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PATIENT FACING SYSTEMS

Blood Glucose Regulation for Post-Operative Patients with Diabetics and Hypertension Continuum: A Cascade Control-Based Approach

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Abstract

Management of glycemic level in post-operative condition is critical for hypertensive patients and the post-operative stress may results in hyperglycemia, hyper insulin and osmotic diuresis. Recent medical research shows that diabetic and hypertension hands together in a significant overlap in its etiology and its disease mechanism. It is clear that there is a call for monitoring in the parameter and controlling the glucose level particularly in the presence of hypertension. This paper proposes the novel complex (cascade) control system to control the insulin infusion level particularly in the presence of hypertension. Based on the requirements the structure has been designed and the simulation results indicates that the proposed control strategy shows better results and may achieve potentially better glycemic control to the hypersensitive diabetic patients.

Keywords Optimal insulin infusion · Cascade control · Hypertension · Mathematical model

Introduction

Over the past 50 years, there is a drastic increase in diabetes mellitus worldwide. The frequency of diabetes in 2000 was approximately 3% and is estimated to grow to 5% by 2030 [1–3]. This increment decodes the diabetes from 171 million in 2000 to well over 350 million in 2030. [4] Guru Shankar *et.* al. tested type 2 diabetes with hypertension from a large prospective data analysis of 12,550 adults and the results were almost three times with the normative counterparts and the results clearly indicates that clear sign of increased trend in hypertension in diabetic persons. Moreover, the amalgamation of diabetes mellitus and hypertension are the important risk factors for heart attacks and strokes, including atherosclerosis and its complications. Also recent medical research proves that there is an extensive overlap between diabetes and hypertension [5], and the same reflects the overlap in their disease mechanisms and etiology between the hypertension and diabetics. A study states that, 58% of people having considerable hypertension with diabetes and 42% people had normal blood pressure in diabetic [6]. Also this research shows the hypertension may occurs in approximately 40% with type I diabetic issues and the average of 50% to 80% of patients with type 2 diabetes accordingly [7]. The result of pathophysiological mechanisms (Fig. 1) shows that disease being serves to aggravate both diabetes and hypertension based on generic and acquired factors which influences to the development of cardiovascular disease (CVD) and renal disease [8–13]. Medical studies clearly depicts that the blood glucose and blood pressure has to be monitored continuously and the glucose level has to be maintained in perioperative condition which is done using complex control (cascade) system in this paper.

The cascade control structure is one of the widespread complex control structures in process industries which is implemented to minimize the disturbance in the form of progressive rejection properties of the controlled system in lieu of two different process parameters [14]. The same is implementation in this paper to control the insulin infusion with the blood pressure which is taken as variation disturbance. The variation of blood pressure and the blood glucose is cumulated that provides a frequent disturbance in the post-operative condition. The average value to be indicated along with an insulin level of further control in the infusion system. The design and investigation of the cascade control is very difficult in its architecture and the detailed parameter estimation often varies in the secondary control and the controller parameters can be

