studying the performance of such an AP in clinical conditions is a challenging task.

Rest of the paper will address the challenges above and propose an AP which performs both insulin administration and food recommendation.

3. SMART ARTIFICIAL PANCREAS WITH FOOD RECOMMENDER SYSTEM

This section presents a smart artificial pancreas which can also perform diet recommendations addressing challenges *(C1) – (C3)*. We use the long-term model proposed in Magdelaine et al. (2015) to model the impact of glucose/insulin dynamics over long-time periods to address challenge *(C1)* . This model is then used as prediction model to compute the insulin infusion rate using MPC. We use the carbohydrate (CHO) information of typical food and its variations to design a diet recommender system overcoming *(C1)* . Finally, we studied the role of recommender system using clinical trials conducted in JDC to address *(C3)* . In the rest of the section, we present the different components of our smart artificial pancreas.

3.1 Long-term Model

Notation: In our analysis, we use $i(t), d(t)$ and $g(t)$ denote the insulinemia, rate of change BGL due to digestion and BGL, respectively. In addition, k_1 represents the endogenous glucose production, k_b glucose absorption rate and the glucose decrease rate is given by $-k_{si}i(t)$. Similarly, T_u represents the second order insulin dynamics, $u(t)$ the insulin infusion rate V_i the insulin volume and CHO in the meal is denoted as $r(t)$

Following Magdelaine et al. (2015) the state-space form of the long term model is

$$\dot{x}(t) = \begin{bmatrix} 0 & -k_{si} & 0 \\ 0 & 0 & 1 \\ 0 & -\frac{1}{T_u^2} & -\frac{2}{T_u} \end{bmatrix} x(t) + \begin{bmatrix} 0 \\ 0 \\ \left(\frac{k_u}{V_i}\right)/T_u^2 \end{bmatrix} u(t) + \underbrace{\begin{bmatrix} (k_1 - k_b) \\ 0 \\ 0 \end{bmatrix}}_{E} + \underbrace{\begin{bmatrix} d\,(t) \\ 0 \\ 0 \end{bmatrix}}_{F} \tag{1}$$

$$y(k) = [1\ 0\ 0]\, x(t)$$

where $x\,(t) = \left[\, g\,(t)\ i\,(t)\ \dot{i}\,(t) \,\right]^T$, u(t) is the insulin infusion and $d\,(t)$ is the "disturbance" from digestion. Besides, digestion dynamics can be represented by the state-space model:

$$\dot{x}_{dig}(t) = \begin{bmatrix} 0 & 1 \\ -\frac{1}{T_r^2} & -\frac{2}{T_r} \end{bmatrix} x_{dig}(t) + \begin{bmatrix} 0 \\ \frac{(k_r/V_B)}{T_r^2} \end{bmatrix} r(t) \tag{2}$$

$$d(t) = [1\ 0]\, x_{dig}(t)$$

where $x_{dig}\,(t) = \left[\, d\,(t)\ \dot{d}\,(t) \,\right]^T$.

3.2 Model Predictive Control of Long-term Model

The MPC uses the long-term model to predict the future blood glucose concentration depending on the insulin infusion rate and CHO of the food using the disturbance model in (2). Since we plan to implement the MPC in a digital computer, the state space model should be discretized. We use k to denote the discrete time-instants where the model evolution is recorded, i.e., the sampling time of the controller. Next, we use N_p and N_c to denote the prediction horizon (i.e., the time steps for which the model is predicted forward in time) and the control horizon (i.e., the time for which we plan to reset the control). Now consider the measurement equation to be

$$y(k) = Cx(k) + E + e(k) \tag{3}$$

where $e(k)$ represents a bounded white noise which is independent and identically distributed with zero mean and a known bounded variance σ^2. The MPCs' objective is to minimize the BGLs' variations from a reference set-point and without significant deviations in insulin infusion by deciding the insulin infusion to the patient. The constraints are the physiological dynamics, limits on the insulin administration, slew-rate on the insulin infusion and the bands within which the BGL has to be maintained. We formulate the MPC design as an optimization problem given by,

$$\begin{aligned} &\min_{U} \ \ \mathcal{J} = (Y - Y_R)^T Q (Y - Y_R) + \Delta U^T R \Delta U \\ &s.t. \\ &\quad x(k+1) = Ax(k) + Bu(k) + E \\ &\quad y(k) = Cx(k) \\ &\quad u_{min} \leq u(k) \leqslant u_{max} \\ &\quad \Delta_{min} \leq \Delta u(k) \leqslant \Delta u_{max} \\ &\quad y_{min} \leq y(k) \leq y_{max} \quad k = 1, \ldots, N_P \end{aligned} \tag{4}$$

