

Symposium Paper

Editorial: Symposium on Algorithms for Continuous Glucose Monitoring and Control

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SYSTEMS AND CONTROL THEORY is the basis for algorithms embedded in many of the products (both high and low “tech”) that we use in our daily lives. While consumers appreciate the relative compactness of CD and DVD players and microdrives, for example, and value the manufacturing technology involved in miniaturization, they probably do not think much about the mathematical algorithms that enable these systems to operate.

There are a number of devices/products in the market, or under development, for continuous glucose monitoring and control. A primary goal of this symposium is to give clinicians a better understanding of how a systems engineering approach can be applied to diabetes technology. A secondary audience consists of systems engineers seeking to understand some of the challenges related to blood glucose monitoring and control in diabetes.

The first two papers study continuous glucose monitoring. Challenges to the use of continuous subcutaneous glucose sensors are that the signals can have substantial measurement noise, they must be calibrated based on a blood glucose measurement, and there is a dynamic lag between the blood and subcutaneous glucose concentrations. The article in this symposium by Palerm et al.¹ focuses on filtering the noisy subcutaneous sensor signal and predicting the future subcutaneous glucose concentration as a function of time to provide a

warning of impending hypoglycemia. This study details the effects of sample time, prediction horizon, and hypoglycemic threshold on the sensitivity and $1 - \text{specificity}$ (rate of false alarms). The analysis is applied to an idealized signal (sinusoid) to understand the inherent limitations of hypoglycemia warning indicators. One of the major uses of continuous glucose monitoring, initially, is for a nocturnal hypoglycemic warning device for juveniles. The approach developed by Palerm et al.¹ should lead to a better understanding of how the parameters affect the rate of false-positives, and thus improve the design of a hypoglycemic alarm. The article by Knobbe and Buckingham² applies optimal estimation techniques to estimate the blood glucose from continuous subcutaneous sensor signals. Their approach accounts for the time lag between blood glucose and the subcutaneous sensor. This approach is applied to patients in the Diabetes Research in Children Network (DirectNet) program using the Medtronic MiniMed (Northridge, CA) continuous glucose monitoring system (CGMS[®]).

One of the long-term goals of continuous glucose monitoring is to provide a sensor signal that can be used in a closed-loop artificial pancreas. In the third article I provide a historical review of feedback control theory and application, and a personal perspective of the challenges in the development of an artificial pancreas.³

Some manufacturing processes (particularly in semiconductor and pharmaceutical industries) operate in a batch-wise fashion, with measurements available only at the end of the batch. Zisser et al.⁴ extend so-called “run-to-run” control techniques to determine the best insulin dose (meal bolus) for each meal. Their clinical study is conducted on 14 type 1 individuals. The paper by Cook et al.⁵ develops an intelligent dosing strategy to suggest the average daily insulin dose between office visits, to patients with type 2 diabetes. This approach is somewhat related to run-to-run control, but leaves decisions about how to distribute the insulin dose throughout the day to the clinician. Concerns about this approach have been delineated in the commentary by Bequette and Desemone⁶ and will not be detailed here.

The next symposium article, by Chassin et al.,⁷ develops a grading system to assess the clinical performance of closed-loop glucose control systems. The proposed approach is applied in simulation studies of a model predictive controller applied to 17 individuals with type 1 diabetes, and compared with other measures of glucose control that have been proposed in the literature.

There has been much effort recently in the development of model-based strategies for closed-loop control. The final two papers of this symposium address the development of models that can be used in a closed-loop artificial pancreas. Hipszer et al.⁸ develop pharmacokinetic models for the intravenous delivery of insulin, for critical care application. They find that a one-compartment model (represented by a single differential equation) adequately describes the dynamics between insulin delivery and blood concentration for four of the five subjects studied. The final paper, by Steil et al.,⁹ provides a detailed analysis of three glucose kinetic models, which relate the insulin concentration in the blood to the glucose concentration. The authors suggest that data from open-loop control of glucose in type 1 diabetes patients can be used to improve these models for use in a fully closed-loop artificial pancreas.

This set of papers represents an overview of algorithms for continuous glucose monitoring and control. Hopefully the papers provide the right combination of depth and breadth to give clinicians a general idea of the application of systems and control techniques to diabetes technology. David Klonoff and I intend to develop similar symposia in the future and welcome your comments and suggestions on the topics covered and the depth of mathematical analysis.

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