Biomedical Signal Processing and Control 38 (2017) 86–99

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

Fault and meal detection by redundant continuous glucose monitors and the unscented Kalman filter

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ARTICLE INFO

Article history:
Received 6 December 2016
Received in revised form 7 April 2017
Accepted 8 April 2017

Keywords:
Continuous glucose monitoring sensor
Fault detection
Unscented Kalman filter
Adaptive filtering
Sensor redundancy

ABSTRACT

The purpose of this study is to develop a method for detecting and compensating the anomalies of continuous glucose monitoring (CGM) sensors as well as detecting unannounced meals. Both features, sensor fault detection/correction and meal detection, are necessary to have a reliable artificial pancreas. The aim is to investigate the best detection results achievable with the proposed detection configuration in a perfect situation, and to have the results as a benchmark against which the imperfect scenarios of the proposed fault detection can be compared. The perfect situation that we set up here is in terms of a patient simulation model, where the model in the detector is the same as the patient simulation model used for evaluation of the detector. The detection module consists of two CGM sensors, two fault detectors, a fault isolator, and an adaptive unscented Kalman filter (UKF). Two types of sensor faults, i.e., drift and pressure induced sensor attenuation (PISA), are simulated by a Gaussian random walk model. Each of the fault detectors has a local UKF that receives the signal from the associated sensor, detects faults, and finally tunes the adaptive UKF. A fault isolator that accepts data from the two fault detectors differentiates between a sensor fault and an unannounced meal appearing as an anomaly in the CGM data. If the fault isolator indicates a sensor fault, a method based on the covariance matching technique tunes the covariance of the measurement noise associated with the faulty sensor. The main UKF uses the tuned noise covariances and fuses the CGM data from the two sensors. The drift detection sensitivity and specificity are 80.9% and 92.6%, respectively. The sensitivity and specificity of PISA detection are 78.1% and 82.7%, respectively. The fault detectors can detect 100 out of 100 simulated drifts and 485 out of 500 simulated PISA events. Compared to a nonadaptive UKF, the adaptive UKF reduces the deviation of the CGM measurements from their paired blood glucose concentrations from 72.0% to 12.5% when CGM is corrupted by drift, and from 10.7% to 6.8% when CGM is corrupted by PISA. The fault isolator can detect 199 out of 200 unannounced meals. The average change in the glucose concentrations between the meals and the detection time points is 46.3 mg/dL.

1. Introduction

As the continuous glucose monitoring (CGM) sensor is one of the main parts of an artificial pancreas (AP), the anomalies and faults associated with the CGM sensor affect the performance and reliability of the AP considerably. Consequently, the safety of patients in an AP is critically connected to the reliability of the CGM sensors [1–4]. Recent advances in sensor technology have made it possible to achieve high accuracy CGM sensors. An example is the CGM sensor under development by Roche (Roche Diagnostics GmbH, Mannheim, Germany), which provides an aggregated mean absolute relative difference (MARD) between the CGM readings and their paired capillary blood glucose (BG) measurements of 9.2% [5]. A study by Bailey et al. [6] also indicated that the FreeStyle Libre Flash glucose monitoring system (Abbott Diabetes Care, Alameda, CA) has an overall MARD of 11.4% without the need for calibration within two weeks. However, the Flash sensor is not suited for the AP application. Dexcom (San Diego, CA) also tested the accuracy of the G4® Platinum (G4P) CGM system with the 505

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http://dx.doi.org/10.1016/j.bspc.2017.05.004
1746-8094/

algorithm, achieving a MARD of 13% [7]. Furthermore, the Dexcom G5® mobile CGM has been recently approved for insulin-dosing in Europe, which indicates the acceptable reliability of the G5® system for nonadjunctive use [8]. Despite these advances in the sensor technology and accuracy, the CGM fault detection is still a challenge that requires attention and it serves as an active research area [9]. In this study, we enhance the CGM data by developing an algorithm for fault and meal detection. Fault detection improves the CGM safety and detection of unannounced meals helps developing a fully automated AP. The faults that we aim to detect are drift and the pressure induced sensor attenuation (PISA) artifact. Drift remains the main reason for sensor calibration [10], and calibration for at least twice a day is recommended to compensate for the sensor drift. Drift is the falsely slow variations of the CGM readings due to foreign body response causing the inflammatory cells to migrate to the sensor insertion site [11]. The inflammatory cells produce compounds that interact with the glucose sensor and erroneously increase or decrease the glucose readings over the course of time. PISA is another sensor anomaly and it is the low signal readings caused by the compression of the sensor insertion site due to pressure on the sensor [12].

Several methods have been proposed for outlier detection and smoothing the CGM data. These methods include finite and infinite impulse response filters [13,14], as well as model-based outlier detection with adaptive and nonadaptive Kalman filters [15–18]. While these denoising methods effectively smooth the CGM signal by filtering out the spiky outliers and noise, they are insufficient to remove the manifestations of the sensor artifacts, such as drift, from the CGM data. The reason is that the time scale of a sensor drift could be comparable with the time scale of the signature of the physiological events such as meal, insulin, exercise, and stress on the CGM signal. This makes it difficult to detect the sensor drift and differentiate it from the metabolic changes in the BG. Consequently, a robust and safe AP requires additional sources of information through physical redundancy (using more than one CGM sensor) and analytical redundancy (using a model in addition to the measurements) to detect and discriminate between drift and the physiological events such as unannounced meals. While previous studies suggest methods for drift and PISA detection [19,20], the literature on filtering out the drift and PISA events upon detection is sparse.

