An Improved PID Switching Control Strategy for Type 1 Diabetes

Gianni Marchetti‡*, Massimiliano Barolo*, Lois Jovanovic†, Howard Zisser†,
and Dale E. Seborg†, Member, IEEE

*Department of Chemical Engineering Principles and Practice, Università di Padova (Italy)
†Sansum Diabetes Research Institute, 2219 Bath St., Santa Barbara, CA 93105
‡Department of Chemical Engineering, University of California Santa Barbara, Santa Barbara, CA 93106-5080

Abstract—In order for an “artificial pancreas” to become a reality for ambulatory use, a practical closed-loop control strategy must be developed and critically evaluated. In this paper, an improved PID control strategy for blood glucose control is proposed and evaluated in silico using a physiologic model of Howorka et al. [1]. The key features of the proposed control strategy are: (i) a switching strategy for initiating PID control after a meal and insulin bolus; (ii) a novel time-varying setpoint trajectory, (iii) noise and derivative filters to reduce sensitivity to sensor noise, and (iv) a systematic controller tuning strategy. Simulation results demonstrate that proposed control strategy compares favorably to alternatives for realistic conditions that include meal challenges, incorrect carbohydrate meal estimates, changes in insulin sensitivity, and measurement noise.

I. INTRODUCTION

People with type 1 diabetes must rely on exogenous insulin for survival. The current treatment method requires either multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII) delivered via a pump. Both treatment modes necessitate blood glucose (fingerstick) measurements throughout the day in order to determine insulin boluses for mealtimes; also, one to three injections or programming continuous infusion of short-acting insulin via CSII are required to maintain normoglycemia between meals. For people with type 1 diabetes, tight glucose control has been difficult to achieve due to the infrequent measurements, patient variability, and changes in insulin sensitivity due to exercise, stress, illness, etc. Consequently, there has been considerable interest in developing an “artificial pancreas”, a portable (or implantable) automated insulin delivery system that consists of three components: a glucose sensor which provides frequent measurements (e.g., every five minutes), an insulin infusion pump, and a control algorithm which calculates the appropriate insulin dosage for the current conditions.

During the past 30 years, a variety of glucose control strategies based on continuous glucose sensing has been reported. Since this literature has been reviewed in recent survey articles [2]–[5], we will not present a detailed review here. In summary, the control strategies include variations of the proportional-integral-derivative (PID) control strategy that is widely used in industrial control applications [6]. A PID control strategy is attractive for glucose control because it mimics the first and second phase responses that the pancreas beta cells use to control glucose.

This paper is concerned with developing an improved glucose controller that is based on a novel PID controller, bolus injections for meals, and a strategy for switching between them. Controller performance is evaluated for realistic conditions such as poor (meal) carbohydrate estimates, changes in insulin sensitivity, and measurement noise.

II. PHYSIOLOGICAL MODEL

Many physiological models have been proposed that describe glucose and/or insulin dynamics [1], [7]–[10]. In this paper, the simulation studies are based on the model developed by Howorka et al. [1] and the modifications reported by Wilinska et al. [10]. This model will be referred to as the “Howorka model”. It represents the relationship between input variables, subcutaneous insulin infusion rates (basal and bolus), and the output variable, intravenous glucose concentration. This model also includes a submodel for meal ingestion. The Howorka model is a nonlinear compartmental model with three subsystems for glucose, insulin, and insulin action. The values of the model parameters were determined from experimental data for both normal and diabetic subjects.

In order to simulate the measurement noise of the glucose sensor, a normally distributed random error, ε, with mean zero and variance equal to 0.00111 was introduced, \( G_m = G(1 + \epsilon) \), where \( G_m \) (mg/dL) is the measured value.

III. PID CONTROLLER DESIGN

A variety of PID control strategies have been developed for diabetes control and described in survey papers and review articles [2]–[5]. Most of the related evaluations have been based on simulation studies but experimental applications to dogs or humans have also been reported.

