

UNIVERSAL MODELS FOR PREDICTING GLUCOSE CONCENTRATION IN HUMANS

I. FIELD OF THE INVENTION

[0001] The present invention is in the field of methodologies, systems, computer program products, and universal models for predicting glucose concentration in humans.

II. BACKGROUND OF THE INVENTION

[0002] Within this application several publications are referenced by Arabic numerals within brackets. Full citations for these, and other, publications may be found at the end of the specification immediately preceding the claims. The disclosures of all these publications in their entireties are hereby expressly incorporated by reference into the present application for the purposes of indicating the background of the present invention and illustrating the state of the art. If however there are any conflicts between this disclosure and text incorporated by reference, then statements made in this document control and supersede the incorporated teachings.

[0003] Minimally invasive continuous glucose monitoring (CGM) devices are instruments utilized to measure and record a patient's glycemic state as frequently as every minute [1]. This information can be utilized to alter or improve the patient's lifestyle, to tighten their glycemic control, or to adjust therapy. These frequent measurements can also be used by data-driven models to forecast future values of subcutaneous glucose concentration and avoid undesired hypoglycemic or hyperglycemic episodes [1]-[4].

[0004] In contrast to intermittent measurements, CGM devices collect information frequently such that consecutive measurements retain a large degree of temporal correlation. This correlation is exploited by data-driven models to infer future values as a function of previous measurements [2]-[4]. However, because of the availability of glucose signals at high sampling rates, developers of data-driven models often implicitly assume that the models need to be tuned for a specific individual, thus increasing the burden of model development and reducing their practical applicability. For example, Sparacino et al. [3] uses an autoregressive (AR) model of order one, AR(1), which continuously adapts the model coefficients to the monitored individual to predict future glucose concentrations up to 30 minutes from the time of prediction. Although such a model can produce acceptable predictions, it needs to be continuously adapted for every individual. Additionally, in spite of the adaptive nature of the model, it introduces a significant delay between predicted and measured values. This delay is caused by the low order of the AR model, because a single AR model coefficient is not sufficient to capture the temporal variations of the time-series glucose signal. In another example, Dua et al. [4] employs a Kalman filter to predict future blood glucose levels by continuously adjusting parameters of a first-principles model. Although the first-principle model is significantly more flexible than the AR(1) model of Sparacino et al., the continuous adaptation also makes the Dua et al. model individual specific.

III. SUMMARY OF THE INVENTION

[0005] At least one embodiment of the invention provides a universal, data-driven model developed based on glucose data from one diabetic subject, which is subsequently applied to predict subcutaneous glucose concentrations of other sub-

jects, even those with different types of diabetes. Three separate studies, each utilizing a different CGM device, were used to verify the model's universality. Two out of the three studies involved subjects with type 1 diabetes and the other study was for type 2 diabetes. The subcutaneous glucose concentration data are filtered (i.e., smoothed) by imposing constraints on their rate of change. Using the filtered data, data-driven autoregressive (AR) models of order 30 are developed and utilized to make short-term, 30-minute-ahead glucose-concentration predictions. Same-subject model predictions are utilized as a reference for comparisons against cross-subject and cross-study model predictions, which are evaluated using the root mean squared error (RMSE). For each studied subject, the average cross-subject and cross-study RMSEs of the predictions are small and indistinguishable from those obtained with the same-subject models. In addition, the predictive capability of the models is not affected by diabetes type, subject age, CGM device, and inter-individual differences. Thus, a stable, universal glucose models is developed that captures the invariant correlations in time-series signals of diabetic patients.

[0006] An embodiment of the invention provides a method for predicting at least one future glucose level in an individual. The method receives glucose signals from a glucose measuring device, wherein the glucose signals represent glucose levels obtained from an individual at fixed time intervals. The glucose signals are converted into numerical values representing the glucose levels obtained from the individual. The glucose signals and/or numerical values are stored in a memory unit housed in the glucose measuring device. In another embodiment, the memory unit is external to the glucose measuring device.

[0007] The method predicts one or more future glucose levels of the individual by weighing the glucose signals by model coefficients of a glucose prediction function. Weighing the previous glucose signals of the individual by the model coefficients reduces a time lag of the predicted future glucose levels. In at least one embodiment, the predicting of the future glucose level is performed with a processor (or programmable data processing apparatus) having code to perform calculations of the glucose prediction function. The glucose prediction function is a universal autoregressive model that is portable between individuals irrespective of health of the individuals. The health of the individual includes a diabetes type of the individual, age of the individual, and/or whether the individual is hospitalized. Moreover, the model coefficients are invariant between the individuals irrespective of the type of the glucose measuring device utilized to measure the glucose signals.

[0008] In addition, the method displays the predicted future glucose levels on a display and generates an alert when the future glucose level of the individual exceeds an upper glucose threshold and/or falls below a lower glucose threshold.

[0009] A method according to another embodiment of the invention obtains first glucose measurements (i.e., training data) via a glucose monitoring device. Current glucose levels are monitored at fixed time intervals in a plurality of individuals having type I and type II diabetes (i.e., test subjects). A programmed processor uses a portion of the first glucose measurements to train a glucose prediction function that is portable between individuals. The training of the glucose prediction function is independent of the type of glucose measurement device utilized to obtain the first glucose measurements, the ages of the individuals, and whether the indi-