(5)

where $Y = [y(k+1), y(k+2).....y(k+N_P)]^T$ are predicted blood glucose concentration, $\Delta U = [\Delta u(k), \Delta u(k+1).....\Delta u(k+N_P-1)]^T$ are slew rate of the insulin administration and $Y_R = [y_R(k+1), y_R(k+2), ..., y_R(k+N_P)]^T$ are the reference trajectory or the desired glucose concentration. The MPC computes the optimal insulin infusion rates based on the current measurements on BGL which is influenced by the food intake. The MPC uses a receding horizon approach, i.e., it uses the first computed insulin infusion rate and discards the other values. In the next step, the prediction step is extended to the next time-horizon and the procedure repeats. This way MPC could correct its future inputs based on current measurements even with an approximate model. This is the feature we make use for providing implicit CHO measurements used in the diet recommender algorithm.

3.3 Diet Recommender Algorithm

Calculating the impact of food intake and its pattern is a complex task. Usually glycemic index is a measure used to indicate whether the diet is good for diabetic or not. However, determining glycemic index is a complex task and while it has been reported for simple foods such as rice or polished rice. Finding glycemic index for mixed meal is a challenging task as it depends on the preparation, recipe used and other factors which are wholly exogenous and time-varying. Therefore, measuring

glycemic index for individual patients is rather difficult to build in an artificial pancreas. Alternatively, approximate CHO measures of food are available and the variance for different preparation could be obtained. This is the basic idea of our diet recommender algorithm.

In the diet recommender algorithm, we use a set of mixed meals is represented by the set $\mathcal{M} = \{m_1, m_2, \ldots, m_l\}$, where $m_i \quad \forall i \in \{1, \ldots, l\}$ represents the mixed meal. In addition, the mean, minimum and maximum values of m_i are denoted by μ_{m_i}, $\min_{m_i}$ and $\max_{m_i}$, respectively. Fusing this information with the long-term model and MPC, we get the implicit CHO rates of the patients' diet. To this extent, we use a stochastic framework wherein the AP computes the optimal insulin infusion using the MPC algorithm in (4). Since the physiological dynamics is very slow, we solve the MPC for μ_{m_i}, $\min_{m_i}$ and $\max_{m_i}$ CHO values and compute the insulin administration. Then we define the diet quality as

$$DQ_i = e^{-\left(\frac{\sum_k^{N_p} \|u_i(k)^* - u_i(k)_j\|}{\mu_u}\right)} \; j \in \mu_{m_i}, max_i, i \in \{1, \ldots, l\} \tag{6}$$

where μ_u and u^* define the average insulin infusion rate and optimal insulin infusion rate, respectively. The above measure provides implicit measurements of CHO using patients long-term model. This way even the influences of multiple drugs or co-morbid conditions could be accommodated as well. This measure will provide the CHO measurements implicitly without having to worry about the recipe or food preparation. This DQ will then serve as a measure to recommend suitable diet for the patient. The flowchart for recommending diet and evaluating quality of food is shown in Fig. 2

Diet Pattern: Diet pattern also has significant influence on BGL as well. To obtain the pattern based on the implicit CHO value obtained from the recommender, we perform analysis for different feasible scenarios (continuously spaced diet or different time-spaced) on the long-term model and compute the optimal diet pattern for either the same mixed meal or for different ones which takes minimum insulin infusion while maintaining patients within the bounds.

4. RESULTS

This section presents the simulation and clinical trial results using the long-term model for T1DM with food intake patterns of an elderly patient taken at JDRC, Trivandrum. The parameters used in our study are shown in Tab. 1.

Table 1. Values of Parameters

Parameter	Value	Units
M	72	kg
k_{si}	197	$(mg/U)min^-1$
T_u	122	min
k_1	1.94	mg/dl/min
k_b	128/M	mg/dl/min
k_u/V_i	0.0556	min/dL
T_r	183	min
k_r/V_B	0.0024	min/dL
V_i	$2.5 * V_M$	dL