The PID controller calculates the insulin infusion rate that is released by the pump into subcutaneous tissues. The velocity form of the PID controller was used [6]. In order to reduce the effect of noise, the measured glucose concentration, \( G_m \), was filtered using a standard first-order filter [6]. Furthermore, a derivative filter was used in the controller itself.
In an initial study, the PID controller was tuned for meal challenges. However, it was not possible to avoid postprandial hypoglycemia unless the reset time was set to very large values (e.g., $\tau_f = 167$ h), which essentially eliminated the effect of integral control action. On the other hand, it is desirable to include integral action to deal with patient variability such as changes in insulin sensitivity. One solution to this problem is to limit the integral term by introducing upper and lower limits. With this constraint, the effect of the integral action for meal challenge is negligible compared to the effects of proportional and derivative action, but integral action will eliminate steady-state error (offset) in $G_m$ after insulin sensitivities changes. Based on these considerations, a novel controller tuning procedure was employed. First, $K_c$ and $\tau_D$ were tuned for meal challenges (correct CHO estimate, and 50% under- and over-estimates) using a simulation; PI and the performance index of equations (1)–(5), were the minimum allowable values of $K_c$ and $\tau_D$. Thus, Strategy C was essentially identical to Strategy A, the bolus-only approach, for these conditions. This experience motivated the development of the switching technique that is a key element of Strategies D and E.

B. PID control only

The PID control algorithm of Section III provides a basis for comparison because many previous studies have considered conventional PID control.

C. Bolus plus PID control

In this approach, the insulin bolus is introduced at meal time and the PID controller operates continuously.

D. Bolus plus PID control with switching criteria

The insulin bolus occurs at meal time but the PID controller is not initiated until a switching criterion is satisfied.

E. Bolus plus PID control with switching criteria and a time-varying glucose setpoint

The novel features of Strategies D and E will now be described in more detail.

First, we consider why a switching strategy is desirable. Preliminary simulations for Strategy C indicated that it is detrimental to have the PID controller active during and immediately after an insulin bolus. For this situation, the PID controller senses the increasing glucose level of the post-prandial response and consequently makes the insulin infusion rate greater than its basal value. This additional insulin release leads to hypoglycemia unless the controller is tuned very conservatively. Consequently, the optimal controller settings for Strategy C and the performance index of equations (1)–(5), were the minimum allowable values of $K_c$ and $\tau_D$. Thus, Strategy C was essentially identical to Strategy A, the bolus-only approach, for these conditions.

Improved glucose control for meal challenges and poor CHO estimates can be achieved by starting the PID controller after the meal and bolus occur. However, the specification of the switching time is important. If the PID controller is started too early, hypoglycemia can occur. On the other hand, if the PID controller is switched on too late, the post-prandial glucose peak may be very large and slowly decrease to the setpoint value. Our simulation studies have indicated that an effective switching strategy is obtained if the PID controller is started when one of two criteria is satisfied:

(i) $G$ reaches its peak value;
(ii) $G > 150$ mg/dL and $dG/dt > 1.5$ mg/dL min.

The 150 mg/dL threshold was selected because it is the peak value of $G$ for a correct bolus and Strategy A. The rate-of-change limit of 1.5 mg/dL min was chosen to be greater than the maximum rate of change for this same situation.

The rationale for these switching criteria is as follows. When the CHO estimate is either correct or too large, the PID controller switches on when criterion (i) is satisfied. Then the insulin infusion rate starts to decrease because $dG/dt < 0$. When the CHO estimate is too small, the bolus is also too small and thus when $G$ reaches the threshold of 150 mg/dL, $dG/dt$ is large. Consequently, after the PID controller is switched on, it immediately increases the insulin infusion rate, which is the correct action.
Next, we consider the rationale for using a time-varying glucose setpoint. During the post-prandial period, the blood glucose concentration is expected to increase, and then decrease. Consequently, it is appropriate to have a time-varying setpoint, $G_{sp}$, that reflects this expected behavior [1], [5]. The following strategy has been devised. When the PID controller is initiated, $G_{sp}$ should be set equal to the current filtered measurement, $G_f$, and then eventually decrease to the desired value of $G$, 80 mg/dL for this study. However, for the case of a CHO under-estimate, $G$ is still increasing when the PID controller is switched on. Thus, it would be inappropriate to force $G_{sp}$ to decrease right away. Extensive simulations have demonstrated that good glucose control is obtained when the setpoint trajectory is specified as:

$$G_{sp}(k^*) = \begin{cases} 
80 \text{ mg/dL} & \text{if } G_f(k^*) \leq 80 \text{ mg/dL}, \\
(G_f(k^*) - 80) \exp \left(-\frac{k^*}{\tau}\right) + 80 & \text{otherwise},
\end{cases} \quad (6)$$

where $k^* = k - k_{sw}$, $k$ (min) is the current sampling instant, $k_{sw}$ (min) is the switching instant, and $\tau$ (min) is a design parameter. For $k^* < 0$, $G_{sp} = G_f$. In order to avoid unexpected hypoglycemia, a lower limit of 80 mg/dL was used. The time-varying setpoint trajectory defined in (6) has the following properties:

- a. It is affected by the actual value of $G_f$, for every $k^*$;
- b. It varies from $G_f(k^* = 0)$ to 80 mg/dL;
- c. As $\tau \to 0$, $G_{sp}(k^*) \to 80$ mg/dL;
- d. As $\tau \to \infty$, $G_{sp}(k^*) \to G_f(k^*)$.

