Model Predictive Control with Learning-Type Set-Point: Application to Artificial Pancreatic β-Cell

Youqing Wang
Dept. of Chemical Engineering, University of California, Santa Barbara, CA 93106-5080
Biomolecular Science & Engineering Program, University of California, Santa Barbara, CA 93106-9611
Sansum Diabetes Research Institute, Santa Barbara, CA 93105-4321

Howard Zisser
Dept. of Chemical Engineering, University of California, Santa Barbara, CA 93106-5080
Sansum Diabetes Research Institute, Santa Barbara, CA 93105-4321

Eyal Dassau, Lois Jovanovič, and Francis J. Doyle III
Dept. of Chemical Engineering, University of California, Santa Barbara, CA 93106-5080
Biomolecular Science & Engineering Program, University of California, Santa Barbara, CA 93106-9611
Sansum Diabetes Research Institute, Santa Barbara, CA 93105-4321

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A novel combination of model predictive control (MPC) and iterative learning control (ILC), referred to learning-type MPC (L-MPC), is proposed for closed-loop control in an artificial pancreatic β-cell. The main motivation for L-MPC is the repetitive nature of glucose-meal-insulin dynamics over a 24-h period. L-MPC learns from an individual's lifestyle, inducing the control performance to improve from day to day. The proposed method is first tested on the Adult Average subject presented in the UVa/Padova diabetes simulator. After 20 days, the blood glucose concentrations can be kept within 68–145 mg/dl when the meals are repetitive. L-MPC can produce superior control performance compared with that achieved under MPC. In addition, L-MPC is robust to random variations in meal sizes within ±75% of the nominal value or meal timings within ±60 min. Furthermore, the robustness of L-MPC to subject variability is validated on Adults 1–10 in the UVa/Padova simulator. *AIChE J,* 56: 1510–1518, 2010
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Introduction

Output regulation is a fundamental issue in control design.[1] For output regulation issue, the control objective is to make the outputs approach a given target Y_r as closely as possible. To achieve the control objective, a command is required to tell the controller what to do, and this command is named set-point. In most cases, the set-point is chosen to be the same as the target Y_r. Logically, this leads to the question of whether the target is the best choice for the set-point.

This prompts an additional question: what is the optimal set-point, and how can it be determined? If a process

Correspondence concerning this article should be addressed to F. J. Doyle at frank.doyle@icb.ucsb.edu.

exhibits a repetitive behavior, e.g., batch processes and periodic continuous processes-iterative learning control (ILC) could be used to update the set-point and search for the optimal one. Therefore, there are two loops in the closed-loop system, as shown in Figure 1: a local controller is used to stabilize the system and regulate the outputs; an ILC is used to optimize the set-point for the local controller.

Generally speaking, there are two ways to use ILC: (1) it is utilized to determine the control signal directly, a method which is called direct ILC[2]; (2) it is used to update some parameters for the local controller, a method which is named indirect ILC.[2] According to this classification method, the algorithm proposed in this work is considered an indirect ILC algorithm. In a recent survey,[2] 207 articles from the Web of Science that featured ''iterative learning control'' in the title were reviewed, and only 16 of them were deemed to focus on indirect ILC. For indirect ILC, two essential issues need to be established: what algorithms are used to design the local control, and which parameters of the local controller are updated by ILC. Among the 16 indirect-ILC-related articles mentioned previously, ILC was used to update the set-point for the local control in only two works.[3,4] In the first study,[3] ILC was used to update the set-point for a PID controller, and then a standard PID with adaptive gain was used to replace the ILC-based PID. In the other work,[4] an anticipatory-type ILC (A-ILC) was used to adjust the set-point for a PID controller, and the proposed scheme was implemented on an X-Y platform.

In the present work, the local control is chosen as model predictive control (MPC) because of its superior abilities in dealing with multivariate processes, constraints, and nonlinearities. Furthermore, the ILC method proposed in this article is much easier to use and more intuitive than that used in the aforementioned references. In this novel combination, MPC is applied to the system and ILC is used to optimize the set-point for MPC. Hence, the proposed algorithm is denoted L-MPC. It should be pointed out that ILC and MPC have long been used together, in combinations such as BMPC,[5] 2D-GPILC,[6] and MPILC.[7] However, in each of these, MPC was used to design the updating law of ILC; therefore, these methods are in the direct ILC category. To the best knowledge of the authors, this article is the first work on ILC-based MPC, or L-MPC.

To evaluate the proposed algorithm, it is applied to closed-loop control of an artificial pancreatic β-cell for Type 1 diabetes mellitus (T1DM). T1DM is a metabolic disease characterized by damaged β-cells, which are responsible for insulin secretion. In 2000, $\sim$17.1 million persons worldwide have Type 1 diabetes mellitus,[8,9] and a clear rising trend in the incidence of the disease has been reported.[10] The hyperglycemia (high blood glucose concentration) resulting from insulin deficiency can cause many serious, long-term complications, such as heart disease, hypertension, retinopathy, nephropathy, and neuropathy. To reduce the glucose level, exogenous insulin delivery is required for subjects with T1DM. However, excessive insulin infusion can result in hypoglycemia (low blood glucose concentration), which will cause impaired brain functions or even death.[11] Hence, managing the insulin delivery to achieve normal glucose levels is a daily challenge.

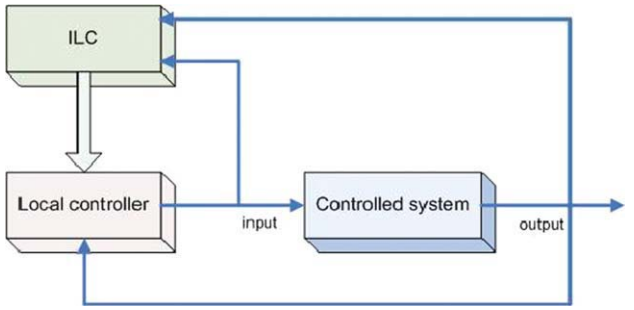

Figure 1. Block diagram of indirect iterative learning control.