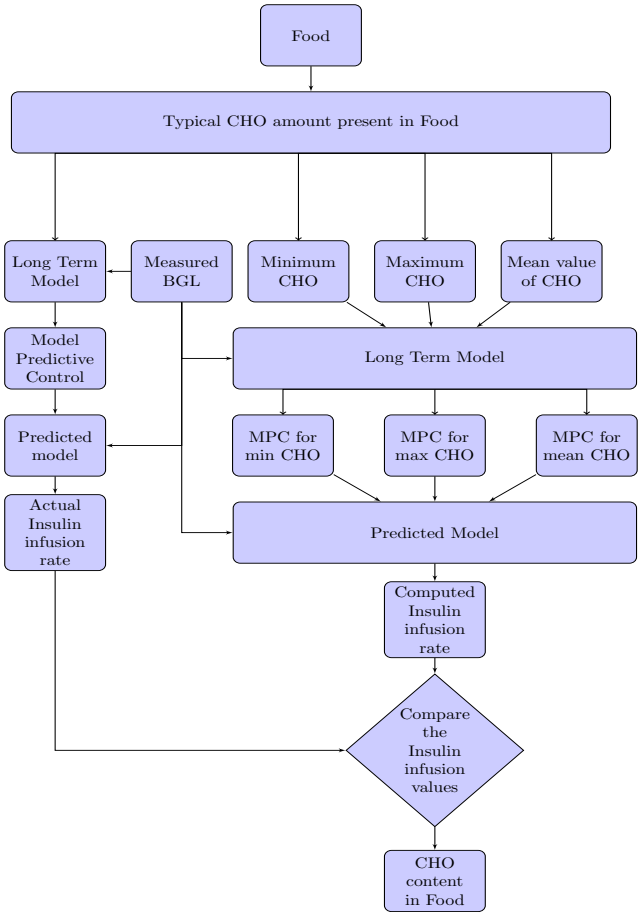

Fig. 2. Flowchart for Diet Recommendation

The results of the MPC for actual blood glucose measurements with mixed meal intake with diet pattern is shown in shown in Fig. 3. It could be observed that the food intake is distributed over time and the MPC maintains the BGL within the bounds for variations of CHO between 5-20 g. This is the optimal insulin infusion rate for the diet considered and its pattern.

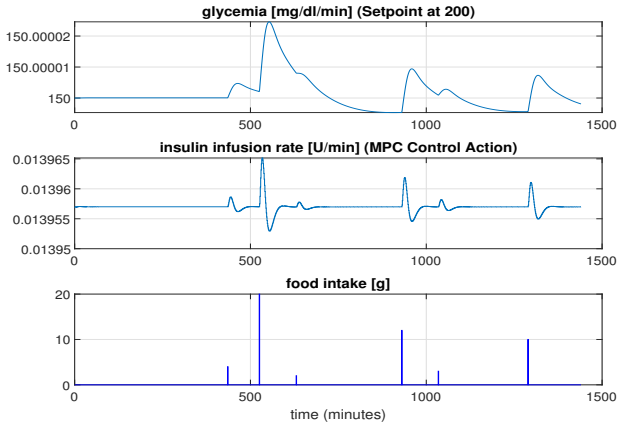

Fig. 3. MPC action on BGL

4.1 Diet Recommender Studies

In our study, we consider the mixed meal with a CHO of 80 g in average preparation and which could go up

to 150 g and a lower bound of 30 g. Assuming that the patient consumes the food at 10 min after the experiment, the variations in the BGL and insulin administration for the maximum and minimum cases are shown in Fig. 4 and Fig. 5, respectively. While explicit measure of CHO is not possible for mixed meal due to variabilities in the preparation. The long-term model based MPC would determine the CHO implicitly using the diet quality. It could be observed from Fig. 4 that the insulin infusion rate is about 0.06483 [U/min] is required after food but drops down to 0.016 [U/min] after the 260 minutes. One can also see the capability of long-term model to capture the influence for longer time-spans. Similarly, the control action for the mixed meal considered for a minimum CHO intake, i.e., 30 g is shown in Fig. 5. The insulin infusion rate is at 0.02573 [U/min] computed by the MPC using the long-term model. The measure DQ is used to ascertain the food quality and CHO content without requiring to measure the CHO levels. Further, the diet recommender could use this value to advise the patient on the diet intake and preparation.

