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Comparison of Linear and Non-Linear Regression Models for Non-Invasive Blood Glucose Measurement

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Abstract: This paper deals with a new approach of non-invasive glucose monitoring based on near infrared spectroscopy. The proposed approach is coupled with a regression analysis in order to improve the predictive capacity of the designed device. Basic spectral data is a comparison that has been established between linear and non-linear machine learning regression algorithms. The experimental results show that feed forward backpropagation neural network improves more the performance of the designed prototype than partial least square models. The squared correlation coefficient and the Root Mean Square Error (RMSE) of the Artificial Neural Network (ANN) regression model built were 0.9804 and 0.0784 respectively. The ANN regression model was then used in the validation step using 300 human serums with a concentration range of 08-297 mg/dl. Clarke Error Grid Analysis (EGA) showed that 97% of the measured concentrations fall within the clinically acceptable regions. Results showed that the created model can open a new path to a non-invasive glucose monitoring.

Keywords: Non-Invasive Blood Glucose Measurement, Near Infrared Spectroscopy, Regression Analysis, Partial Least Square, Artificial Neural Networks

Introduction

Diabetes has become an epidemic affecting more than 422 million people worldwide (WHO, 2018). Diabetes is a metabolic disorder, caused by a dysfunction in the insulin section. Insulin is produced by the pancreas. Its interaction with glucose allows the body's cellular energy. The problem is that the patient's body does not produce insulin accurately throughout the day, hence the importance of insulin to regulate blood sugar level, avoiding making it too high or too low (Joseph and Golden, 2014).

Therefore, diabetes is a degenerative disease that without treatment can have very serious consequences, such as blindness, kidney failure and nerve damage. There can also be a tooth and gum damage, skin disease, thyroid problem and sexual dysfunction (ADA, 2011).

The latest technologies give every diabetic the chance to survive by controlling their blood glucose levels continuously and non-invasively (Khalil, 1999). To reach this goal, several techniques have been proposed, such as mathematical modeling, artificial intelligence and advanced signal processing techniques.

Al-Mbaudeen *et al*. (2010) proposed the technique of principal component regression coupled with a filter module to predict blood glucose concentration. These approaches have reduced the Standard Error (SE) from 40 mg/dL using unfiltered module to 15.63 mg/dL using a Chebyshev filter.

Parab *et al*. (2010) used the Partial Least Squares (PLS) regression model to design a noninvasive glucometer. The experimental results were satisfying, with values of 3.459 for the RMSE.

Uwadaira *et al*. (2015) exploited logistic regression analysis to identify the factors affecting the development of non-invasive blood glucose calibration model. In addition, PLS is used to correlate data with blood glucose concentration. These statistical approaches were successfully developed with a Standard Error of Cross-Validation (SECV) of 25.0 mg/dL and 80% of the validation samples falling within the zone A of the Clarke Error Grid.

Artificial Neural Networks (ANN) have also been applied in the prediction of blood glucose concentrations. Indeed, (Mougiakakou *et al*., 2006), (Perez-Gandia *et al*., 2010), (Robertson *et al*., 2011), (Pappada *et al*., 2011) and

(Zecchin *et al*., 2012) exploited ANN to provide short-term prognosis of blood glucose levels. The RMSE of model predictions was reported to be 13.65, 9.7, 10.09, 43.9 and 14 mg/dL respectively.

More elaborate research based on Support Vector Regression (SVR) have also been proposed for real-time glucose prediction (Eleni *et al*., 2013; Bunescu *et al*., 2013; Hamdi *et al*., 2018; Eleni *et al*., 2015).

To choose the best calibration, (Ming and Raveendran, 2009) used two different techniques: PLS and feed forward backpropagation neural network. The RMSE is around 0.5282 mmol/L and 0.2952 mmol/L, respectively. Therefore, ANN proved its effectiveness, with a correlation of 0.9863.

Hidalgo *et al*. (2017) proposed a comparative analysis of several machine learning techniques. The four models are based on Genetic Programming (GP), Random Forests (RF), K-Nearest Neighbors (KNN) and Grammatical Evolution (GE). For the analysis of experimental results, authors used the Clarke Error Grid in different forecasting horizons (t +30 min, t +60 min, t +90 min and t +120 min). Results show that GE and GP are better than KNN and RF since they perform well for short-term prognosis (30 min and 60 min).

