Journal of Diabetes Science and Technology
Volume 7, Issue 1, January 2013

ORIGINAL ARTICLE

Multilevel Model of Type 1 Diabetes Mellitus Patients for Model-Based Glucose Controllers

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Abstract

Background:

Glucose homeostasis is the result of complex interactions across different biological levels. This multilevel characteristic should be considered when analyzing and designing closed-loop glucose control algorithms. Classic control schemes use only a pharmacokinetic-pharmacodynamic (PKPD) perspective to describe the glucoregulatory system.

Methods:

A multilevel model combining a PKPD model with an insulin signaling model is proposed for patients with type 1 diabetes mellitus T1DM (T1DM). The PKPD Dalla Man model for T1DM is expanded to include an intracellular level involving insulin signaling to control glucose uptake through glucose transporter type 4 (GLUT4) translocation. A model-based controller is then designed and used as an example to illustrate the feasibility of the proposal.

Results:

Two significant results were obtained for the controller explicitly utilizing multilevel information. No hypoglycemic events were registered and an excellent performance for interpatient variability was achieved. Controller performance was evaluated using two indexes. The glucose was kept inside the range (70–180) mg/dl more than 99% of the time, and the intrapatient variability measured using control variability grid analysis was solid with 90% of the population inside the target zone.

Conclusions:

Multilevel models open new possibilities for designing glucose control algorithms. They allow controllers to take into account variables that have a strong influence on glucose homeostasis. A model-based controller was used for demonstrating how improved knowledge of the multilevel nature of diabetes increases the robustness and performance of glucose control algorithms. Using the proposed multi-level approach, a reduction of the hypoglycemic risk and robust behaviour for intrapatient variability was demonstrated.

J Diabetes Sci Technol 2013;7(1):193–205

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Abbreviations: (CVGA) control variability grid analysis, (GLUT4) glucose transporter type 4, (MPC) model predictive control, (PKPD) pharmacokinetic/pharmacodynamic, (T1DM) type 1 diabetes mellitus, (UVa) University of Virginia

Keywords: artificial pancreas, glucose closed-loop control, model predictive control, multilevel model

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