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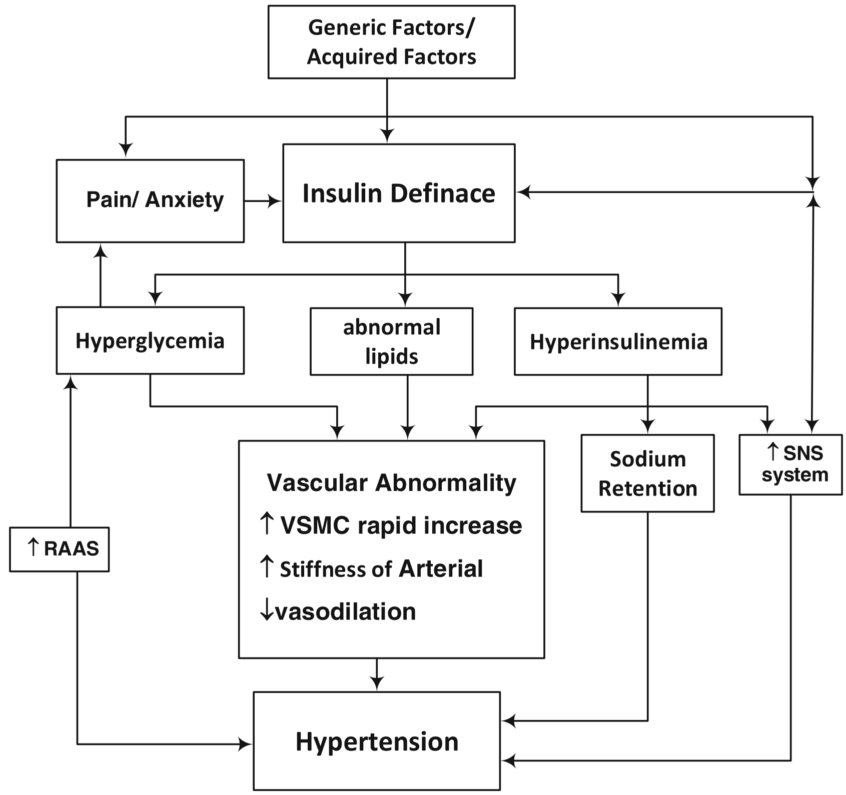

Fig. 1 An overview of pathophysiologic mechanism and development of hypertension in diabetic mellitus. (Chapter 34: Hypertension and Diabetes Mellitus. Hypertension: A Companion to Braun Wald's Heart Disease. PP 406–417 Copyright Elsevier, 2007 [113])

tuned in a conventional manual tuning to achieve the optimal insulin level [15].

With the concern of 25 different subjects, the post-operative BG and BP samples for every one hour were taken from various hospitals and the insulin infusion rate is determined with the average value of the BG variation cascaded with hypertension.

Materials and methods

Diabetic model

Basically the human body is a multi-dimensioned stochastic system depends on its generic factors, in that the pancreas is a system that works independently to control the blood glucose level in the human body. When the pancreas not generate insulin properly, the human body requires manually and the insulin has to be inject with the help of injection or using pump artificially to the patient which plays an important role called as artificial pancreas [16]. Based on the observations the model has to be established and the mathematical model finds the insulin and its resistance correlation to find its relationship, also the system describes the human diabetic system dynamics and the control system is designed based on human diabetic system cycle [17]. In this paper Bergman minimal model is used for insulin regulation and the dynamics of process indicates the mathematical model importance of diabetes and its management. Based on the observed parameters are approximated for a steady state process with the observed values for the post-operative patient and the frequently measured data along with sensor system errors with insulin availability and glucose compactness of the human system [18, 19].

$$\frac{dG_{Di}(t)}{dt} = -p_1 \;\; [G_{Di}(t) - G_{bd}] - x(t)G_{Di}(t) + [d(t) + U_{ic}(t)] \tag{1}$$

$$\frac{dX}{dt} = -p_2 X_{pg}(t) + p_3 I \tag{2}$$

$$\frac{dI_{Di}(t)}{dt} = -n[I_{ic}(t) - I_{bd}] + \gamma[G_m(t) - h] + r(t) \tag{3}$$

In the model G $_{Di}$(t) is considered as plasma glucose concentration in (mg/dl) and I_{ic}(t) & U_{ic}(t) signifies concentration of insulin in (μU/ml) & r called as external input insulin (U/h), The I is considered as basal value of insulin level in (ml U/L), G $_{d\ i}$(t) is external input glucose of the human body (mm/min)I $_{db}$ and G are glucose and insulin concentration before infusion of the insulin. The patient random sample parameters are considered as P1, P2, P3 in Table 1 and finally 'n' is narrated as rate of change of insulin, which is used in plasma layer (Min^{-1}). Values for the model parameters are estimated by Bergman theory denotes *in* a study of diabetic and normal human subjects are as follows [7, 20–22],

Table 1 Patient model Parameters

	P1	P2	P3
Sensitive Patient	0.028	0.025	0.000013
Hyper sensitive Patient	0	0.025	0.000013