The work of Falco *et al*. (2019) established a type of symbolic regression named Multigene Symbolic Regression. This technique develops a linear model of the transformations of the input variables. Experimental results showed that this combination could predict blood glucose levels since they were sensitive to 91.03% in the samples of A and B regions of the Clarke Error Grid analysis.

To develop a solid prediction, a recent work based on the linear ARMAX model was advanced in (Kamuran *et al*., 2013). Kamuran *et al*. suggested a Savitzky-Golay filter and a Kalman filter to treat the problem of noise in patient data. Results showed that the proposed alarm system gives a good performance with the value of 11.7 mg/dL for RMSE.

Simon *et al*. (2013) proposed the technique of Fuzzy Lattice Reasoning (FLR) to predict blood glucose concentration. The experimental results were satisfying, with an accuracy value of 0.93.

Zhua *et al*. (2019) used the logistic regression model to predict blood glucose using the Pima Indians Diabetes dataset. The accuracy and precision are around 0.9739 and 0.97, respectively.

Wu *et al*. (2017) exploited k-means algorithm and logistic regression algorithm to utilize the regression model for more than one dataset. The experimental results were successfully developed. The accuracy rate was 95.42% with an increase of 3.04% in comparison with other researches.

The work of Tronstad *et al*. (2018) exploited PLS and ANN regression models to predict blood glucose concentration. Their invented sensor is based on Near-Infrared (NIR), bioimpedance and skin temperature measurements. Experimental results showed that this combination could predict blood glucose levels since they were sensitive to 88% in the samples of A and B regions of the Clarke Error Grid analysis.

A better prediction performance was obtained as well in (Jensen *et al*., 2013; Anas *et al*., 2012). Thus Jensen *et al*. (2013) suggested an optimized real time hypoglycemia detection using Linear Regression (LR). The results showed that LR was able to obtain a good performance with a sensitivity of 81%. Using the same technique LR Anas *et al*. (2012) present the prediction of blood glucose levels in 10 patients. Although these results are promising, the technique needs to be validated with the Clarke Error Grid.

As seen in the literature, linear and nonlinear regression algorithms have been applied extensively to predict blood glucose concentration. However, different models have rarely been compared in terms of their predictive ability.

This research suggests the reliability of different types of regression models in the prediction of blood glucose. This paper aims to verify the predictive capability of our non-invasive prototype combined with linear and non-linear regression models. A comparison will be established to built and choose the best regression model in blood glucose concentration measurement. Hence, the best technique will be demonstrated in 300 human serums of different concentration ranges.

The plan of this work is organized as follows: Section 2 clarifies the basic principle of the measurement, Section 3 presents the various materials and methods used in this work, section 4 provides the main results, section 5 illustrates the comparison between linear and nonlinear regression models and Section 6 includes the conclusion and prospects.

Basic Principle of the Measurement

Over the years, researchers have sought to develop their work to avoid the painful measurement of glucose level in diabetics. The development began in 1980 while the execution was undertaken after twenty years (Djakouré-Platonoff *et al*., 2003; Benhamou *et al*., 2012).

Several body parts were used to detect blood glucose, such as tears, saliva, earlobe etc. An American team at Purdue University compared different body zones and proved that the glucose measurement system is more effective in blood than in saliva, tears or urine. Therefore, we focus to study the blood glucose concentration as a function of light variation through human serum. Among

the invented sensor for continuous glucose monitoring, NIR spectroscopy caught so much attention. Thus far, many researchers tried to prove the feasibility of NIR spectroscopy (Lu *et al*., 2016; Goodarzi *et al*., 2015). In addition, recent research has shown that the most informative region for blood glucose concentration prediction is 940-1500 nm regions (Islam, 2015). This explains why NIR spectroscopy is used throughout this paper. The designed device is based on NIR spectroscopy, which is a proprietary technology aiming at ensuring painlessness, comfort and accuracy.

The essence of the new device is to take advantage of the proportionality between blood glucose concentrations and the attenuation of travelling light through body zones. Consequently, experiment set up is based on the Beer-Lambert law given in Equation (1):

$$A = -\log_{10}\left(\frac{I}{I_0}\right) = \alpha C d \quad (1)$$

Where A is the Absorbance; I_0 and I are the incident and transmitted light intensity; α is the specific extinction coefficient of the compound; C is the concentration of the absorbing compound; finally d is the optical path length.

To briefly illustrate, blood glucose prediction is divided into four main parts as shown in Fig. 1.

