DEVELOPMENT OF CONTROL ALGORITHMS FOR BLOOD GLUCOSE REGULATION IN THE CRITICALLY ILL

By

Jing Sun

A Thesis Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: CHEMICAL AND BIOLOGICAL ENGINEERING

Approved by the
Examining Committee:

____

B Wayne Bequette, Thesis Adviser

____

Cynthia Collins, Member

____

Pankaj Karande, Member

____

Anak Agung Julius, Member

Rensselaer Polytechnic Institute
Troy, New York

September 2011
(For Graduation December 2011)

ABSTRACT

Management of blood glucose is a much focused topic of pivotal importance in helping improve the quality of life in health care. Various challenges could be encountered in different clinical circumstances in maintaining "euglycemia" (a normal basal BG level in the range of 80 to 100mg/dl). This research is focused on glycaemic control for the critically ill.

Individuals who are critically ill may suffer from hyperglycemia (could be much higher than 200mg/dl) and insulin resistance, even with no history of diabetes. A landmark study by Van den Berghe showed that maintaining blood glucose below 110 mg/dl reduced dramatically overall in-hospital mortality and morbidity. Although this study is not without controversy, a lot of efforts are still focused on the realization of "tight" glucose control (close-to-normal) in the ICU.

A body of literature shows that model-based glucose control strategies work better than the sliding scale/titration approaches and estimator-based approaches. Thus, a classical Internal Model Control (IMC)-based Proportional-Integral-Derivative (PID) controller is designed based on one standard patient and compared with commercial Columnar Insulin Dosing (CID), Glucose Regulation for Intensive Care Patients (GRIP), Biostator II and Yale Protocol algorithms. Simulation results on 15 in silico patients using a three-state physiological model show that the IMC-based PID controller outperforms other control approaches in both glucose tracking and management of hypoglycemic episodes.

Additionally, more advanced model-based control strategies are developed. In this work, the controller is divided into two essential components: control law and predictor. The control law makes decision on the appropriate amount of manipulated input (IV insulin and nutrition included) to be infused into the patient, meanwhile the predictor feeds the control law information of the predicted BG level for the future steps. While the focus is often on regulating blood glucose by infusing insulin, it should be recognized that ICU patients also have nutritional needs that are satisfied by both enteral (feeding tubes) and parenteral (IV) delivery. Therefore,

the habituating control law developed includes glucose feedrate as another manipulated input, in addition to insulin infusion. These ideas can be considered extensions of the habituating control strategy proposed by Henson, which uses an additional degree of freedom to improve disturbance rejection. In order to handle the wide variability in insulin sensitivity from patient-to-patient, as well as for specific individuals during the course of their hospital stay, we design our predictor based on the multiple model Kalman filter strategy. Finally, a controller is established with the combination of the habituating control law and multiple model Kalman filter predictor, which leads to better performance than fixed-model and single input control strategies in inducing less hypo-and hyperglycemia (smaller BGRI) and less variability (bigger minimum and smaller maximum values) in our simulation studies.