journal homepage: www.intl.elsevierhealth.com/journals/cmpb

# Profiling intra-patient type I diabetes behaviors

*Iván Contreras* [a,*], *Carmen Quirós* [b], *Marga Giménez* [b], *Ignacio Conget* [b], *Josep Vehi* [a]

[a] *Institut d'Informática i Aplicacions, Universitat de Girona, Campus de Montilivi, Girona, Spain*
[b] *Diabetes Unit, Endocrinology and Nutrition Department, Hospital Clínic i Universitari, Barcelona, Spain*

ARTICLE INFO

*Article history:*
Received 8 March 2016
Received in revised form
22 July 2016
Accepted 29 August 2016

*Keywords:*
Type 1 diabetes
Continuous glucose monitoring
Insulin pumps
Time series prediction
Clustering

ABSTRACT

*Background:* The large intra-patient variability in type 1 diabetic patients dramatically reduces the ability to achieve adequate blood glucose control. A novel methodology to identify different blood glucose dynamics profiles will allow therapies to be more accurate and tailored according to patient's conditions and to the situations faced by patients (exercise, weekends, holidays, menstruation, etc).

*Materials and methods:* A clustering methodology based on the normalized compression distance is applied to identify different profiles for diabetic patients. First, the methodology is validated using "*in silico*" data from 10 patients in 3 different scenarios: days without exercise, poor controlled exercise days and days with well-controlled exercise. Second, we perform a series of *in vivo* experiments using data from 10 patients assessing the ability of the proposed methodology in real scenarios.

*Results:* *In silico* experiments show that the methodology is able to identify poor and well-controlled days in theoretical scenarios. *In vivo* experiments present meaningful profiles for working days, bank days and other situations, where different insulin requirements were detected.

*Conclusions:* A tool for profiling blood glucose dynamics of patients can be implemented in a short term to enhance existing analysis platforms using combined CGM-CSII systems. Besides coping with the information overload, the tool will assist physicians to adjust and improve insulin therapy and patients in the self-management of the disease.

© 2016 Elsevier Ireland Ltd. All rights reserved.

## 1. Introduction

Integrated systems using continuous glucose monitors (CGM) and continuous subcutaneous insulin infusion (CSII) have had a significant impact in type 1 diabetes (T1D) management. The use of CSII-CGM systems was shown to reduce HbA1c without increasing the time spent in hypoglycemia [1]. Subsequently, CSII-CGM systems with automatic features such as automatic suspension of insulin delivery during hypoglycemia and predictive low glucose suspend have shown to reduce nocturnal hypoglycemia without increasing mean glucose substantially [2,3]. Furthermore, the recent advances in CGM have led to more robust and portable devices which have demonstrated their value in improving the glycemic control working with closed-loop algorithms [4,5]. The integration of data originating from

*Abbreviations:* AUC180, the area under the curve above 180; AUC70, the area under the curve below 70; BG, blood glucose; BGV, the blood glucose variability; CGM, continuous glucose monitors; CHO, the daily carbohydrates; CSII, continuous subcutaneous insulin infusion; I:C, the insulin to carbohydrates ratio; ISIG, the average interstitial signal for Enlite sensors; ISIGV, the ISIG variability; NCD, normalized compression distance; T1D, type 1 diabetes; TDD, the total diary dose of insulin.

* *Corresponding author.* Institut d'Informática i Aplicacions, Universitat de Girona, Campus de Montilivi, Girona, Spain. Fax: +34 972 41 82 59.
E-mail address: ivancontrerasfd@gmail.com (I. Contreras).

http://dx.doi.org/10.1016/j.cmpb.2016.08.022
0169-2607/© 2016 Elsevier Ireland Ltd. All rights reserved.

sensor-based systems and electronic health records combined with smart data analytics methods and powerful user centered approaches enables the shift toward preventive, predictive, personalized, and participatory diabetes care [6]. However, the limited capacity of current solutions to process the data extracted from glucose monitors limits the development of enhanced diabetes management solutions.

Nowadays, companies commercializing CSII-CGM systems offer software platforms that provide tools to upload data from sensors, to share information with physicians and give patient support to diabetes management. These platforms are currently integrating methodologies to support treatment management by analyzing the data generated by the CGM. A notable example is the Medtronic software CareLink Pro/Personal® which provides functionalities to analyze BG values depending on the events occurring at specific periods, assisting patients and physicians with recommendations, which can lead to an improved insulin therapy. However, these features are still unable to detect the majority of scenarios with high impact in the blood glucose variability such as exercise, menstrual period, seasons, diet disturbances, or habits among other factors. Thus, the complexity of generating accurate treatments is accentuated when we have to deal with disturbances that can arise in the same patient. This intra-patient variability has different effects on BG levels altering the patterns usually generated by patients with T1D. The ability to identify such patterns would allow generating temporal profiles, which in turn can assist in identifying the causes of poor glycemic control and aid in the therapy adjustment. With the objective of analyzing similarities among time series we use a hierarchical clustering methodology based on an innovative similarity measure.