Based on the observations and available values, Lynen and Banquette elaborated and formulated diabetic model process transfer function along with the process parameters [23]. in this model the intake meal has consider as meal difference and the related pulse value considered as scale of 3.33 g/min and the same duration the glucose along with the 5- g glucose meal consumed in 15 min time lag [24–26],

$$G_{pDi}(s) = \frac{-3.79}{(40s+1)(10.8s+1)} \tag{4}$$

Also the meal intake transfer function to be consider as follows

$$G_{pDi\ (Meal)}(s) = \frac{8.44}{s(20s+1)} \tag{5}$$

Blood pressure (SNP) model

The post-operative hypertension management is a complex task in surgery patients and need to maintain the diet level as per the patient's history and recommended values. In this condition blood pressure variation continuously monitored along with blood glucose to find the frequent variation and to stable the blood pressure need to infuse sodium nitro prusside (SNP) drug. SNP is considered as a significant drug of widely used for hypersensitive emergencies and this drug has immediate reaction within two minutes of time and it will reduce the blood flow rate based on the skull pressure rate, the infusion dose starts from 0.5 μg /kg/min and it can go up to 1 μg /kg/ min and this level depends on the requirement and control.

The Blood pressure modeling is a challenging task in biomedical instrumentation region and the control of blood pressure. Slate and co-authors (1980) [27] has developed the SNP infusion dynamic patient model with the help of associated data analysis for hypertension stabilization. Based on the behavioral properties the model as described below,

$$G_{PBP}(s) = \frac{\triangle Pdc\ (s)}{I_{snp}(s)} = \frac{ke^{-T_i s}\left(1+\alpha e^{-T_c s}\right)}{\tau s+1} \tag{6}$$

The descriptions of the model as follows;

- $\Delta P_{dc}(s)$ is denotes as variation in blood Pressure (mmHg)
- $I_{snp}\ (s)$ SNP Amount of infusion rate o (ml h^{-1}),
- k considered as sensitivity of the patient
- α denotes as index of recirculation,
- τ time constant,
- T_i signifies transport delay
- T_c time of recirculation.

The model has categorized in three different scenario like normal, sensitive and insensitive and these models will be measured in terms of sec. The model parameters [28–30] are shown in below Table 2 and the typical values are approximated value will vary based on person to person.

Control scheme (cascade control)

Cascade controller is one of the most popular and complex control system commonly used in process industries with the single manipulated output with the advantage of multiple measurements in the process. Cascade control was first introduced by Franks and worley [31] to improve the system performance with disturbances and to reduce the passive disturbances in the process.

In feedback system the disturbance corrective action will not happened until variable deviates from the set point and the control action happened after the deviation. So based on the discrepancies and improve the feedback control, an additional measurement introduced and this secondary controller, $Gc2{=}G_{c(Bp)}(s)$ is included in cascade form and the main controller, $G\ c_{di}$, as shown in Fig. 2, this modification will improve the response of the combined system. The proposed control scheme brings together in cascade and smith predictor merits and brings its best merits. Also the proposed PID based cascade structure provides the better closed loop performances with strained time constants process transfer functions and complex poles, with unstable poles or an integrator [32], similarly the outer loop controller design provides the better parameter identification with the help of simple algebraic approach. This design method creates the advantage of the standard forms and this will predict better performance of closed loop system. This paper uses the blood glucose level control of its primary blood pressure as a secondary parameter by which insulin can be infused [33, 34].