The narrow arrow lines denote the measurement information; the wide arrow line denotes the management decision. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

MPC has been used previously for glycemia control.[12,13] Because of the clinical disturbances, e.g., meals, the glucose level controlled by MPC is not flat enough if the set-point is fixed to be the target. On the other hand, people generally consume meals at the similar time from day to day; hence the glucose-meal-insulin dynamics can be considered a continuous process with periodic disturbances. This is the main motivation for using L-MPC for the artificial pancreatic β-cell. The following simulation results will illustrate that the ILC-based set-point can substantially improve the control performance of MPC.

The rest of this article is organized as follows: A nonlinear physiological model describing the virtual subject and an auto-regressive exogenous (ARX) model for control design are introduced in ''Virtual Subject and ARX Model.'' The controller is designed in ''Learning-Type Model Predictive Control,'' where the MPC-based local controller and the ILC-based set-point are introduced separately. ''Experiment Results'' presents numbers of simulation results that demonstrate the excellence of the proposed method. Finally, some conclusions are provided in ''Conclusions.''

Virtual Subject and ARX Model

In previous studies,[14–16] an *in silico* model for T1DM was proposed. This *in silico* subject is comprised of three subsystems: the glucose subsystem, the insulin subsystem, and the meal subsystem. The glucose subsystem is described as a two-compartment model (glucose mass in plasma and rapidly equilibrating tissues; glucose mass in slowly equilibrating tissues); another two-compartment model (periphery degradation and liver degradation) is used to describe insulin kinetics, and the meal subsystem is also assumed to be two compartments (one for the liquid and another for the solid phase). On the basis of this model, a simulation environment was built by researchers from University of Virginia and University of Padova,[17] named the UVa/Padova diabetes simulator for short. The core of the simulation environment is a set of *in silico* subjects. In this work, 11 *in silico* subjects (adults 1–10 and adult average) from the simulator were used in a virtual subject platform built in MATLAB® (The MathWorks, Natick, MA).

An identification technique is required to develop a model of the virtual subject for controller design, because the aforementioned physiological model serves only as the virtual subject. In clinical practice, the available variables for model identification are insulin delivery rate, glucose concentration, and carbohydrate (CHO) count; however, the CHO count needs to be estimated by a human, so an accurate value is difficult to determine. Therefore, an ARX model will be used to approximate the relationship between the insulin and the glucose levels. For this study, the input, insulin delivery rate, is denoted as $u(t)$ and the output, glucose concentration, is denoted as $y(t)$, where t is the time step index. The sample time is set at 5 min, in accordance with the DexCom Seven® system.[18]

To develop the model between insulin and glucose levels, an open-loop experiment without meals (i.e., fasting condition) is conducted on the virtual subject for 24 h. The insulin delivery rate has a step change, so the step-response identification method can be used to identify the model between $u(t)$ and $y(t)$. For simplicity, an ARX model is used to approximate this relationship, as shown here.

$$A(z^{-1})y(t) = B(z^{-1})u(t - nd) + w(t) \tag{1}$$

where z^{-1} is the backward shift operator, nd is the time delay, and $w(t)$ denotes uncertainties or disturbances.

Learning-Type Model Predictive Control

Model predictive control

A short overview of the basic MPC algorithm is provided here; a more detailed overview of MPC can be found in textbooks, for example the book.[19] The key algorithmic components of MPC include: prediction model, cost function, and receding horizon optimization. On the basis of the ARX model in Eq. 1, the prediction model can be built. Given that the set-point for MPC is $y_r(t)$, the cost function is given as

$$\Omega \hat{=} \sum_{j=1}^{N} \alpha_1 (y_r(t+j) - \hat{y}(t+j|t))^2 + \sum_{i=0}^{M} \left[\alpha_2 (u(t+i|t))^2 + \alpha_3 (\Delta u(t+i|t))^2 \right] \tag{2}$$

where the integers N and M ($N > M$) are referred to, respectively, as the prediction horizon and control horizon. $\hat{y}(t+j|t)$ denotes the prediction of $y(t+j)$ based on the known information at time t. $u(t+i|t)|_{i=0}^{M}$ denotes the possible control sequence in the control horizon, and Δu denotes variations of the control signal over time. Weights α_1, α_2, and α_3 adjust the relative importance of tracking error suppression, input penalty, and input variation penalty, respectively. Guidelines for choosing $\{N,M,\alpha_1,\alpha_2,\alpha_3\}$ can be found in the literature.[19] The following optimization problem is solved to obtain the updating law:

$$u(t+i|t)|_{i=0}^{M} = \arg\min_{u(t+i|t)} \Omega \tag{3}$$

In this work, the optimization problem (3) is solved using the MPC toolbox in MATLAB. After a feasible solution $u(t+i|t)|_{i=0}^{M}$ is obtained, only the first term $u(t|t)$ is implemented; at time $t + 1$, the optimization procedure will be repeated.

