Estimation-based Model Predictive Control of Blood Glucose in Type I Diabetics: A Simulation Study

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ABSTRACT A constrained state space model predictive controller, designed based on a 3-state model of the human glucose-insulin interaction, was implemented on a 19-state simulation model of a Type I Diabetic patient. The controller maintained the blood sugar level of the patient plant between the values of 60 and 130 mg/dl, when subjected to a meal disturbance of 50g, significantly lowering the risk of hypoglycemia/hyperglycemia.

INTRODUCTION

Diabetes Mellitus is characterized by insufficiency of the pancreas to produce enough insulin to regulate the blood sugar level. In Type I Diabetes the pancreas produces no insulin, and the patient is totally dependent on insulin from an external source to be infused at a rate to maintain blood sugar levels at normal levels. Hyperglycemia occurs when blood glucose level rises much higher than the norm (> 8mmol/L) for prolonged periods of time; hypoglycemia occurs when the blood sugar level falls below values of 3mmol/L. Both situations can be deleterious to the individual's health. Hyperglycemia can lead to blindness, kidney failure, and other complications on a long-term basis. The effects of hypoglycemia are more critical on a short-term basis, leading to loss of consciousness and coma within a few hours. The normal range of blood sugar falls between 3.8-5.6 mmol/L, the target range for a controller regulating blood sugar [1].

The normal body has a natural feedback regulation system where high glucose levels stimulate the production of insulin from the pancreas. The goal of our research is to regulate blood sugar level in a Type I diabetic by manipulating the insulin infusion rate, that is, produce an "artificial pancreas". In this preliminary study, the efficacy of a Model Predictive Control (MPC) strategy is shown by computer simulation of a diabetic patient.

BERGMAN MODEL

Many models have been developed to describe the human-glucose insulin system. Of these the Bergman [2] model presents a minimal model composed of 3 equations to describe the dynamics of the system.

These modeling equations are:

$$\frac{dG}{dt} = -P_1 G - X(G + G_b) + D(t) \quad (1)$$

$$\frac{dX}{dt} = -P_2 X + P_3 I \quad (2)$$

$$\frac{dI}{dt} = -n(I + I_b) + U(t)/V_I \quad (3)$$

where the states are:

G - plasma glucose conc. (mmol/L) above basal value
X - proportional to I in remote compartment (mU/L)
I - plasma insulin conc. (mU/L) above basal value

The inputs are:

D(t) - meal glucose disturbance (mmol/Lmin)
U(t) - manipulated insulin infusion rate (mU/min)
G_b, I_b - basal values of glucose and insulin conc. (4.5mmol/L, 15mU/L)

The parameter values for a Type I diabetic are:

$P_1 = 0\text{min}^{-1}$ $P_2 = 0.025\text{min}^{-1}$
$P_3 = 0.000013\text{mU/L}$ $V_I = 12\text{L}$ $n = 5/54$ min

This model is linearized about the steady-state values of G = I = X = D= 0, U=16.667mmU/min to give the following discrete state space matrices (sample time =5 minutes).

$$x_{k+1} = \Phi x_k + \Gamma u_k + \Gamma_d d_k \quad (4)$$

$$y_{k+1} = C x_{k+1} \quad (5)$$

$$\Phi = \begin{pmatrix} 1.00\text{x}10^{0} & -2.12\text{x}10^{1} & -6.04\text{x}10^{-4} \\ 0 & 8.82\text{x}10^{-1} & 4.87\text{x}10^{-5} \\ 0 & 0 & 6.29\text{x}10^{-1} \end{pmatrix}$$

$$\Gamma = \begin{pmatrix} -8.80\text{x}10^{-5} \\ 1.12\text{x}10^{-5} \\ 3.34\text{x}10^{-1} \end{pmatrix} \qquad \Gamma_d = \begin{pmatrix} 5 \\ 0 \\ 0 \end{pmatrix}$$

$$C = [1 \quad 0 \quad 0]$$

The term d_k is an input disturbance (glucose meal) to the system.