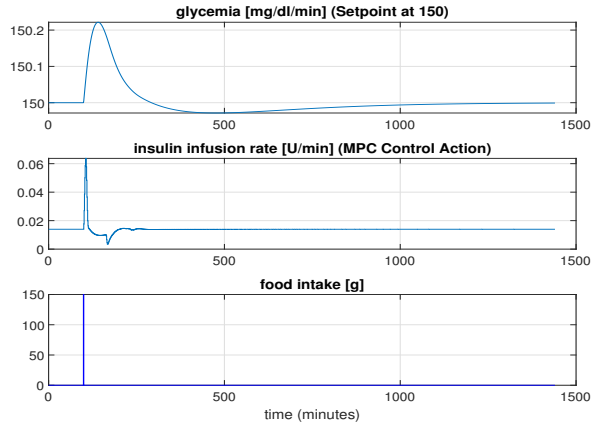

Fig. 4. MPC action for maximum CHO Food

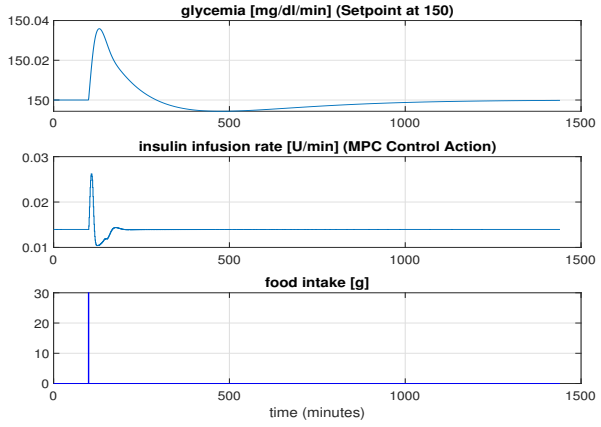

Fig. 5. MPC action for Minimum CHO Food

4.2 Recommender for Diet Pattern

To anlyze the food pattern, we consider two scenarios wherein the patient takes a diet with 154 g per day. We consider two scenarios wherein the patient consumes the food with CHO content being 54 g, 48g, 24g, and 28g, respectively. Instead of one time-step input as before. We first consider the scenario wherein the food is consumed in an interval of 1 hour as shown in Fig. 6, we see that the insulin infusion of 0.118 is required for the considered duration. Second scenario we consider the patient to consume food in a 2 hour interval and the insulin infusion rates are computed as shown in Fig. 7. One could see that the insulin administration rate comes down to 0.0914 U for the same time-period. This results shows that fasting for long time-slots even after high CHO inputs helps in reducing the insulin intake significantly. This could be identified from off-line simulation on the food CHO estimated by the recommender system. Based on the food preparation and patient requirement different patterns could be recommended.

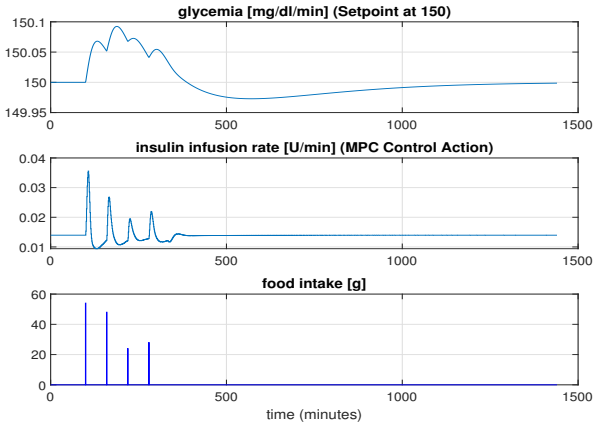

Fig. 6. MPC action for CHO with 1 hour time-span

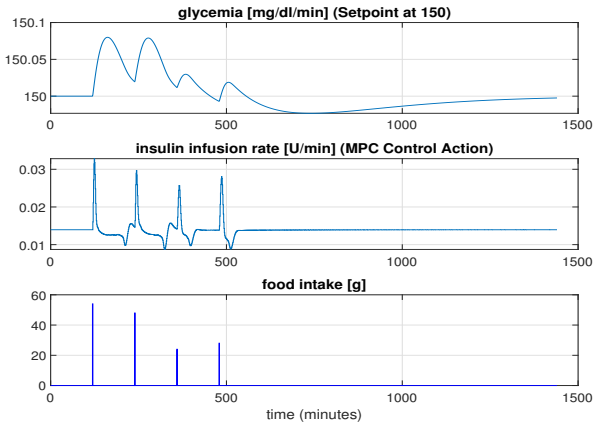

Fig. 7. MPC action for CHO with 2 hour span

The results demonstrated that the proposed smart artificial pancreas can simultaneously perform insulin administration and also recommend suitable diet and its pattern. Furthermore, we also obtain an implicit method to understand CHO levels in the food without having to measuring them. Moreover, as CHO depends on numerous factors such as preparation, recipe and others, the proposed smart artificial pancreas will help reduce the complexities associated with its measurement using

diet quality measure. Furthermore, our studies showed that long fasting times could reduce blood glucose levels significantly which was found using our long-term model and smart artificial pancreas.

5. CONCLUSION

This paper presents a smart artificial pancreas which can simultaneously determine the optimal insulin infusion and also acts as a diet recommender. It had three main components: long-term model, model predictive control and recommender algorithm. Using the insulin infusion rate from the MPC, the food CHO was measured implicitly. Then this was used to determine the diet and its pattern. We showed through simulations on actual data that the proposed smart artificial pancreas is suitable for simultaneously maintaining blood glucose levels and also recommending diet and its pattern. Consequently, the proposed smart artificial pancreas could help reduce deaths and serious complications due to diabetes. Extending the proposed approach using a stochastic MPC approach is the future course of this investigation.

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