Learning-type set-point

Because of the repetitive nature of meal intake, glucose measurement, and insulin delivery over a 24-h period, the glucose-meal-insulin dynamics can be interpreted as a continuous process with periodic disturbances. Therefore, the tracking error from the previous day can be used to adjust the set-point in the current day. Because the period of the characteristic dynamics is 24 h and the sample time is 5 min, the period for time step t is $T = 288$. Hence, t and $t-T$ correspond to the same moment in two neighboring days, so the meal disturbances at these two points are the same or similar. It is reasonable to assume that

$$y_r(t) - y(t) \approx y_r(t-T) - y(t-T) \tag{4}$$

On the basis of this assumption and given the tracking error $e(t - T) = Y_r - y(t - T)$, one obtains

$$\begin{aligned} e(t) &= Y_r - y(t) = Y_r - y_r(t) + y_r(t) - y(t) \\ &\approx Y_r - y_r(t) + y_r(t-T) - y(t-T) \\ &= e(t-T) + y_r(t-T) - y_r(t) \end{aligned} \tag{5}$$

Letting $e(t) = 0$ in (5), the "optimal" choice for the set-point $y_r(t)$ is

$$y_r(t) = y_r(t-T) + e(t-T) \tag{6}$$

however, this aggressive scheme might lead to overshoot, which should be avoided; hence, a more reasonable and robust scheme is introduced for updating the set-point

$$y_r(t) = y_r(t-T) + Ke(t-T); \quad y_r(t) \equiv Y_r, \text{ when } t \in [0, T) \tag{7}$$

This is a typical P-type ILC,[20,21] where $0 < K < 1$ is the learning gain.

In the literature,[22] a sufficient condition for asymptotical stability of a closed-loop system under indirect ILC was established. Under this condition, the tracking error $e(t)$ will converge to zero. Therefore, according to (7), $y_r(t)$ will be similar to $y_r(t - T)$, in other word, the ILC-based set-point will converge to a periodic profile. The range of the limit periodic profile could be great, which is a potential risk when there exist batch-wise variations; hence, some constraints on the set-point is introduced in (12).

In other words, within the L-MPC framework, MPC works as the local control; an ILC is used to update the set-point for MPC. For clarity, the block diagram of L-MPC is shown in Figure 2.

Experiment Results

Controller design

The following simulations are completed on the Adult Average subject from the UVa/Padova diabetes simulator. An open-loop simulation is performed to identify the model in Eq. 1. The insulin delivery rate is chosen as

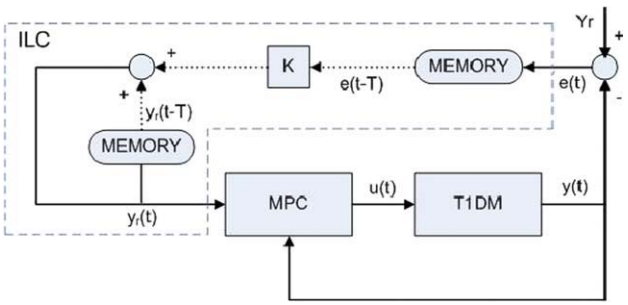

Figure 2. Block diagram of learning-type model predictive control.

The solid arrow lines denote the real-time information; the dotted arrow lines denote the information in the previous cycle; components in the dashed frame comprise an iterative learning controller (ILC). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

$$u(t) = \begin{cases} 0.6\,\mathrm{U/h}, & 0 \le t < 60 \\ 0.5\,\mathrm{U/h}, & 60 \le t \le 144 \end{cases} \tag{8}$$

Then, the ARX model can be obtained as shown below

$$\begin{aligned} A(z^{-1}) &= 1 - 1.9860z^{-1} + 0.9864z^{-2}; \\ B(z^{-1}) &= -0.0030;\ nd = 1 \end{aligned} \tag{9}$$

Obviously, it is impossible to describe the virtual subject (comprised of three nonlinear sub-models introduced in "Virtual Subject and ARX Model") accurately by using this simplified model. Next, the control law will be designed, based on the simplified model in (9).

To compare the tracking performance in different cases numerically, the following criterion is introduced

$$\mathrm{ATE}(k) \hat{=} \sum_{t=(k-t)T+1}^{kT} |y(t) - Y_r|/T \tag{10}$$

which is the average tracking error (ATE) for kth day. Obviously, a smaller ATE equates to a better tracking performance.

Because the glucose-insulin dynamics are relatively slow, the prediction horizon is chosen as 50; for tuning, the control horizon is chosen as 5. In the MPC module, three weights need to be designed: the tracking error weight α_1, the input penalty weight α_2, and the input variation penalty weight α_3. Three parameters can be combined to yield two degree of freedom: if α_3 is fixed to be unit, only α_1 and α_2 should be tuned. The ATE values of MPC and L-MPC are compared in Figure 3 under four groups of weights: $\{\alpha_1,\alpha_2,\alpha_3\} = \{2.5,1,1\}$, $\{10,1,1\}$, $\{5,0.5,1\}$, or $\{5,2,1\}$, respectively. It is clear that MPC is robust to different weight settings and L-MPC can improve the closed-loop performance in all cases. On the basis of the simulation results, intermediate values are chosen in this study: $\alpha_1 = 5$, $\alpha_2 = 1$, and $\alpha_3 = 1$. To guarantee continuous insulin delivery, the following constraint is introduced:

$$u(t) \ge 0.24\,\mathrm{U/h} \tag{11}$$

Other than the set-point, all parameters are the same for L-MPC and MPC.

Repetitive diets

In this section, it is assumed that the subject consumes three meals a day at {7:00, 13:00, and 18:00} with fixed amounts of carbohydrate, {60 g, 100 g, and 70 g}, respectively. In the first day, an optimized basal and bolus open-loop therapy is used as follows: the basal rate is subject-specific as defined in the UVa/Padova simulator, and meal-related boluses are calculated using subject-specific insulin-to-carbohydrate ratios and meal sizes. The feedback control is engaged on the second day. The target for output is chosen as $Y_r = 110$ mg/dl. In this work, hyperglycemia is defined as blood glucose concentration greater than 180 mg/dl.[23] While the definition of hypoglycemia has a wide range (60–70 mg/dl)[24] and is associated with or without clinical symptoms. For simplicity, we have selected 60 mg/dl as hypoglycemia threshold where any deviations below this level are termed significant hypoglycemia.[24,25] Accordingly, blood glucose concentrations between 60 mg/dl and 180 mg/dl are considered to be within the safe range for T1DM.

