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Improved blood glucose control for critically ill subjects

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ABSTRACT

For patients in intensive care units (ICUs), control of blood glucose level is an important factor in reducing serious complications and mortality. Standard protocols for glucose control in ICUs have been based on infrequent glucose measurements, look-up tables to determine the appropriate insulin infusion rates, and bedside administration of the insulin infusion by ICU staff. In this paper a new automatic control strategy is proposed based on frequent glucose measurements and a self-tuning control technique. During a short initial time period when manual glucose control is performed using a standard protocol, a simple dynamic model of the glucose–insulin system is identified in real time using recursive least squares. Then an adaptive PID controller is tuned, based on the model parameters, and the controller is turned on. A simulation study based on detailed physiological models of the glucose–insulin dynamics demonstrates that the proposed control strategy performs better than standard protocols for insulin infusion.

1. Introduction

In healthy individuals, blood glucose (BG) concentration usually stays within an interval of about 60–150 mg/dL. This euglycemic state is maintained thanks to the action of a complex endogenous glucose regulation system, where insulin (an endogenous hormone produced by the pancreas) plays a central role. BG levels persistently larger than the upper threshold correspond to a state known as *hyperglycemia*. Although this state is typical of diabetes (a metabolic disease resulting from defects in insulin production, insulin action, or both), in individuals who are critically ill, hyperglycemia can be induced by acute stress even if they have no prior history of diabetes [1–3]; for example, for a critically ill, non-diabetic subject entering an intensive care unit (ICU), the BG level can easily be higher than 200 mg/dL.

The hyperglycemic response to acute stress can be ascribed both to endogenous contributors (e.g., increased counter-regulatory hormones, increased insulin resistance, decreased glucose uptake) and to exogenous contributors (e.g., medications) [4]. Stress-induced hyperglycemia is strongly associated with adverse outcomes in subjects with acute myocardial infarction, stroke and trauma. Furthermore, in heterogeneous ICU populations hyperglycemia has been associated with increased hospital mortality and increases in other negative clinical outcomes, including severe infection, sepsis, as well as multiple organ failures [1–5]. In past years, there was a widespread consensus that strict glycemic control should be maintained in a critically ill patient [2,5]. The NICE-SUGAR trial [6] challenged this thesis recently, but the results of the trial itself were criticized by many [7] in terms of the adopted methodology. Thus, despite the widespread consensus that hyperglycemia should be treated within ICUs [7,8], an appropriate glucose target (or range) to achieve is still under discussion.

Stress-induced hyperglycemia management in an ICU resembles the management of glycemia for a person with type 1 diabetes or insulin-dependent, type 2 diabetes, to whom exogenous insulin must be administered in order to control his/her BG level. However, additional challenges are present with respect to diabetes management, because the basal state (nominal BG level) and insulin sensitivity of a critically ill patient may be not known in advance, especially so if the patient is admitted to an ICU from an emergency room.

Several techniques have been proposed to control BG in a critically ill patient, ranging from nurse-implemented *insulin infusion protocols* (IIPs) to conventional and advanced automatic controllers. The IIPs are generally in the form of look-up tables that are used by the nursing staff to specify the exogenous insulin infusion rate according to glucose measurements taken every 1–4 h (e.g., by point-of-care glucose meters via capillary (fingerstick) measurements). The insulin infusion recommendations generated

Abbreviations: ARX, autoregressive with exogenous input; BG, blood glucose; GIM, glucose–insulin model; ICU, intensive care unit; IIP, insulin infusion protocol; IV, intravenous; PID, proportional-integral-derivative; RLS, recursive least-squares.

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