METHODOLOGY

In MPC the value of the output (glucose) is predicted P sample times into the future, based on model of the process. The objective is to minimize the square of the deviations of the model-predicted output from the desired setpoint trajectory, by adjusting M future control (insulin infusion) moves:

$$J = \sum_{i=1}^{P} (r_{k+i} - \hat{y}_{k+i})^2 + \lambda \sum_{i=1}^{M} \Delta u_{k+i-1}^2 \quad (6)$$

where J is the objective function
P is the prediction horizon
M is the control horizon
k is the sample time index

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λ is the weighting on the manipulated input
Δu is the manipulated input increment
r is the desired glucose setpoint
$\hat{y}$ is the predicted glucose output

Only the first control move in the sequence is implemented, and at the next step the optimization is repeated. This approach is also known as receding horizon control. The predicted output trajectory is given by the state space formulation:

$$\hat{y}_{k+i|k} = C\Phi^{i}\hat{x}_{k|k} + \sum_{j=1}^{i} C\Phi^{j-1}\Gamma u_{k-1} + \sum_{j=1}^{i} C\Phi^{j-1}\Gamma_d \hat{d}_{k|k} + \sum_{j=k}^{k+i-1}\left(\sum_{q=1}^{i-j+k} C\Phi^{q-1}\Gamma\right)\Delta u_j \quad (7)$$

A clear advantage of MPC is that the control algorithm can explicitly enforce constraints. Physiological constraints are necessary in the diabetic system, encompassing the limits of hyperglycemia/hypoglycemia. The following constraints were imposed.

$$0 \le u \le 80\text{mU/min} \quad (8)$$

$$3\text{mmoles/L} \le y \le 15\text{mmoles/L} \quad (9)$$

$$-16.7\text{mU/min} \le \Delta u \le 16.7\text{mU/min} \quad (10)$$

Not all states are measured, so state estimation is used to determine the best estimate of the current state vector, which is used as the initial condition for the future predictions. The Kalman Filter (KF) used is of the following form:

$$\hat{x}^{a}_{k|k-1} = \Phi^{a}\hat{x}^{a}_{k-1|k-1} + \Gamma^{a}u_{k-1} \quad (11)$$

$$\hat{x}^{a}_{k|k} = \hat{x}^{a}_{k|k-1} + L(y_k - C^{a}\hat{x}^{a}_{k|k-1}) \quad (12)$$

where $\hat{x}_{m|n}$ represents the estimate at time step m, given measurements up to time step n, y_k is the actual measured value with 2% sensor noise, and L is the steady-state KF gain. Superscript a indicates that the input disturbance is augmented into the state space matrices as a fourth state. See [3] for a discussion of this approach.

SORENSON PLANT

This model also describes the glucose-insulin dynamics of the human body but is composed of 19 state equations, describing insulin and glucose concentrations in various areas of the body and also incorporates the effect of glucagon, another regulatory hormone [4].

RESULTS AND DISCUSSION

The controller designed based on the linearized 3-state Bergman model was tested on the nonlinear 19-state Sorenson plant (after appropriate changes in units), with the purpose of controlling blood sugar level to the desired range of 3.5 – 6.5 mmoles/L (63 – 120 mg/dl). A meal disturbance given by the form D(t) = 1.157exp(-0.05t) was implemented at 200 minutes, to test the disturbance rejection of the system. The results are shown in Fig. 1. There is an initial dip below the setpoint value of 77mg/dl, but hypoglycemic levels are not reached. This might indicate that the dynamics of the Sorenson model are slower than that of the Bergman model, with the controller action taking effect before the meal substantially influences the glucose level. The maximum rise is to 130 mg/dl (7.2mmoles/L). The settling time is just over three hours, but the blood sugar level is back in normoglycemic range within two hours, similar to the behavior of a non-diabetic person. In spite of plant-model mismatch (both parametric and structural), the performance of the estimation-based model predictive control strategy is quite good. It should be noted that a similar simulation-based study was performed by Parker et al. [5], who used the 19-state model for both the plant (patient) simulation and controller design; their approach was based on unconstrained MPC, however, which does not yield optimal results when constraints are encountered.

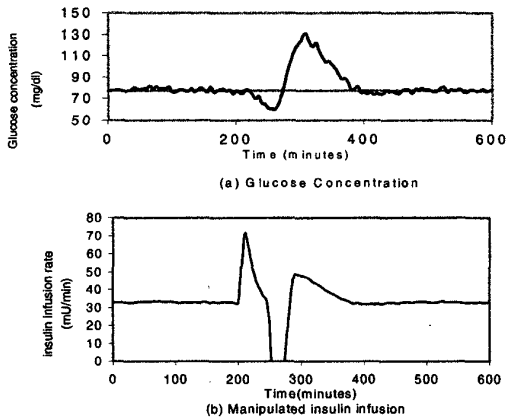

Fig 1. Control response to a 50g glucose meal disturbance at 200 minutes

The simulation-based results we have presented represent a first-step towards our long-term objective of combining a robust glucose sensor with an insulin infusion pump (external or internal) to form an artificial pancreas. A current research focus includes the development of low-order, patient specific models, including estimation of parameters for a Bergman-type model as well as subspace identification.

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