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Development of a multi-parametric model predictive control algorithm for insulin delivery in type 1 diabetes mellitus using clinical parameters

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ABSTRACT

A multi-parametric model predictive control (mpMPC) algorithm for subcutaneous insulin delivery for individuals with type 1 diabetes mellitus (T1DM) that is computationally efficient, robust to variations in insulin sensitivity, and involves minimal burden for the user is proposed. System identification was achieved through impulse response tests feasible for ambulatory conditions on the UVa/Padova simulator adult subjects with T1DM. An alternative means of system identification using readily available clinical parameters was also investigated. A safety constraint was included explicitly in the algorithm formulation using clinical parameters typical of those available to an attending physician. Closed-loop simulations were carried out with daily consumption of 200 g carbohydrate. Controller robustness was assessed by subject/model mismatch scenarios addressing daily, simultaneous variation in insulin sensitivity and meal size with the addition of Gaussian white noise with a standard deviation of 10%. A second-order-plus-time-delay transfer function model fit the validation data with a mean (coefficient of variation) root-mean-square-error (RMSE) of 26 mg/dL (19%) for a 3 h prediction horizon. The resulting control law maintained a low risk Low Blood Glucose Index without any information about carbohydrate consumption for 90% of the subjects. Low-order linear models with clinically meaningful parameters thus provided sufficient information for a model predictive control algorithm to control glycemia. The use of clinical knowledge as a safety constraint can reduce hypoglycemic events, and this same knowledge can further improve glycemic control when used explicitly as the controller model. The resulting mpMPC algorithm was sufficiently compact to be implemented on a simple electronic device.

1. Introduction

People with type 1 diabetes mellitus (T1DM) may have a life expectancy ten years less than their normal glucose tolerant counterparts due to complications resulting from chronic hyperglycemia, such as cardiovascular disease and strokes [1]. Hyperglycemia is an elevated blood glucose (BG) concentration, with a threshold defined as BG greater than 180 mg/dL [2]. Aggressive treatment with intensive insulin therapy (IIT), involving up to a total of 12 manual capillary glucose measurements and insulin injections per day, reduces hyperglycemia and can lead to a reduction in the prevalence of these complications [2]. IIT also increases the risk of hypoglycemic events and increases the burden on the caregiver and/or patient administering the therapy [3]. Hypoglycemia is any lower than normal BG; symptoms of hypoglycemia, such as tachycardia and nausea, occur at around 50–70 mg/dL [4,5].

The attraction of an efficient closed-loop device is thus threefold: increased life expectancy, decreased hypoglycemia, and reduction in the burden of administering effective therapy. Innovations in real-time continuous glucose monitoring (CGM) sensors and continuous subcutaneous insulin infusion (CSII) pumps mean that the components necessary for a closed-loop device suitable for use in ambulatory conditions are maturing [6], leaving the control algorithm as the limiting factor in development.

CGM sensors and CSII pumps use the subcutaneous (SC) route for glucose measurement and insulin delivery, respectively. Other routes, such as intravenous and intraperitoneal [7,8], offer

Abbreviations: BG, blood glucose; CGM, continuous glucose monitoring; CF, correction factor; CHO, carbohydrate; CSII, continuous subcutaneous insulin infusion; FDA, Food and Drug Administration; ICR, insulin-to-carbohydrate ratio; IIT, intensive insulin therapy; IV, intravenous; SC, subcutaneous; T1DM, type 1 diabetes mellitus.

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