If $G$ increases, $u$ should increase as well. But when the time-varying setpoint trajectory defined in (6) is used, the error begins to decrease as soon as the controller is switched on. By contrast, for constant $G_{sp}$, the error would increase. Thus, for the new setpoint trajectory in (6), the derivative term in (5) was modified as,

$$D(k) - D(k-1) = \frac{\alpha \tau_D}{\Delta t + \alpha \tau_D} (D(k-1) - D(k-2))$$

$$-K_c \frac{\tau_D}{\Delta t + \alpha \tau_D} (G_f(k) - 2G_f(k-1) + G_f(k-2)). \quad (7)$$

Therefore, if the controller is switched on at the peak in $G$ (switching criterion 1 is satisfied), $G$ starts decreasing and the setpoint trajectory in (6) gradually causes $G_f$ to decrease to 80 mg/dL. In the case of a CHO under-estimate, the PID controller is switched on when $G_f$ reaches 150 mg/dL (switching criterion 2 is satisfied). But since $G$ is still increasing, the setpoint trajectory will initially increase and then eventually decreases to 80 mg/dL.

### V. SIMULATION RESULTS

The five glucose control strategies of Section IV were evaluated for two situations:

(i) Meal challenges and either a correct insulin bolus, a 50% under-bolus, or a 50% over-bolus;

(ii) Changes in insulin sensitivity during basal conditions: a 50% increase or a 50% decrease.

The incorrect boluses represent situations where the diabetic subject incorrectly estimates the CHO content of the meal.

The changes in insulin sensitivity were simulated by making the indicated change in all three of the insulin sensitivities for the Hovorka model [1]. In order to provide a fair comparison of Strategies A–E, each PID controller was tuned using the method described in Section III.

#### A. Results for meal challenges

The simulation results for a 75 kg patient and a 60 g CHO meal challenge are shown in the left side of Fig. 1 and in Table I. Results for Strategy C are not included in Fig. 1 because they are identical to those for Strategy A, as indicated in Table I and discussed in Section IV. Table I includes several metrics: the maximum and minimum glucose concentrations for each response, $G_{max}$ and $G_{min}$; the settling time $t_s$, and the total amount of insulin that was administered, $I_{tot}$. The settling time was defined to be the time at which the glucose concentration entered and remained with the desired range, 75 to 85 mg/dL.

Figure 1 and Table I indicate that the new switching control strategies (D and E) are superior to the standard control strategies (A, B, and C) for these meal challenges due to their smaller IAE values, shorter settling times, and smaller $G_{max}$ value for the under-estimated bolus. Strategy E provides the best control based on these criteria. The $I_{tot}$ values for the five control strategies do not differ significantly. Table I indicates that the $G_{min}$ values for Strategies D and E include small violations of the lower constraint of 60 mg/dL that was used in the controller tuning of Section IV. However, these violations can be eliminated by increasing the weight in the soft constraint for $G_{min}$ in (3) (e.g., use a value of 10,000 instead of 100).

#### B. Results for insulin sensitivities changes

The simulation results for the two insulin sensitivity changes during basal conditions and no meal are shown in the right side of Fig. 1. As described in Section IV, the tuning procedure for each controller determined the optimal value