The insulin infusion rate is adjusted with the help final control element in the system by manipulating the obtained

Table 2 Hypertensive Patient model Parameters

Parameter	Hyper Sensitive	Sensitive	Insensitive
k	−9	−0.714	−0.179
α	0	0.4	0.4
τ	20	30	60
T_i	30	45	75
T_c	30	40	60

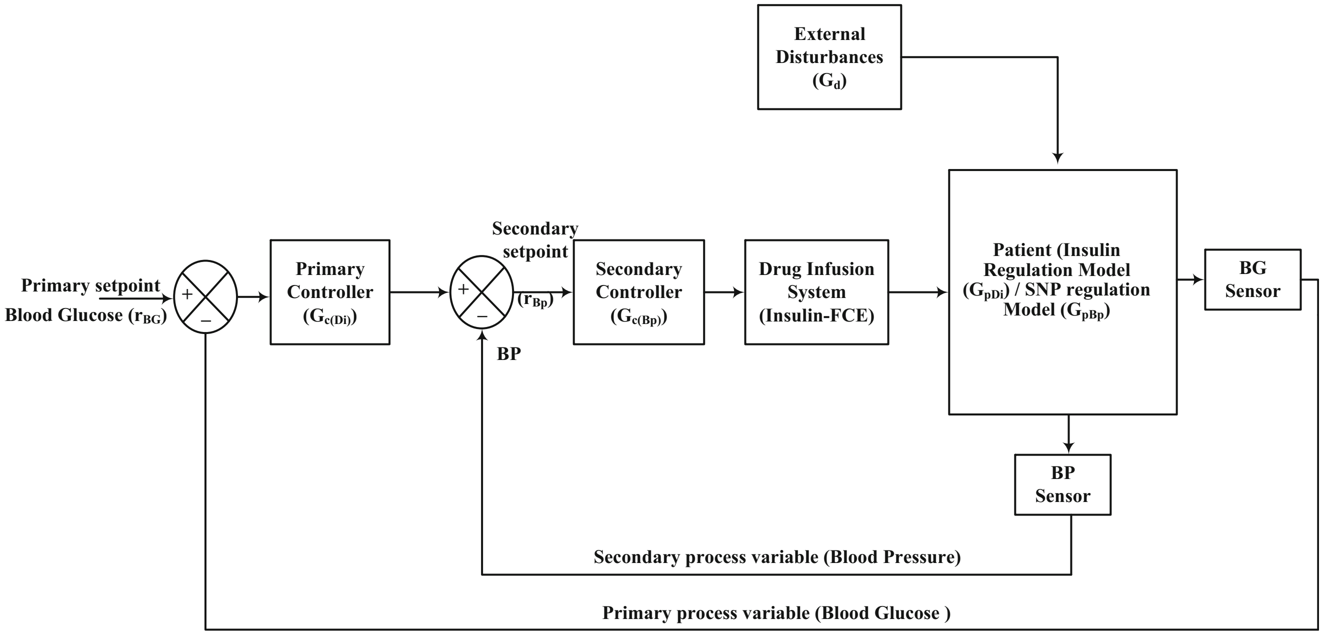

Fig. 2 Proposed Cascade control structure for blood glucose and hypertension kinetics

variables. Therefore, the detailed parameters are shown in Fig. 2 and the detailed descriptions of the control loop as illustrated as below.

- Set point – Desired value of Blood Glucose to the human system (r_{bg})
- Primary controller (master) - measures blood Glucose and asks the secondary controller for more or less insulin infusion ($G_{c\ (Di)}$)
- Secondary controller (slave) - measures Blood Pressure (G_{cbp})
- Actuator – Insulin Pump (FCE)
- Secondary process – Blood Pressure in Patient (G_{pBp})
- Inner loop disturbances - fluctuations in glucose variation
- Primary process – Blood Glucose stability (G_{pDi})
- Outer loop disturbances - fluctuations in the diabetic level,especially fluctuations in hypoglycemia (G_d)

Cascade control design

Tuning the cascade controller is a complex task and it follows two different stages. Initially need to tune the inner-loop controller [$G_{c(Bp)}(s)$] analyzed and tuned based on the secondary process values, based on the process parameters the secondary loop (inner) transfer function as described in [Equation (7)], to secondary process transfer considered is [Equation (8)] designed for outer-loop controller tuning [$G_{c(Di)}(s)$]. Based on the outer loop prediction the inner loop control design implemented based on PID controller using normalize tuning methods to obtain the desired output [28]. Once the secondary loop is tuned, the primary control loop also tuned with its effectiveness and the outer loop transfer function can be used to tune the controller performance.

