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A probabilistic soft alert method for abnormal glycemic event by quantitative analysis of prediction uncertainty for type 1 diabetes

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ABSTRACT

Alerting abnormal glycemic event is of importance for people with type 1 diabetes mellitus (T1DM) using continuous glucose monitoring. The traditional deterministic hyper/hypoglycemia predictive alert methods do not consider the presence of prediction errors resulting from model inaccuracy and external disturbances and may lead to false positive alerts resulting in incorrect therapeutic actions. To address this problem, a probabilistic soft alert method is proposed to quantify the prediction uncertainty of hyper/hypoglycemic events. This method evaluates uncertainty caused by prediction errors and the probability density function of prediction errors is estimated using the Gaussian mixture model (GMM). Thus, a soft confidence interval can be set and the probability of the hyper/hypoglycemia alert can be calculated. The parameters of GMM can be updated to revise the probability density function and confidence interval in order to capture changes of prediction uncertainty with time. The proposed method is investigated using data collected from thirty *in silico* subjects and ten adults with type 1 diabetes. For the *in silico* subjects, the proposed method reduced missed alerts by 57.1%, false alerts by 73.3% and time delay by 42.3% for hypoglycemia alert utilizing autoregressive models with exogenous inputs model. For the adult subjects, the time delay of hyperglycemia alert was reduced by 33.2% and the time delay of hypoglycemia alert was reduced by 41.6% utilizing subject-dependent autoregressive model. The proposed method is demonstrated to be able to improve the alert performance of the abnormal glycemic events.

1. Introduction

Diabetes mellitus is a group of metabolic diseases resulting from either insulin secretion deficiency or inappropriate insulin action. There are two main types of diabetes mellitus: Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) [1]. People with T1DM suffer from long-term complications including heart disease, stroke and foot ulcers [2], because the pancreas fails to produce enough insulin to manage blood glucose levels adequately. Typical treatment for T1DM is multiple insulin injection with three to four subcutaneous insulin injections per day mimicking normal endogenous insulin secretion in order to maintain euglycaemia [3,4]. Continuous glucose monitoring (CGM) devices have been developed to provide minute-to-minute subcutaneous glucose concentration readings and have opened up a new gate for diabetes treatment in T1DM [5–7]. CGM device is an important component of an 'artificial pancreas' [8,9] which is a novel and promising way for the personalization treatment of T1D [10]. The CGM devices are also used to closely monitor the change in glucose levels and predict hyper/-hypoglycemic events [11].

Predicting future blood glucose with historical CGM data for optimal therapy has become an important option in glucose management to avoid abnormal glycemic events. Previous work [11] has shown future glucose can be predicted if recent glucose measurements follow a certain known pattern. Several methods have been proposed for glucose prediction. Data-driven (or empirical) models have been widely used for time-series signal analysis in many applications [12–14]. They can be used to explore the internal relationship between the blood glucose dynamics and outside stimuli such as insulin, meals and so on. The data-driven prediction models [15–21] can be divided into two types: linear models and nonlinear models, including regression prediction [15–19], artificial neural networks [20,21], etc.

One application of glucose prediction is to generate early alert to help T1DM subjects make optimal therapeutic options. Traditional alert method is to compare the predicted glucose values against a predefined