<table>
<thead>
<tr>
<th>Control Strategy</th>
<th>Estimation</th>
<th>IAE $(10^{-4})$</th>
<th>$G_{max}$ (mg/dL)</th>
<th>$G_{min}$ (mg/dL)</th>
<th>$t_s$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>correct</td>
<td>1.40</td>
<td>150</td>
<td>64</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>under</td>
<td>4.69</td>
<td>202</td>
<td>80</td>
<td>&gt;18</td>
</tr>
<tr>
<td></td>
<td>over</td>
<td>1.68</td>
<td>122</td>
<td>40</td>
<td>&gt;18</td>
</tr>
<tr>
<td>B</td>
<td>-</td>
<td>1.97</td>
<td>228</td>
<td>67</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>correct</td>
<td>1.40</td>
<td>150</td>
<td>64</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>under</td>
<td>4.69</td>
<td>202</td>
<td>80</td>
<td>&gt;18</td>
</tr>
<tr>
<td></td>
<td>over</td>
<td>1.68</td>
<td>122</td>
<td>40</td>
<td>&gt;18</td>
</tr>
<tr>
<td>C</td>
<td>correct</td>
<td>1.08</td>
<td>150</td>
<td>68</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
<td>under</td>
<td>1.71</td>
<td>192</td>
<td>58</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>over</td>
<td>1.10</td>
<td>122</td>
<td>51</td>
<td>12.8</td>
</tr>
<tr>
<td>D</td>
<td>correct</td>
<td>0.99</td>
<td>150</td>
<td>78</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>under</td>
<td>1.61</td>
<td>192</td>
<td>56</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>over</td>
<td>0.79</td>
<td>122</td>
<td>56</td>
<td>8.4</td>
</tr>
</tbody>
</table>

*Glucose values under 60 mg/dL are reported in boldface.
of $\tau_I$ for insulin sensitivity changes. The simulation results in Fig. 1 are for the optimal value of $\tau_I$ for that specific change in insulin sensitivity.

The results in Fig. 1 demonstrate that Strategies A and C are not able to cope with these sensitivity changes and result in undesirable glucose excursions, which include hypoglycemia. For Strategy B and the 50% decrease in insulin sensitivity, $G$ eventually returns to the desired value of 80 mg/dL but only after a large, slow response. Strategy E provides the best response to the insulin sensitivity changes based on its small IAE values and short settling times. The total insulin utilization is essentially the same for all five control strategies. For strategies D and E, the optimal $\tau_I$ values were similar for both insulin sensitivity changes. For example, the optimal values of $\tau_I$ for Strategy E were 3.7 h for the increase and 2.6 h for the decrease.
VI. DISCUSSION OF RESULTS

The simulation results demonstrate that an insulin bolus for a meal challenge is required in order to avoid the large glucose peak that occurs when a bolus is not used (Strategy B). However, the bolus-only approach (Strategy A) results in poor glucose control for incorrect boluses and for insulin insensitivity changes. Thus, a combination of insulin boluses for meals and PID control is desirable. But for meal challenges, the PID controller should be switched on at an appropriate time after the bolus is introduced (Strategies D and E); otherwise, it will result in insulin overdosing and hypoglycemia unless it is tuned very conservatively, as was necessary for Strategy B. Furthermore, for the successful application of PID control, it is important to limit the integral control action in order to avoid insulin overdosing. In this study, the integral control action was limited by imposing the constraints in (6). Alternatively, classical “anti-reset-windup” approaches [6] could be considered.

For this simulation study, the proposed Strategy E gave the best performance for both meal challenges and changes in insulin sensitivity. Furthermore, Strategy E is quite robust, that is, insensitive to various types of changes. For example, gain margin calculations [6] for the two insulin sensitivity changes demonstrated that the optimal value of the controller gain $K_c$ could be increased by a factor of five before instability occurred in the form of a sustained glucose oscillation. Strategy E also performed well for measurement time delays of 6 to 12 minutes, without having to re-tune the controller. These time delays correspond to the approximate lags associated with the best available subcutaneous glucose sensors. Longer measurements delays could be accommodated by re-tuning the PID controller. Finally, Strategy E is not unduly sensitive to the numerical value of $\tau$, the tuning parameter for the $G_{sp}$ trajectory. Also, it can be used as a convenient tuning parameter because reducing $\tau$ makes the controller more aggressive.

The reason that Strategy E outperforms the other four strategies is that the combination of the switching criterion and the time-varying glucose setpoint allows more aggressive controller settings to be used without sacrificing robustness.

VII. CONCLUSIONS

A new glucose control strategy has been proposed based on a novel combination of insulin boluses for meals and an improved PID control algorithm. The key features of the control strategy are (i) a switching strategy for determining when to initiate PID control action after a meal, (ii) a novel time-varying trajectory for the glucose setpoint, and (iii) a limit on the integral control action that greatly reduces the possibility of insulin over-dosing. The new control strategy has been compared to four alternatives in a simulation study based on Hovorka’s physiological model [1], [10], and was shown to be superior for both insulin sensitivity changes and meal challenges with poor CHO estimates.