$$Y_{Bp}(s) = \frac{G_{c(Bp)}(s)\ G_{pBp)}(s)}{1+G_{c(Bp)}(s)\ G_{pBp}(s)}\ r_{Bp}(s) + \frac{G_d(s)}{1+G_{c(Bp)}(s)\ G_{pBp}(s)}\ I_d \tag{7}$$

The inner loop (secondary) transfer function can be derived as

$$G_{c\ (Bp)\ Cl}(s) = \frac{G_{c(Bp)}(s)\ G_{pBp}(s)}{1+G_{c(Bp)}(s)\ G_{pBp}(s)} \tag{8}$$

Based on the above equation, the further analysis drives

$$Y_{BG}(s) = \frac{G_{c(Bp)}(s)\ G_{pBp}(s)}{1+G_{c(Bp)}(s)\ G_{pDi}(s)}\ r_{Bp}(s) + \frac{G_d(s)\ G_{pDi}(s)}{1+G_{c(Bp)}(s)\ G_{pBp}(s)}\ I(s) \tag{9}$$

$$G_{pDi(eff)}\ (s) = \frac{G_{c(Bp)}(s)\ G_{pDi}(s)G_{pBp}(s)}{1+G_{c(Bp)}(s)\ G_{pBp}(s)} = G_{c(Bp)}(s)\ G_{pBp}(s) \tag{10}$$

The relationship of the primary closed loop set point change has derived as,

$$Y_{BG}(s) = \frac{G_{c(Di)}(s)\ G_{pDi(eff)}(s)}{1+G_{c(Di)}(s)\ G_{pDi(eff)}(s)}\ r_{BG}(s) = \frac{G_{c(Di)}(s)\ G_{c\ (Bp)\ Cl}(s)G_{pDi}(s)}{1+G_{c(Di)}(s)\ G_{c\ (Bp)\ Cl}(s)G_{pDi}(s)}\ r_{BG}(s) \tag{11}$$

The observed equation clearly shows that the primary transfer function affected by secondary control loop. As per observations the primary controller response is slower compare to secondary control and the this control action is much faster than the primary loop to maintain the proper control strategy, so the secondary control consider as $G_{c\ (Bp)\ Cl} = 1$, based on available description of the primary control loop transfer function is defined as

$$Y_{BG}(s) \approx \frac{G_{c(Di)}(s)\ G_{pDi}(s)}{1 + G_{c(Di)}(s)\ G_{pDi}(s)}\ r_{BG}(s) \tag{12}$$

Results and discussion

The observation of proposed cascade model preserved and treated with both the diabetic, hypertension measurements are shown in Fig. 1. The cascade protocol not only reduced the disturbance in the system also improve the insulin infusion rate to hyper and hypo glycemic levels. Meanwhile, the results has been compared with the conventional feedback control along with the insulin infusion rate. This proposed system is considered the average value of carbohydrates intake along with the average glucose and blood pressure (BP) for simulating the control strategies shown in Table 3.

In this proposal PID based feedback method is used to compare with the proposed cascade model, also the diabetic patient model parameters are identical with cascade control, because the results need to compare the proposed scheme with the same model for further simulation. The cascade and feedback procedures adopted different type of patient parameters to deal with hyperglycemia along with periodic glucose level maintenance for post-operative patients. While the cascade control provides the enteral feed rate along with the hypertension input and the insulin infusion rate decreases based on the target, and the feedback control deliver higher insulin infusion rate compared with the proposed system and this action proves the cascade control performance.

This observation might be due to variation of the measuring parameters and the cascade system have the opportunity to reduce the insulin rate to $\pm 10\%$ compare with conventional methods, if the glucose increases in the blood afar from the upper limit (> 200 mol /L) the cascade provide the immediate response and infuse the insulin and control the HGI value along with the blood pressure variation, since the conventional control system loops does not consider hypertension variation and this negligence will infuse more insulin in volume infused while calculation, and it this variation considerably monitored to avoid uncertain glycemic levels. However, the new proposed methodology shows the noticeable difference between the feedback and cascade control results shown in Fig. 3.