For ILC, only the learning gain needs to be designed. The ATE values for three different learning gains are compared in Figure 4. The ILC does not begin to adjust the set-point in the first day, so the ATE values in this day are the same and, hence, are omitted. Evidently, larger K values result in faster convergence rates in the cycle direction; however, larger K values will induce worse robustness to variations. In this article, an intermediate value of $K = 0.5$ is chosen to strive a compromise between these two effects.

The control results under L-MPC for 20 days are given in Figure 5: Figure 5a shows the glucose levels for 20 days; Figure 5b shows the insulin delivery rates; for clarity, the glucose and insulin curves in the last day are enlarged in Figures 5c, d, respectively. For comparison, Figure 6 shows the control results under MPC for 20 days. From Figure 6a,

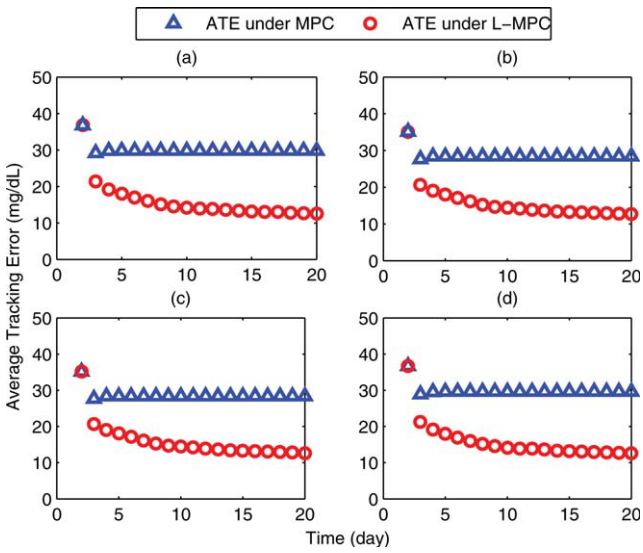

Figure 3. Comparison of average tracking error under different weights.

Where △ denotes ATE for MPC and ○ denotes ATE for L-MPC: (a) {α1, α2, α3} = {2.5,1,1}; (b) {α1, α2, α3} = {10,1,1}; (c) {α1, α2, α3} = {5,0.5,1}; (d) {α1, α2, α3} = {5,2,1}. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

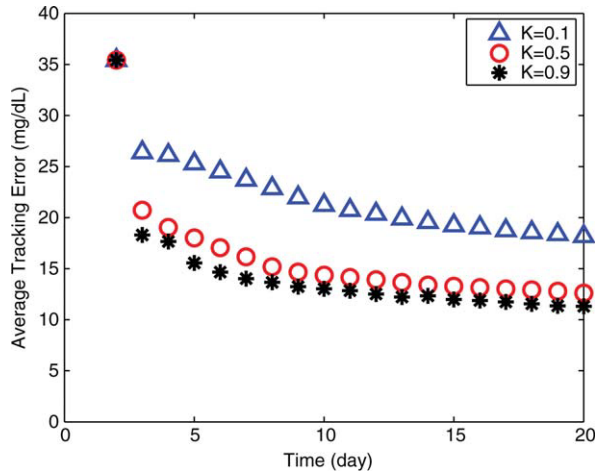

Figure 4. Comparison of average tracking error for three different learning gains.

[Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

one can see that the control performance becomes steady after the 3rd day. As shown in Figure 6c, the range of glucose concentrations under MPC is about 68–201 mg/dl. For the L-MPC case, as shown in Figure 5a, the control performance keeps improving from day to day, and the glucose level in the last day can remain in the range of about 68–145 mg/dl, as shown in Figure 5c, which is excellent for T1DM. Clearly, L-MPC can improve the control performance over MPC.

In most cases, it is difficult or even impossible to achieve exact tracking due to unmeasured disturbances, constraints, and other uncertainties. Therefore, the set-point will keep updating such that it has a large variation, as shown in Figure 5a. The excessive range of the set-point creates potential risks, especially in the presence of non-repetitive variations, such as meal amount and timing variations. To avoid the potential risks and improve L-MPC's robustness, some limitations are added to the ILC-based set-point:

$$y_r(t) = \max\{\delta_1 Y_r,\ \min[\delta_2 Y_r,\ y_r(t-T) + Ke(t-T)]\} \quad (12)$$

where $0 < \delta_1 < 1$ and $\delta_2 > 1$ are designed parameters. In fact, these limitations conduce a boundary layer for the set-point, and the thickness of the layer is $(\delta_2 - \delta_1)Y_r$. Therefore, a larger $\delta_2 - \delta_1$ will introduce more freedom for L-MPC but may result in worse robustness. In practice, δ_1 and δ_2 can be designed based on the acceptable range for the output. As an example, because the immediate danger from hypoglycemia (glucose concentrate lower than 60 mg/dl) is much greater

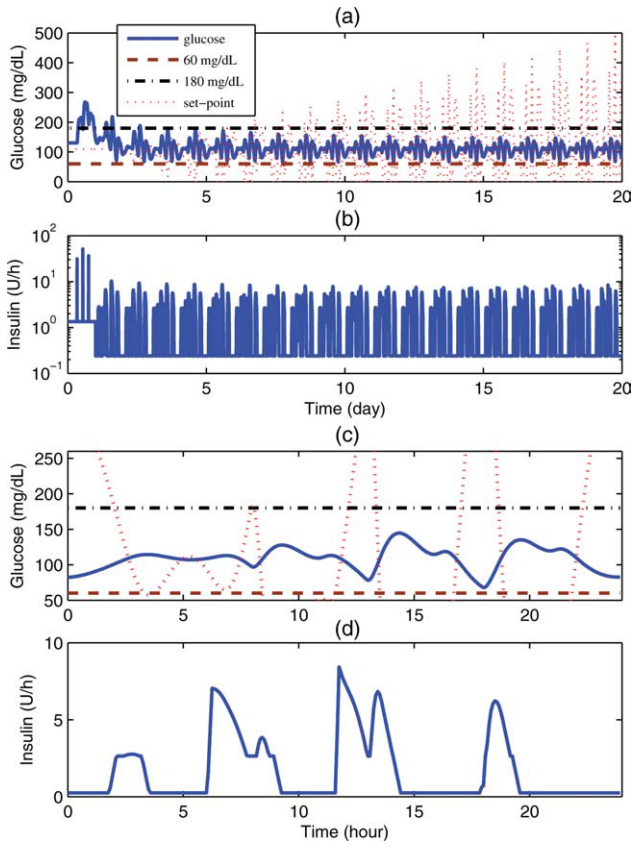

Figure 5. Control performance under L-MPC in 20 days.

