Optimal blood glucose control in diabetes mellitus treatment using dynamic programming based on Ackerman’s linear model

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Abstract. Determination of insulin injection dose in diabetes mellitus treatment can be considered as an optimal control problem. This article is aimed to simulate optimal blood glucose control for patient with diabetes mellitus. The blood glucose regulation of diabetic patient is represented by Ackerman’s Linear Model. This problem is then solved using dynamic programming method. The desired blood glucose level is obtained by minimizing the performance index in Lagrange form. The results show that dynamic programming based on Ackerman’s Linear Model is quite good to solve the problem.

1. Introduction
Diabetes mellitus is a disease where the blood glucose level cannot be maintained in the normal range, i.e. 60 – 110 mg/dl as stated in [2]. Diabetes mellitus affects insulin production or the insulin response ability to the body. On the other hand, insulin hormone is responsible for the glucose absorption. Insulin injection is one of the most common diabetes mellitus treatments. In this research, the optimal insulin dose for diabetes mellitus treatment is determined based on the optimal control of blood glucose level.

The use of dynamic programming based on Ackerman’s linear model to solve the optimal blood glucose control problem will be discussed in this paper. A MATLAB program is built based on the dynamic programming principle to solve the optimal control problem representing the problem. In this case, Ackerman’s linear model is chosen to represent the regulation of glucose concentration in blood.

2. Ackerman’s linear model
Ackerman’s linear model is able to simulate glucose regulation system although this model is an abstraction of the reality as stated in [1]. Ackerman’s linear model based on [1] and [3] is as follows.

\[
\frac{dg}{dt} = -m_1 g - m_2 h + J \tag{1}
\]

\[
\frac{dh}{dt} = -m_3 h + m_4 g + K \tag{2}
\]

It is defined that \( g \equiv G - G_0 \) where \( G \) is glucose concentration and \( G_0 \) is fasting glucose concentration. Furthermore, \( h \) is defined as \( h \equiv H - H_0 \) where \( H \) is blood hormone concentration (including insulin) and \( H_0 \) is fasting blood hormone concentration.
The parameters in (1) and (2) as given in [1] and [3] are:

- **m**: constant rate for the removal of glucose above the initial (fasting) level due to its own excess above the initial level
- **m** \(_{2}\): constant rate for the removal of glucose above the initial level due to blood-hormone concentrations above the initial level
- **m** \(_{3}\): constant rate for the removal of hormone above the initial (fasting) level due to its own excess above the initial level
- **m** \(_{4}\): constant rate for the release of hormone above the initial level due to blood-glucose concentrations above the initial level

In this paper, the exogenous glucose infusion rate \(J\) is not considered. \(J\) is set to 0 because it is assumed that there is no given exogenous glucose. Both \(h\) and \(K\) are assumed as insulin where \(K\) is the insulin infusion rate.

### 3. Dynamic programming

The general problem of optimal control is to minimize the following function:

\[
I(x(0), t_f) = \int_0^{t_f} \psi(x, u, t) \, dt + \phi(x(t_f))
\]

subject to:

\[
\frac{dx}{dt} = f(x, u, t), \quad x(0) = x_0
\]

\[
a_i \leq u_i(t) \leq \beta_i, \quad i = 1, 2, 3 \ldots m
\]

where \(I: \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R} \to \mathbb{R}, f: \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R} \to \mathbb{R}^n, x = (x_1, \ldots, x_n) \in \mathbb{R}^n, u = (u_1, \ldots, u_m) \in \mathbb{R}^m\).

Dynamic programming that is implemented in this research is based on iterative dynamic programming introduced by Luus in [4]. In the dynamic programming, the optimal control problem is set up into a sequence of stages. The optimal control problem with \([0, t_f]\) time interval is then approximated by a piecewise constant control \(u\) over \(P\) stages with length \(L = t_f / P\). The performance index is estimated by

\[
I(x(0), P) = \psi(x(t_f)) + \sum_{k=1}^{P} \int_{t_{k-1}}^{t_k} \phi(x(t), u(k-1), t) \, dt
\]

Each state component \(x_i\) of \(x\) takes \(N\) values over a region at each time stage except for the first stage which is the given initial condition. Hence, stage 2 until \(P\) has each \(N^n\) grid points. Each control component \(u_i\) of \(u\) takes \(M\) values over a region at each stage. Thus, each state grid point is allowed to take \(M^m\) control vector values.

The calculations are started from stage \(P\) corresponding to time interval \(t_f - L \leq t < t_f\). For each grid point of state \(x\), \(M^n\) values of the performance index are evaluated

\[
I(x(t_f - L), 1) = \psi(x(t_f)) + \int_{t_f - L}^{t_f} \phi(x(t), u(P - 1)) \, dt
\]

where \(M^n\) control values used for \(u(P - 1)\). These \(M^n\) values of the performance index are compared to determine the particular value of \(u(P - 1)\) which gives the minimum value. This particular value is the best control to use at that particular grid point of state \(x\). By repeating the same procedure for all \(N^n\) grid points, the optimal control to use at this last stage can be determined.