The simulation of the proposed model has been carried out with MATLAB using diabetic and hypertension models to regulate the desired glycemic levels along with proper insulin infusion in the presence of blood pressure variation and meal disturbance. The performance of the cascade feedback control methods were verified and the response of each model is obtained and compared with each other. The achieved results are shown the levels of glucose for various patients patient's parameters and the combined responses shows the significant difference compare with feedback control strategy, especially the multiple disturbance process needs minimum settle down time by the proposed control scheme.

Figure 3 presents the combined simulations for the sensitive and hypersensitive respectively. The meal carbohydrates intakes considered as three times as breakfast, lunch and dinner and the glucose deviation has been considered as disturbance function, based on the simulations the insulin scaling factors has decide depends on the hypertension variation along with plasma glucose concentration. The simulation results are shown in Table 4 for the glucose regulation and the minimum and maximum glucose level and inulin level to accomplish the hypoglycemic scenarios. The maximum plasma glucose was detected when the insulin level in created during simulations. In Fig. 4, shows the combined simulation Meld response of continuous plasma glucose measurement and insulin infusion level, based on the scenario the details are observed that there is no instability in the system granting the observation error can be as high as 15%. In fact, a minor oscillatory actions were observed during the simulations mainly at the time of meal.

The controller parameters are tuned and injected based on the patient medical requirement and the Fig. 4 shows the performance of insulin level and the corresponding glucose variation for both control strategies as proposed, based on the outcome, the blood glucose variation depends on the sudden hypertension along with meal inputs, correspondingly the insulin infusion also increases to get back

Table 3 The analysis condition used for simulating the control strategies, here g cho consider as intake of carbohydrates in Grams

	Time	BreakFast in gcho	Plasma Glucose	BP	Time	Lunch in gcho	Plasma Glucose	BP	Time	Dinner in gcho	Plasma Glucose	BP
Diabetic Patient	8 AM	50	140	120/80	1 PM	65	135	120/90	8 PM	55	120	120/80
Diabetic + Hypertension patient	8 AM	50	160	140/90	1 PM	55	145	140/90	8 PM	50	135	140/90

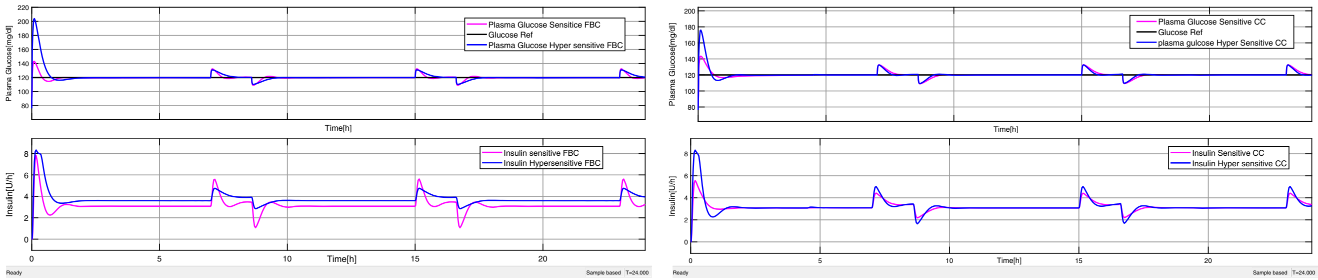

Fig. 3 Closed loop response of Feedback and cascade control loops with sensitive (Rose lines) and hypersensitive (blue lines) and black line denote as reference glucose mean value

Table 4 Comparison between the controls (Feedback- FBC and Cascade Control -CC) with the average values obtained based on the proposed control strategy