(a) Glucose level, safe range, and set-point; (b) insulin delivery rate, where logarithmic scale was used for the Y-axis; (c) last day's results; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

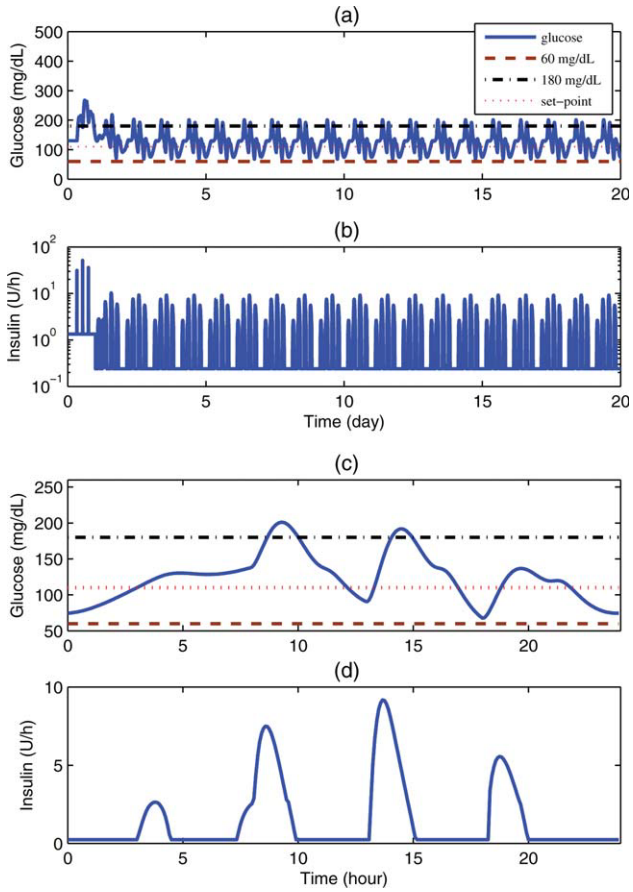

Figure 6. Control performance under MPC in 20 days.

(a) Glucose concentration; (b) insulin delivery rate, where logarithmic scale was used for the Y-axis; (c) last day's glucose; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

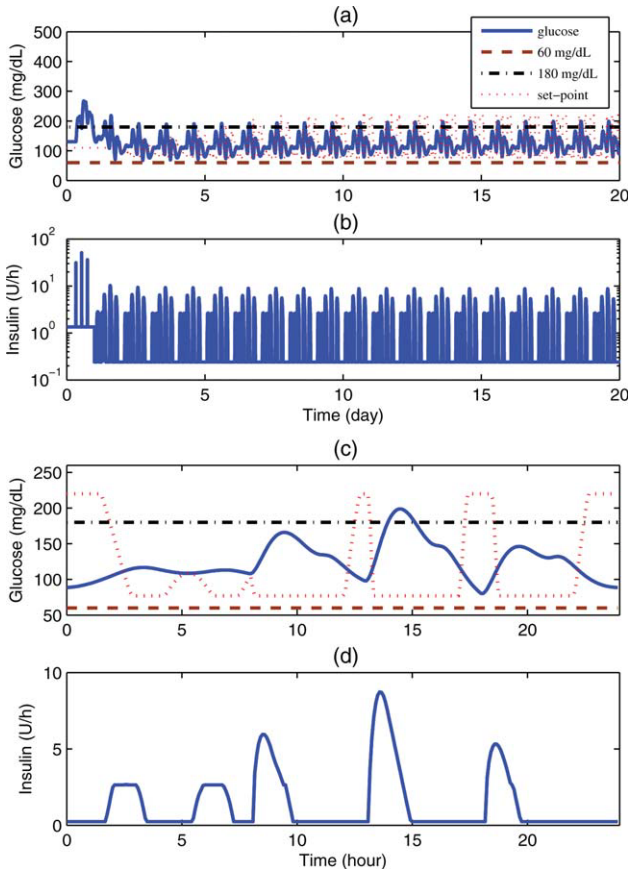

Figure 7. Control performance under constrained L-MPC in 20 days.

(a) Glucose concentration; (b) insulin delivery rate, where logarithmic scale was used for the Y-axis; (c) last day's glucose; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

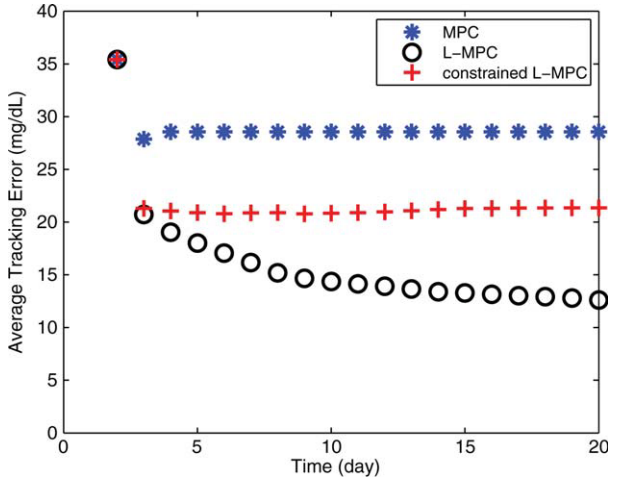

Figure 8. Comparison of average tracking error for MPC, L-MPC, and constrained L-MPC.

[Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Table 1. Robustness Statistic Results for L-MPC

	Mean ATE (mg/dl)	Percentage of Hyperglycemia	Percentage of Hypoglycemia	Percentage in Safe Range
Nominal	21.45	4.85%	0.00%	95.15%
±25%	21.60	4.05%	0.00%	95.95%
±50%	22.51	5.52%	0.51%	93.97%
±75%	24.62	7.05%	2.12%	90.84%
±20 min	22.05	4.89%	0.16%	94.95%
±40 min	23.04	4.69%	1.07%	94.24%
±60 min	24.32	4.51%	1.96%	93.53%
±50% and ±40 min	24.81	6.55%	1.65%	91.81%

For each case, 110 days' simulations were done, and the last 100 days' simulation results are analyzed in this table. Mean ATE is the average of the last 100 days' ATE.

than that from hyperglycemia (glucose concentration higher than 180 mg/dl), $\delta_1 = 0.7$ and $\delta_2 = 2$ were chosen in this work, so the range for the set-point is between 77 mg/dl (>60 mg/dl) and 220 mg/dl. The control results under constrained L-MPC are shown in Figure 7.

As shown in Figures 5 and 7, L-MPC eventually gives bolus-like patterns to compensate for meals. In addition,

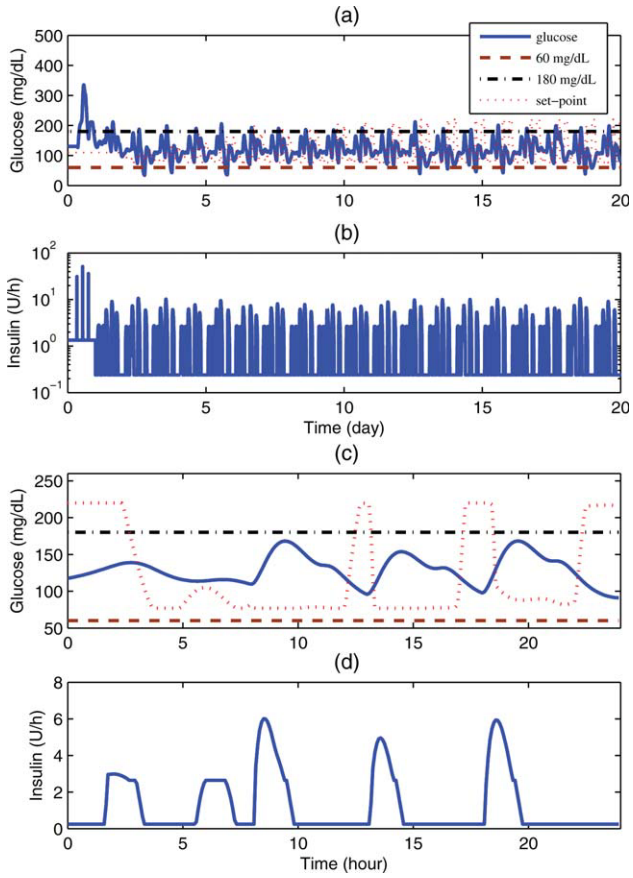

Figure 9. Control results of average subject with ±75% variation in meal amounts.

(a) Glucose curve; (b) insulin curve, where logarithmic scale was used for the Y-axis; (c) last day's glucose; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

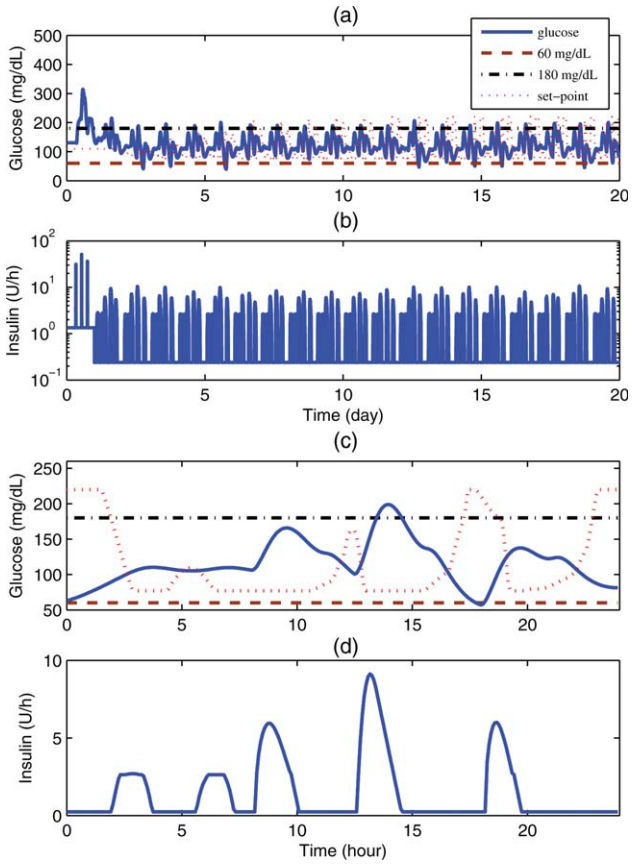

Figure 10. Control results of average subject with ±60 min variation in meal times.

(a) Glucose curve; (b) insulin curve, where logarithmic scale was used for the Y-axis; (c) last day's glucose; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

nocturnal insulin delivery has been redesigned by the algorithm in the form of extended bolus to optimize fasting insulin requirements for a set-point of 110 mg/dl.