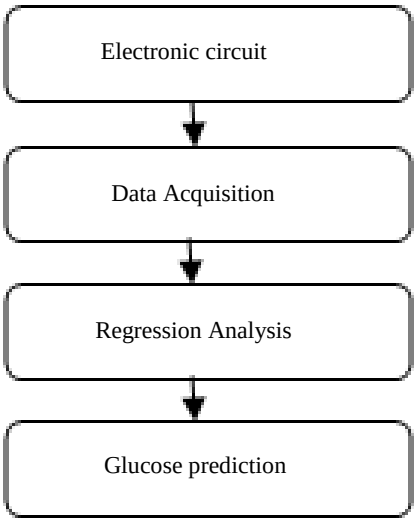
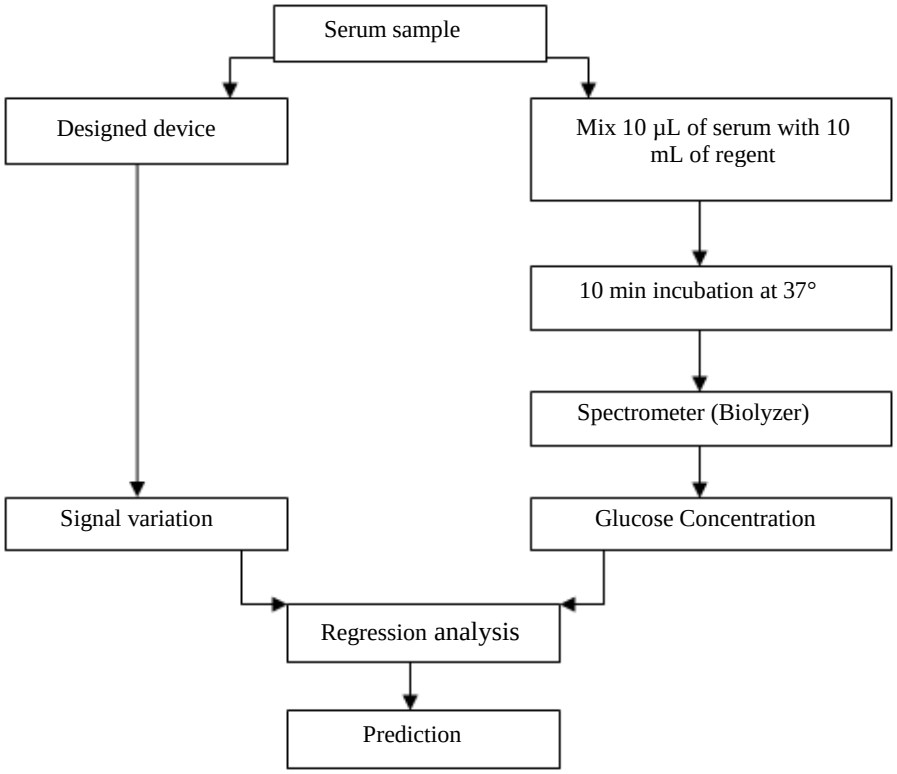


Fig. 1: The block diagram of the design system



(1) Glucose + O_2 + H_2O → Acide gluconique + H_2 O_2

(2) 2 H_2O_2+Phénol +4-Amino-antipyrine → Quinoneimine rose +4H_2O

Fig. 2: The flowchart of the experiment set up

Materials and Methods

Measurement Setup (Prototype Device)

The prototype described here utilizes a NIR led operating at a wavelength of 950 nm and an infrared photodiode since the technology chosen is based on passing NIR light through blood or serum zone; on the other side, the amount of light will be detected. The NIR led is positioned in parallel with the photodiode, so that almost all emitted light reaches the photodiode. Thus, an invisible line is created between the two sides.

The output signal is amplified and filtered using a precision electronic circuit. Indeed, the signal conditioning part comports a differential amplifier and a low-pass filter. This section is achieved using OPA4227. Once done, Analog-to-Digital Converter (ADC) conversion is performed using the microcontroller board Arduino Uno. Finally, we can display blood glucose levels on the computer as well as a tablet or smart phone.

Data Collection

The quality of data affects the predictive capability of the sensor. In vitro experiment setup is considerable regarding the accuracy of noninvasive glucose measurement sensor. Thus, the engineering and algorithmic concepts can be validated. In this work, we used our prototype device and a conventional spectrometer Biolyzer 100 to make in vitro data collection procedure. The spectrometer Biolyzer 100 is a semi-automated clinical chemistry analyzer.