In the medical field, clustering methodologies are used in problems such as identifying effective treatments, recognition of diseases and detection of best practices. Broadly speaking, clustering methodologies are used to discover and study the macroscopic structure and relations between objects. The hierarchical clustering family of methods is defined by the method used to compute distances and a linkage criterion. A well-known distance metric is the normalized compression distance (NCD). The NCD is a compression-based similarity distance based on the Kolmogorov complexity [7]. This determines the similarity in terms of information distance between pairs of objects according to the most dominant common features. Previous studies have demonstrated that the NCD is a reliable tool for classification on a number of domains (see Ref. [8]). Furthermore, NCD has been applied successfully in many areas such as classification of genomes [9], protein structure comparison [10], genotyping [11], tumor subclassifications [12] or virus detection [13] among many others. In this study, we are presenting a new methodology that may provide a novel tool capable of extracting information on glucose profile of patients using CGM. This tool can help physicians and patients to detect patterns of poor glycemic control easily, providing useful information for the therapy adjustment.

## 2. Materials and methods

We have used a data mining technique aimed to identify time series following different patterns despite the seemingly

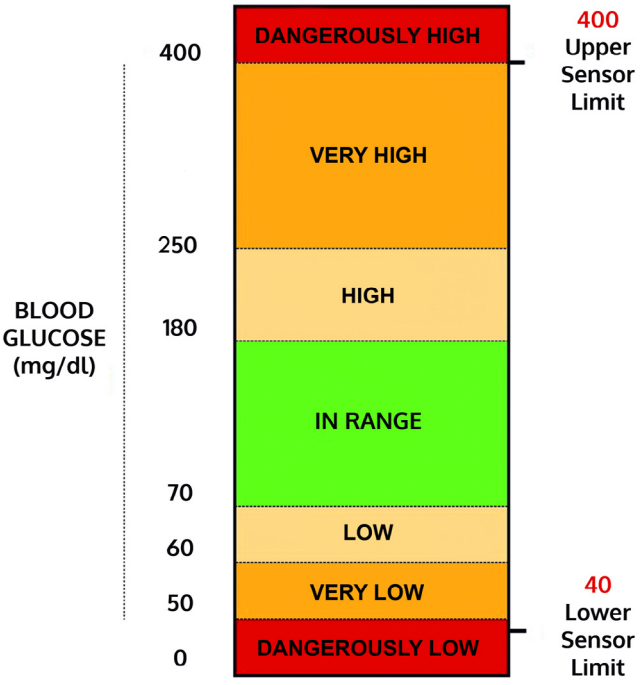


**Fig. 1 – Blood glucose ranges: The 7 ranges of blood glucose applied in this work to discretize the time series of blood glucose extracted with continuous glucose monitors. The recommendation ranges for the standardization of blood glucose was proposed in Ref. [6]. The lower and upper thresholds are fixed by the limits of current commercialized systems in 40 and 400 mg/dl.**

uncorrelated behavior of the BG series. The clustering process can be summarized as a method that builds a binary tree from individual elements by progressively merging the clusters containing the two closest elements. Thus, we consider a set of N time series to be clustered and a distance matrix, also called dis-similarity matrix, with N*N measurements. The distance measure used to build the distance matrix is the modified normalized compression distance, which was proposed in Ref. [8]. The NCD approach is a similarity distance that exploits the management of the different dictionaries used by a compressor to reduce the redundancy. The process of merging clusters is guided by the complete linkage method [14] due to compromise between simplicity, ease of analysis and its ability to obtain quality solutions.

In order to discretize the values representing the BG of each day and calculate the NCD, we transformed the information by a symbolic representation of time series. Thus, BG values are transformed into sequences of characters by the application of threshold levels representing the related glucose profiles. To this end, we follow the recommended standardization of glucose ranges in Ref. [15], which allow us to analyze the values of time series by the six intervals presented in the Fig. 1.

The method builds hierarchical distance trees for daily time series sets of BG values and is able to divide any cluster further to observe its underlying structure. Therefore, in the same way that songs of same music style share patterns, or malicious software and viruses share common features, we expect multiple BG time series to share patterns that are invisible at usual

Download English Version:

https://daneshyari.com/en/article/4958285

Download Persian Version:

https://daneshyari.com/article/4958285

Daneshyari.com