ATE values for MPC, L-MPC, and constrained L-MPC are compared in Figure 8. The ATE values under MPC remain constant from the 4th day, while the ATE values under L-MPC and constrained L-MPC continuous to decrease. The ATE values in the last day are 12.6, 21.4, and 28.6, respectively, under L-MPC, constrained L-MPC, and MPC. L-MPC exhibits better performance than constrained L-MPC, which may be explained by the difficulty of obtaining rapid insulin boluses without allowing large variations in the set-point. Both L-MPC and constrained L-MPC have superior performance over MPC. In subsequent sections, only constrained L-MPC is used; for convenience, the terminology "constrained" is omitted.

Robustness to meal variations

In the previous sections, it is assumed that the sizes and timings of meals remain the same from day to day. For practical application, the proposed algorithm should be able to remain effective in the presence of significant variations. Hence, the robustness of L-MPC in the presence of variations in meal amounts and meal timings must be studied. The effects of each factor on the control performance are considered separately at first, then in combination. The nominal values for meal amounts and meal timings are still set at {60 g, 100 g, 70 g} and {8:00, 13:00, 18:00}.

To study the effects of variations in meal amounts, the meal times are fixed. A uniform distributed random variable is added independently to the nominal meal amount. The statistical results are given in Table 1. For variations as large as ±75%, the minimum size of lunch is 25 g and the maximum size is 175 g, which is quite a large difference; however, the control performance is still acceptable. The glucose and insulin curves over 20 days are given in Figures 9a, b, respectively. For clarity, the control results in the last day are shown in Figures 9c, d. The proposed scheme has excellent robustness in the presence of meal amount variations.

Now, the meal amounts are fixed in nominal values so that the effects of meal time variations may be studied. As shown in Table 1, the robustness of L-MPC to meal time variations is impressive: performance indices in all cases are very close to those in nominal cases. If the variation range is ±60 min, the duration between two meals in some cases will be as short as 3 h or as long as 7 h. According to our experience, this is wide enough to describe real life uncertainties for most individuals.

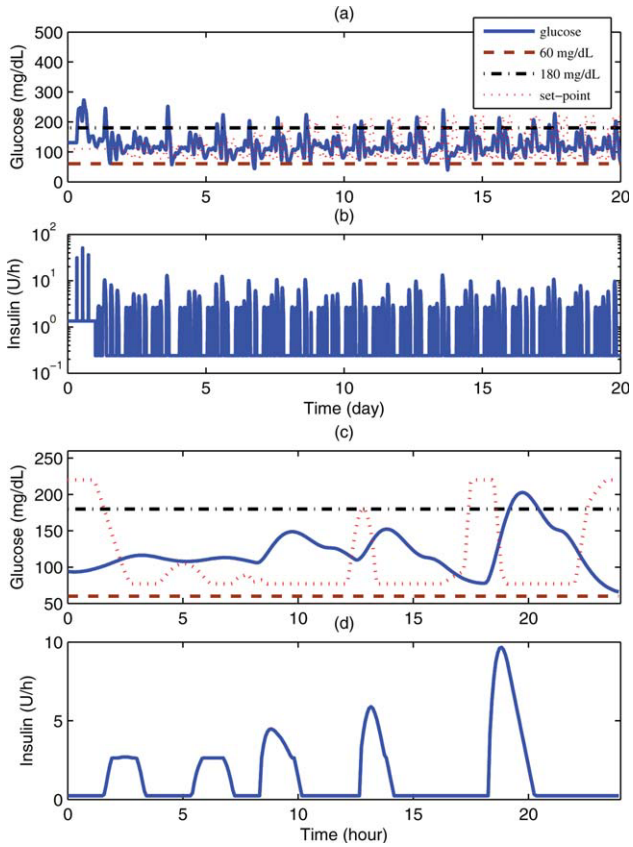

Figure 11. Control results of average subject with (±50%, ±40 min) meal variations.

(a) Glucose curve; (b) insulin curve, where logarithmic scale was used for the Y-axis; (c) last day's glucose; (d) last day's insulin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

The control results with ±60 min variations are shown in Figure 10, which validates the superior robustness of L-MPC to account for meal timing variations.

The previous results consider the robustness of L-MPC to meal amount and meal timing variations separately; however, these variations can appear together in real life. In the next phase, it is assumed that there are both meal size variations within ±50% and meal timing variations within ±40 min. The control performance indices are also included in Table 1. The control results for 20 days are shown in Figure 11. These results demonstrate that L-MPC has very good robustness to real-life variations in diet.

Robustness to subject variations

The preceding results were all conducted on the Adult Average subject. In clinic, biometric values such as weights, insulin resistances, and ages have wide distributions. A good therapy should be robust enough to treat a reasonable distribution in the population.

In this section, Adults 1–10 are tested under L-MPC. Except for the ARX models identified by using the step-response identification method, all other parameters for L-MPC are the same as those used for the Adult Average subject. All control results for the 10 subjects under L-MPC are shown in Figure 12.

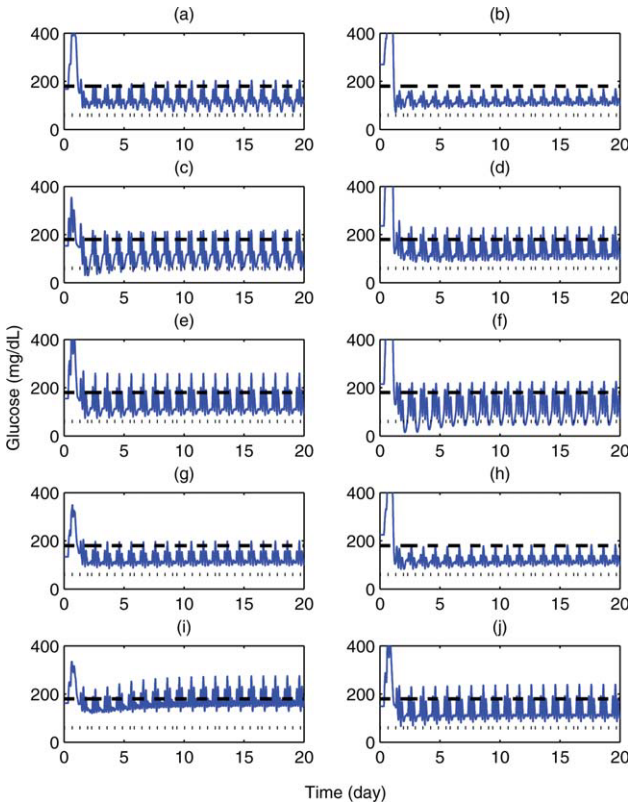

Figure 12. Control results of 10 subjects under L-MPC.