The study was performed in accordance with Biomaghreb Tunisia which has been assessed and found to meet the requirement of the international organization for standardization ISO 9001. It is a private industrial company specialized in the manufacturing of laboratory reagent and medical analysis reagent. All experimental setups were carried out in accordance with the guidelines approved by Biomaghreb rules. Serum samples were obtained from patients with different health statuses to present a comprehensive offer to glucose tests. Therefore, we assure top-level quality, reliable diagnosis and easy interpretation.

Prior to the experiments with the serum samples, test tubes were carefully rinsed out with distilled water before measurement. All procedures and conditions were identical. To develop the system, it is divided into two main parts as explained in Fig. 2. The first part shows the non-invasive technique to measure serum glucose by sensing the change in output signal. In the second part, a conventional spectrometer (Biolyzer 100) was used as a reference to acquire the exact serum glucose concentration. NIR spectroscopic data are used to establish a regression model using machine learning algorithms.

Linear and Non-Linear Machine-Learning Algorithms

Diverse mathematical functions were tested to represent multiple relationships. They are not always sufficient to reflect the uncertainty and the inaccuracy of reality (Xizhao and Minghu, 1992). Hence, regression algorithm choice is decisive to guarantee prediction quality. In recent years, Machine Learning (ML) algorithms are the best solution to improve the prediction performance (Hidalgo *et al*., 2017). ML is an artificial intelligence field that allows users to learn without using explicit instruction. In this study, numerous regression models were generated and compared based on ML algorithms: Linear Partial Least Square (Linear-PLS), Polynomial Partial Least Square (Poly-PLS) and Artificial Neural Network (ANN).

Linear Machine-Learning Algorithms

The PLS algorithm is an old method (Wold, 1966) widely used, especially for the exploration, the comparison or the integration of two datasets. PLS is the most powerful linear machine-learning algorithms used in many areas like spectral and chemical engineering, where numerous experimental measurements need regression and modeling analysis. Linear PLS is very used in blood components prediction considering that its model conforms with the form of Beer Lambert Law (Wold, 1966; Xu *et al*., 2018). The PLS is characterized by its simplicity; it is a developed form of multiple linear regression models.

The PLS model is defined as:

$$\begin{aligned} X &= T * P^T + E \\ Y &= U * Q^T + F \end{aligned} \tag{2}$$

where, X and Y are two matrices of predictors and responses respectively; T and U are the X-scores and Y-scores matrices respectively; P and Q are the X-loadings and Y-loadings matrices respectively; finally, E and F are the X-residuals and Y-residuals matrices respectively.

PLS algorithms endeavor to maximize covariance between the two matrices X-scores (T) and Y-scores (U).

Non-Linear Machine-Learning Algorithms

Non-linear machine learning includes numerous regression techniques such as Artificial Neural Network (ANN), kernel methods, graphical models, Monte Carlo, etc. To handle the complexity of prediction problems, we are interested in this work to artificial neural network techniques. ANN is a computational model inspired by the comportment of the human brain.

ANN techniques have been used for several tasks like medical diagram, machine translation, computer vision, etc.

Among the different architecture, Multilayer Perceptron (MLP) is the most favored in prediction research. In this study, feed forward backpropagation MLP is used with two layers. MLP neural networks can be defined as follows (Equation 3):

$$\hat{y}_t = \alpha_0 + \sum_{j=1}^{q} \alpha_j . g\left(\beta_{0j} + \sum_{j=1}^{p} \beta_{ij} y_{t-i} \right) \quad (3)$$

where, $\hat{y}_t$ is the output, $y_{t-1},\ldots\ldots y_{t-p}$ are the inputs. p and q denote the number of inputs and hidden layer respectively. α_0 defines the weight between bias of the input and the output; β_{0j} is the connection weight of bias and hidden layer. α_j and β_{ij} are the weights of each node. Finally, g is the transfer function.

Metrics Performance

To evaluate the created regression models as well as the blood glucose concentration prediction, two main evaluation metrics were employed: Accuracy metrics and Clarke metrics.