We previously developed a fault detector for the CGM data using the extended Kalman filter (EKF) [21], which we further improved by using an unscented Kalman filter (UKF) [22]. In the current study, we use the fault detector with the UKF for the detection of drift, PISA, and unannounced meals, and also for tuning an adaptive UKF upon fault detection, in a two-CGM sensor configuration. Fig. 1 depicts the schematic configuration of the two CGM sensors, the insulin pump, and the signal processing unit, for the proposed method in a single-hormone AP. The adaptive UKF allows modifying the covariance of the measurement noise in case the CGM sensors are fault-corrupted. This mitigates the signature of a fault on the filtered CGM data. We also designed a fault isolator unit to discriminate between a sensor fault and a change in the CGM signal due to the patient's metabolism variations. Examples of metabolic variations are meal, exercise, stress, and variation of the insulin sensitivity. Any of these events, if not correctly announced to the model, manifests itself in the CGM signal in a way that is similar to the manifestation of a sensor anomaly. As different treatment should be applied for a sensor anomaly and a metabolic change, it is also important that these two categories of events are detected and differentiated accordingly. In our method, the UKF is tuned only if the fault isolator indicates a sensor fault.

The rest of the paper is structured as follows. Section 2 describes the Medtronic virtual patient (MVP) model for type 1 diabetes [23], and our methods for simulating sensor drift and PISA. The MVP model is used for patient simulation and also in the UKFs. Section 3 explains the UKF for filtering, fault detection, and fault isolation and meal detection. At the end, Section 3 presents the method for tuning the measurement noise covariance with the local UKFs of the fault detectors. Section 4 presents the results followed by the discussions in Section 5 and concluding remarks in Section 6.

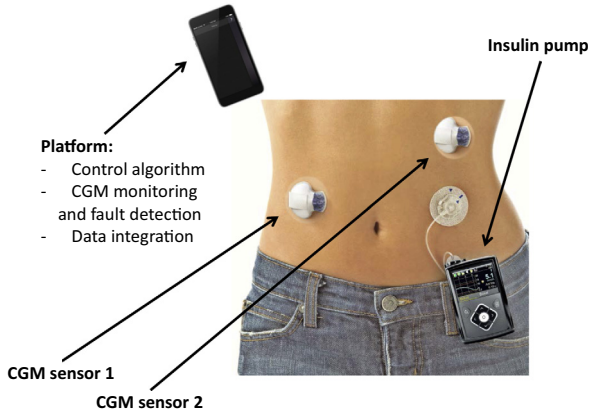

Fig. 1. Configuration of the two continuous glucose monitoring sensors, the insulin pump, and the signal processing platform-implemented in a smart phone – for an artificial pancreas.

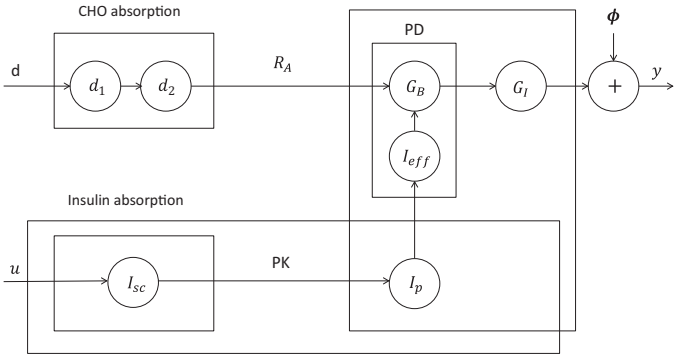

Fig. 2. The Medtronic virtual patient model for type 1 diabetes [23]. d: CHO ingestion rate; d_1 and d_2: glucose masses (mg) in the stomach and small intestine compartments, respectively; R_A: glucose appearance rate; G_B: blood glucose concentration; G_I: interstitial glucose concentration; u: insulin input rate; I_{SC}: SC insulin concentration; I_p: plasma insulin concentration; I_{eff}: insulin effect; ϕ: measurement noise; y: CGM measurement.

2. Simulation

2.1. Virtual patient model

We simulated the MVP model [23], and the two-compartmental model of carbohydrate (CHO) absorption [24], by means of stochastic differential equations (SDEs). The model is based on the work by Hovorka and associates [24–26]. Fig. 2 depicts the model and Appendix A describes the model equations. In Fig. 2, u is the subcutaneous (SC) insulin input rate (μU/min) and contains both basal and bolus insulin administrations. I_{SC}, I_p, and I_{eff} are the SC insulin concentration (mU/L), the plasma insulin concentration (mU/L), and the effect of insulin (min^{-1}), respectively. G_B is the blood glucose concentration. Glucose diffuses from capillary blood into interstitial fluid and the CGM sensor measures the interstitial glucose (G_I) concentration (mg/dL). The input d denotes the CHO ingestion rate (g/min), d_1 and d_2 are the glucose masses (mg) in the stomach and small intestine compartments, and R_A is the glu-