Where a constant insulin delivery rate, 0.6 U/h, was used in the first day to challenge the proposed algorithm. Subfigures (a)–(j) correspond to Adults 1–10 respectively. The meals are repetitive and the same in all cases. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

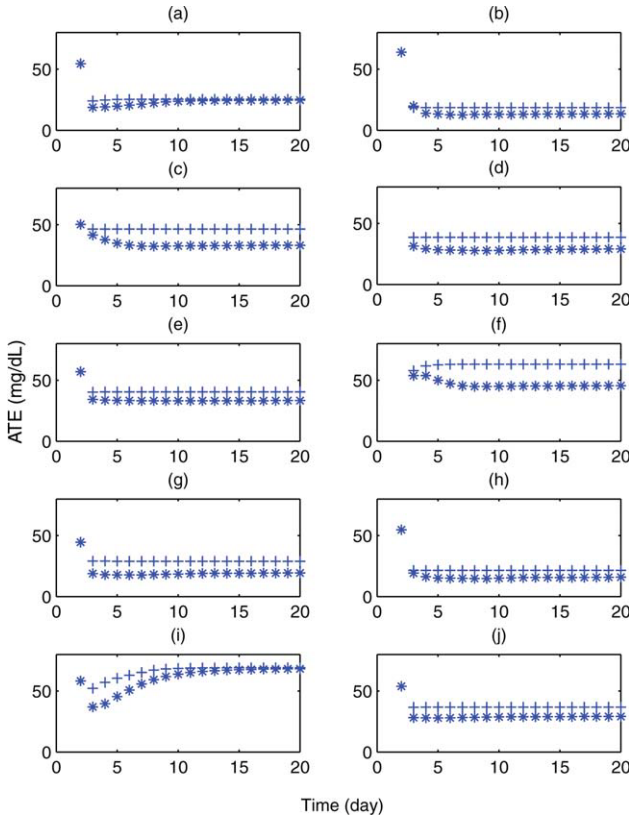

Figure 13. Comparison of tracking performance for 10 subjects under MPC and L-MPC, respectively.

'+' denotes ATE for MPC; '*' denotes ATE for L-MPC. Subfigures (a)–(j) correspond to Adults 1–10 respectively. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

From Figure 12, it is seen that the control performance can be improved from day to day for most subjects, which is one of the advantages of L-MPC. After a few days, an absolute majority of glucose values have converged within the safe range with little variation in all 10 cases. This demonstrates that L-MPC has good robustness to subject variations. It should be noted that using fixed parameters for all subjects results in suboptimal control results for some cases (e.g., Adult 9), which can be easily fixed by adjusting controller parameters. To highlight the function of learning, Figure 13 compares the ATE values for 10 subjects under L-MPC and MPC. In all cases, the tracking performance under L-MPC is better than that under MPC, due to the function of ILC-based set-point. The values of ATE in the last day for two control algorithms are compared for the 10 cases, and L-MPC reduce ATE by 21.1% in average.

Conclusions

This is the first work using ILC to adjust the set-point for MPC, a method termed L-MPC in this work. To validate this novel combination, the proposed method was implemented in the artificial pancreatic β-cell for T1DM. By exploiting the repetitive nature of the glucose-meal-insulin dynamics, the control performance under L-MPC can be improved from day to day. It has been shown that the proposed algorithm is robust to meal variations and subject variability. In addition, this

algorithm does not rely on the subject's intervention, so, it will be suitable for pediatric populations and for those who do not wish to take control of their diabetes.

The design of ILC is independent of the local controller, so the proposed ILC can be transplanted to combinations with other methods, such as internal model control, PID control, and H_∞ control. In addition, whereas only output regulation is considered in this article for simplicity, the proposed idea can be implemented for output tracking issue.

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Notation

Indices

$A(z^{-1})$ = auto-regressive function for ARX model, dimensionless
ATE = average tracking error, mg/dl
$B(z^{-1})$ = exogenous function for ARX model, dimensionless
nd = time delay, dimensionless
T = period for the continuous process, dimensionless
t = time-step index, multiplier of the sample time (5 min), dimensionless
z^{-1} = backward shift operator, dimensionless
Ω = cost function for MPC, dimensionless

Parameters

K = learning gain, dimensionless
M = control horizon, dimensionless
N = prediction horizon, dimensionless
α_1 = weight for tracking error suppression in the cost function, dimensionless
α_2 = weight for input penalty in the cost function, dimensionless
α_3 = weight for input variation penalty in the cost function, dimensionless
δ_1 = a design parameter for the lower boundary of the set-point, dimensionless
δ_2 = a design parameter for the upper boundary of the set-point, dimensionless

Variables

$e(\cdot)$ = output tracking error, mg/dl
$u(\cdot)$ = input, insulin delivery rate, U/h
$w(t)$ = uncertainties or disturbances, dimensionless
Y_r = target for the output, mg/dl
$y(\cdot)$ = output, glucose concentration, mg/dl
$y_r(\cdot)$ = set-point for MPC, mg/dl
$\hat{y}(\cdot)$ = the prediction of the output $y(\cdot)$, mg/dl

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