Accuracy Metrics

The evaluation metrics of the regression models are the Root Mean Square error (RMS), the R-square (R2) and the correlation coefficient (r). The equations are often quantified by:

$$RMSE = \sqrt{\frac{\sum_{i-1}^{N} \left(\hat{y}_i - y_i \right)^2}{N}} \quad (4)$$

$$R^2 = \left(\frac{N \sum_{i=1}^{N} \hat{y}_i y_i - \sum_{i=1}^{N} \hat{y}_i \sum_{i=1}^{N} y_i}{\sqrt{N \sum_{i=1}^{N} \hat{y}_i^{\,2} - \left(\sum_{i=1}^{N} \hat{y}_i^{\,2} \right)} \sqrt{N \sum_{i=1}^{N} y_i^{\,2} - \left(\sum_{i=1}^{N} y_i^{\,2} \right)}} \right)^2 \quad (5)$$

$$r = \sqrt{\frac{\sum_{i=1}^{N} \left(\hat{y}_i - y_i \right)^2}{\sum_{i=1}^{N} \left(\hat{y}_i - y_i \right)^2}} \quad (6)$$

Where:

$\hat{y}_i$ = The predicted value from the regression model
$\hat{y}_i$ = The measured data from the standard instrument
N = The sample number of the data set

Clarke Metrics

To evaluate our blood glucose concentration prototype, Clarke metric is established. The Clarke Error Grid approach was developed to assess the clinical accuracy of the invented glucometer (Clarke *et al*., 1987).

Based on a Cartesian diagram, X-axis displays the reference value that is measured by an invasive glucometer, whereas the predicted values are displayed on Y-axis. The predicted measures are calculated from the evaluated glucometer. The grid is broken down by five zones:

- Zone A includes the concentration value within 20% of the invasive glucometer. The measures within this zone are on-target
- Zone B represents measures outside of the 20%. The points in zone A and B are appropriate
- Zone C contains values leading to needless treatment
- Zones D-E contain values that are potentially dangerous

Statistical Analysis and Software

In electronic setup, the conversion of an analog signal into digital signal was performed by using the popular software ARDUINO 1.8.1.

Furthermore, statistical analysis was achieved by MATLAB version 8.5.0 (R2015a). MATLAB results were used to compare linear and nonlinear machine learning regressors.

Results

In this section, we will evaluate linear and non-linear machine learning models. The evaluation is based on the accuracy metrics introduced in section 3.3.3. Based on performance comparison, we will choose the best for the validation of the non-invasive blood glucose measurement device.

Pls Regression Models

Firstly, we will evaluate the performance of the PLS models within its linear and polynomial forms. 24 samples were used as a calibration dataset. Table 1 shows the accuracy parameters for the estimated PLS regression models. The R squared and the correlation coefficient for linear PLS are 0.9605 and 0.9792 respectively, which shows a good relationship between the real blood glucose concentration values and the linear PLS prediction values. On the other hand, the R squared and the correlation coefficients for quadratic PLS are 0.9609 and 0.9794 respectively. As it is seen, R2 and r are very close to the two PLS regression models. The RMSE values are 0.425 and 0.0125 for linear PLS and polynomial PLS respectively. Therefore, we can clearly see that the RMSE is lower for the nonlinear PLS which means that quadratic PLS performed better than the linear PLS. To

clarify these deductions, Fig. 3 and 4 were plotted. The Figures show that Poly-PLS regression model presents a high correlationship between the measured blood glucose concentration and the predicted Blood Glucose Concentration (BGC) compared to the Linear-PLS regression model.

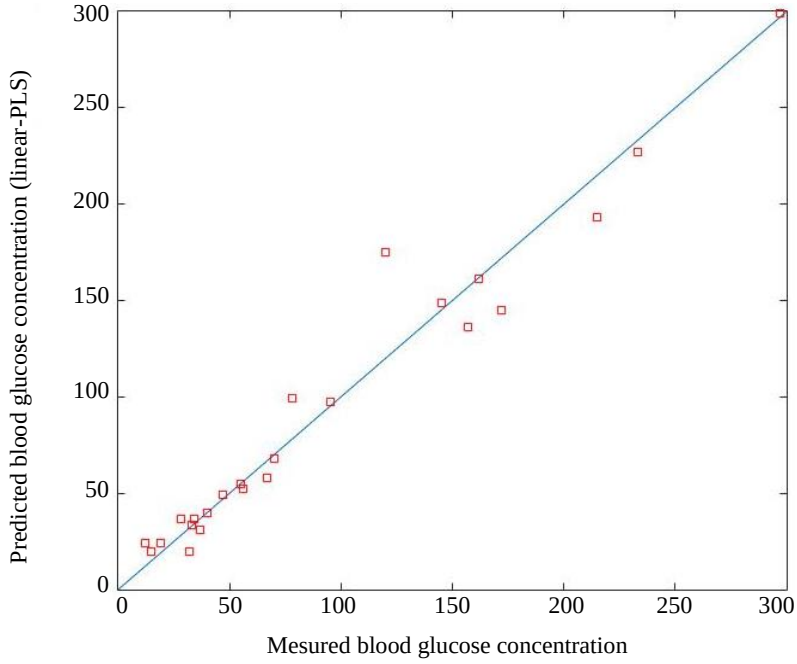


Fig. 3: Comparison of predicted BGC using Linear-PLS regression model with measured BGC using invasive device

