

Analysis, Modeling, and Simulation of the Accuracy of Continuous Glucose Sensors

Marc Breton, Ph.D. and Boris Kovatchev, Ph.D.

Abstract

Background:

Continuous glucose monitors (CGMs) collect a detailed time series of consecutive observations of the underlying process of glucose fluctuations. To some extent, however, the high temporal resolution of the data is accompanied by increased probability of error in any single data point. Due to both physiological and technical reasons, the structure of these errors is complex and their analysis is not straightforward. In this article, we describe some of the methods needed to obtain a description of the sensor error that is detailed enough for simulation.

Methods:

Data were provided by Abbott Diabetes Care and included two data sets collected by the FreeStyle Navigator™ CGM: The first set consisted of 1032 time series of glucose readings from 136 patients with type 1 diabetes and parallel time series of reference blood glucose (BG) collected via self-monitoring at irregular intervals. The average duration of a time series was 5 days; the total number of sensor-reference data pairs was approximately 20,600. The second data set consisted of 56 time series of glucose readings from 28 patients with type 1 diabetes and a parallel time series of reference BG measured via the YSI 2300 Stat Plus™ analyzer every 15 minutes. The average duration of a time series was 2 days; the total number of sensor-reference data pairs was approximately 7000.

Results:

Three sets of results are discussed: analysis of sensor errors with respect to the BG rate of change, mathematical modeling of sensor error patterns and distribution, and computer simulation of sensor errors:

1. Sensor errors depend nonlinearly on the BG rate of change: Errors tend to be positive (high readings) when the BG rate of change is negative and negative (low readings) when the BG rate of change is positive, which is indicative of an underlying time delay. In addition, the sensor noise is non-white (non-Gaussian) and the consecutive sensor errors are highly interdependent.

continued →

Author Affiliation: University of Virginia, Charlottesville, Virginia

Abbreviations: (ACF) autocorrelation function, (ARMA) autoregressive moving average, (BG) blood glucose, (CGM) continuous glucose monitor, (iid) independent identically distributed, (IG) interstitial glucose, (PACF) partial autocorrelation function, (SMBG) self-monitored blood glucose

Keywords: accuracy, continuous glucose monitoring, time series

Corresponding Author: Marc Breton, Ph.D., University of Virginia Health System, Box 400888, Charlottesville, VA 22908; email address mb6nt@virginia.edu

Abstract cont.

2. Thus, the modeling of sensor errors is based on a diffusion model of blood-to-interstitial glucose transport, which accounts for the time delay, and a time-series approach, which includes autoregressive moving average (ARMA) noise to account for the interdependence of consecutive sensor errors.
3. Based on modeling, we have developed a computer simulator of sensor errors that includes both generic and sensor-specific error components. A χ^2 test showed that no significant difference exists between the observed and the simulated distribution of sensor errors and the distribution of errors of the FreeStyle Navigator ($p > .46$).

Conclusions:

CGM accuracy was modeled via diffusion and additive ARMA noise, which allowed for designing a computer simulator of sensor errors. The simulator, a component of a larger simulation platform approved by the Food and Drug Administration in January 2008 for pre-clinical testing of closed-loop strategies, has been successfully applied to *in silico* testing of closed-loop control algorithms, resulting in an investigational device exemption for closed-loop trials at the University of Virginia.

J Diabetes Sci Technol 2008;2(5):853-862