Next, the integration is done backward to stage \(P - 1\) corresponding to time interval \(t_f - 2L \leq t < t_f - L\). For each grid point, compare \(M^n\) control values to minimize the performance index. However, it is possible that when the integration from \(t_f - 2L\) to \(t_f - L\) is done, the state \(x(t_f - L)\) is not one of the grid points at state \(P\). In this case, the optimal control policy corresponding to the closest grid point to the state \(x(t_f - L)\) is taken. The same calculation procedure is continued to stages \(P - 2\), \(P - 3\), and so on until reaching the first stage. Grid points at stage 1 corresponding to the time interval \(0 \leq t < L\) consists of the initial condition \(x(0)\) as a single grid point. \(M^n\) performance index values are compared to determine the control policy giving the minimum value. See figure 1, for the case \(n = 2, N = 5, m = 1\) and \(M = 4\).
Finally, the state values at the beginning of each stage are stored to generate state trajectories by doing a forward integration. The trajectories store states with controls giving the minimum value performance index.

4. Simulation results

Ackerman’s model diabetic patient parameters as stated by Yipintsoi et al. in [5] is used in the program simulation, i.e. \( m_1 = 0.0009, m_2 = 0.0031, m_3 = 0.0415, \) and \( m_4 = 0. \) Hence, the Ackerman’s linear model becomes

\[
\frac{dg}{dt} = -0.0009g - 0.0031h \tag{5}
\]

\[
\frac{dh}{dt} = -0.0415h + K \tag{6}
\]

The program is simulated over \( P = 250 \) with final time \( t_f = 300, \) number of state \( g \) and \( h \) grid points \( N = 10, \) and control discretization \( M = 10. \) The optimal control problem is solved by minimizing the performance index in Lagrange form, i.e.

\[
J = \int_0^{t_f} \rho_1 |K| + \rho_2 |G - G_T| \, dt \tag{7}
\]

where \( \rho_1 \) is control \( u \) weight factor, \( \rho_2 \) is state \( g \) weight factor, and \( G_T \) is desired glucose level. Weight factors \( \rho_1 = \rho_2 = 1 \) used in this simulation means that minimizing the dose of insulin injection is as important as minimizing glucose concentration. The initial glucose level is \( g(0) = 300 \) and the initial hormone level is \( h(0) = 60. \) The control vector is bounded by \( 0 \leq u \leq 10 \) and the desired glucose level as the target is \( G_T = 100. \) The simulation results are shown in figure 2, figure 3, and figure 4.
Figure 2. Glucose level graph.

Figure 3. Hormone level graph.

Figure 4. Insulin injection control graph.
From the graphs, it is clearly seen that the final state glucose level approaching the desired level could be reached with the obtained insulin injection control behaviour. When \( t \) is less than 20 the maximum value of control is used to decrease the blood glucose level rapidly. At the same time, this causes the increase of hormone level till reach the steady state condition around \( t = 150 \). On the other hand, the control chooses the minimum value after \( t > 50 \). The glucose concentration at the final stage is \( g(t_f) = 108.5668 \) and the final hormone level is \( h(t_f) = 106.9235 \). Therefore, the glucose concentration change is 191.4332.

5. Conclusions

It could be concluded from the result that Ackerman’s linear model could represent the regulation of glucose concentration quite well. The results also show that the used method, i.e. dynamic programming, could be applied to solve the blood glucose optimal control problem discussed in this paper. The desired glucose level could be approached by the achieved final glucose level with the determined control policy by minimizing the performance index in Lagrange form. An insulin infusion therapy can be practiced based on the resulted insulin injection control behaviour in this paper. Nevertheless, several kinds of adjustments to the real problem are still needed to apply this result.

References

[1] Ackerman E, Gatewood L C, Rosevear J W and Molnar G D 1965 Model studies of blood-glucose regulation Bulletin of Mathematical Biophysics 27 pp 21-37
[2] Brand-Miller J, Foster-Powell K and Mendosa D 2006 The New Glucose Revolution: What Makes My Blood Glucose Go Up...and Down? (New York: Marlowe & Company)
[3] Chee F and Fernando T 2007 Closed-Loop Control of Blood Glucose (Springer)
[4] Luus R 2000 Iterative Dynamic Programming (Boca Raton: Chapman & Hall/CRC)
[5] Yipintsoi T, Gatewood L C, Ackerman E, Spivak P L, Molnar G D, Rosevear J W and Service J V 1973 Mathematical analysis of blood glucose and plasma insulin responses to insulin infusion in healthy and diabetic subjects Computers in Biology and Medicine 3 pp 71-78