Control strategy	Feedback Control - FBC	Cascade Control - CC
Mean Blood Glucose [mg/dl]	158	142
Max Blood Glucose [mg/dl]	205	178
Min Blood Glucose [mg/dl]	85	81
% of time reach in [70–180] mg/dl	67.5	71.2
Mean Insulin [U/h]	1.3–5	0.83–4.5
Max Insulin level [U/h]	7.8	8.1

the desired blood glucose level. In that scenario the response time is very much important and the controller action should be fact and the lagging creates the unstable glycemic level, similarly this process inclination continues for multiple meals and reaches the maximum level in the presence of hypertension especially post-operative condition. To overcome this the cascade Controller is used to cast-off the disturbance and produce the stable insulin response are shown in Fig. 4, and the disturbance rejection minimize the sudden change and this will desired level of glucose. Finally, the unpredicted stress in physiologic parameters will influence clinical results variation. In addition, the hypertension to be continuously monitored and need to control the with help of additional drug infusion to the human body, also the excess of insulin infusion to the human body will increase the biologic effect like renal failure and need to monitor and infuse the proper insulin level to the human body.

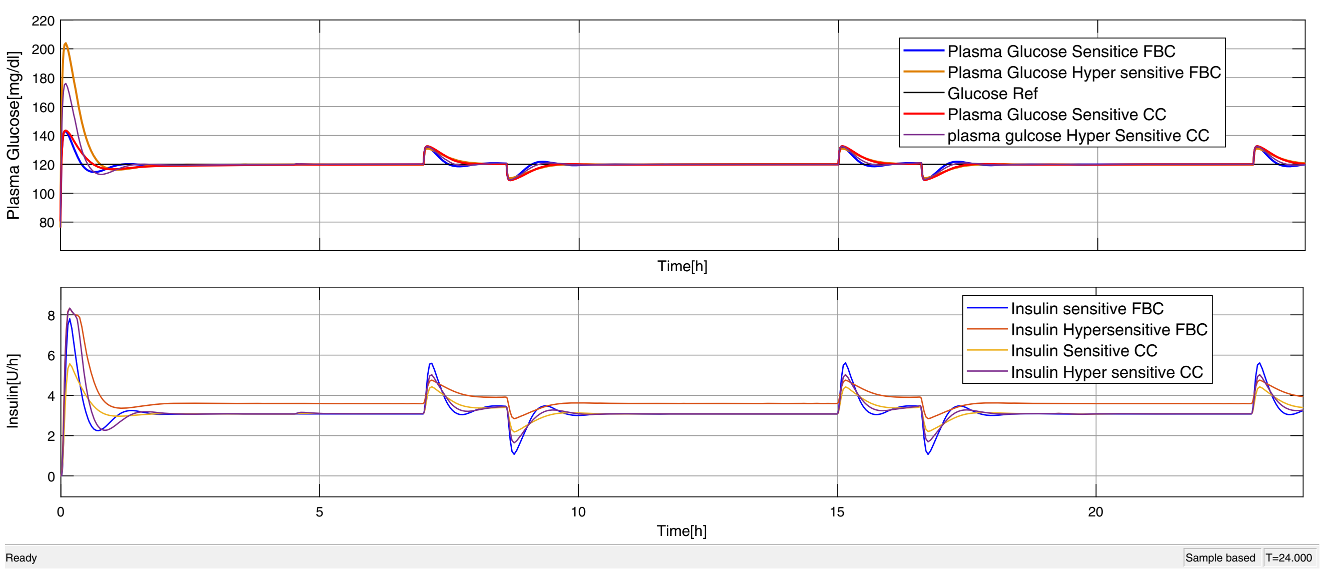

Fig. 4 Meld response of continuous plasma glucose measurement and insulin infusion level for feedback and cascade control strategies via simulated monitoring

Conclusion

This proposal introduces complex (cascade) control strategy of insulin infusion in lieu of plasma glucose stabilization along with blood pressure variance as disturbance. PID controller is proposed for secondary (inner) & primary (outer) control loop to achieve the optimal performance and robustness of the designed system and its parameters were tuned with the guarantee of convergence and stability of the insulin level. Blood pressure fluctuation plays a significant role in the simulation results and insulin control performance is optimized and compared with the classical feedback control system for Plasma glucose identification along with the disturbance rejection.

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