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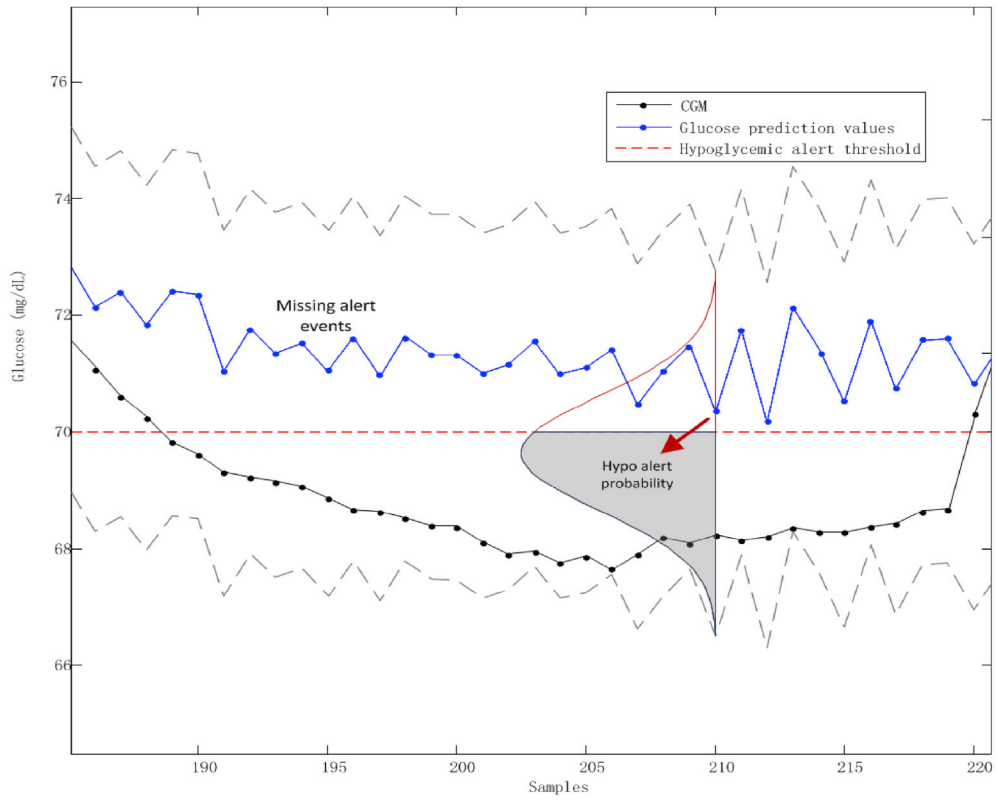
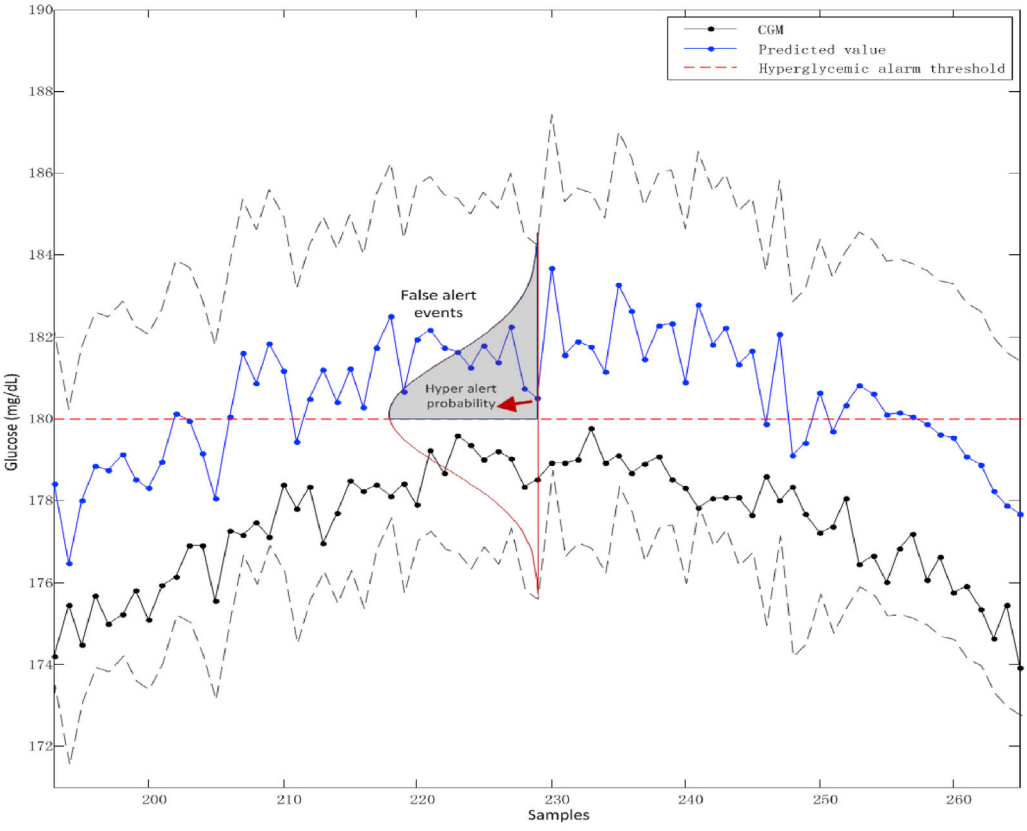


(a)



(b)

Fig. 1. The illustration of (a) missing hypoglycemia alert and (b) false hyperglycemia alert (The grey dashed line is the confidence interval of the predicted glucose values and the grey shaded area is the geometric visualization of the probability of hypo and hyper alert).