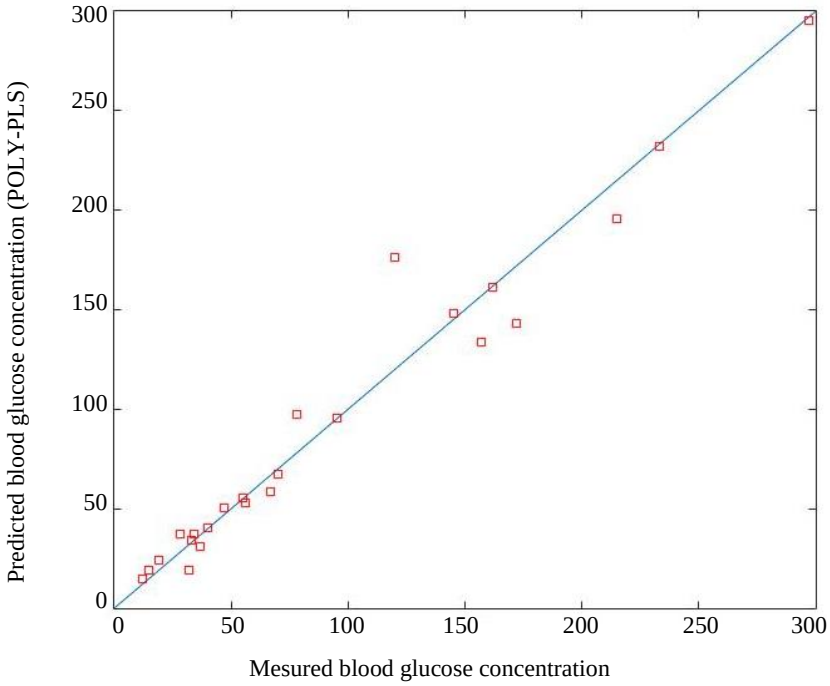


Fig. 4: Comparison of predicted BGC using POLY-PLS regression model with measured BGC using invasive device

ANN Regression Model

In this work, a multilayer perception neural network was implemented as a second model of a non-linear regression model. A feed forward backpropagation neural network with one hidden layer and 24 nodes is adopted to build to predict blood glucose concentration non-invasively. Weights and bias values are updated according to the Levenberg-Marquardt optimization.

Furthermore, we utilized the following specifications: A hyperbolic tangent sigmoid transfer function is used in the hidden layer and a linear transfer function in the last layer. Using MATLAB, a feed forward backpropagation neural network is built and is trained randomly to create a predicted data using ANN regression.

Figure 5 shows a high correlation between the real blood glucose concentrations and the predicted blood glucose concentration using ANN. Based on accuracy metrics, results show a high predictive capacity with values of 0.9804 for R-squared, 0.0784 for RMSE of and 0.99 for correlation as provided in Table 2.

Discussion

In section 3.1, the prediction capacity of linear and quadratic PLS regression models in blood glucose concentration has been evaluated and compared. We deduced that Quadratic PLS performed better than linear PLS. So we will now compare the two non-linear regression models (ANN and Poly-PLS).

As seen in Table 1 and 2, the correlation coefficients are 0.9794 and 0.99 for quadratic PLS and ANN models respectively. Similarly, the R squared values are 0.9609 and 0.9804 for quadratic PLS and ANN models respectively. Therefore, we can clearly see that the correlationship is higher in ANN prediction. On the other hand, the average errors are 0.0125 and 0.0784 for quadratic PLS and ANN models respectively, which means that Poly-PLS regression model has the lower RMSE value. To clarify our comparison, Fig. 5 is plotted. Figure 4 and 5 show that ANN regression model presents its higher correlationship between measured blood glucose concentration and predicted Blood Glucose Concentration (BGC) compared to Poly-PLS regression model.

Table 1: Performance metrics of PLS models

	Fit type	r	R-square	RMSE
Linear PLS	linear	0.9792	0.9605	0.4250
Poly-PLS	Quadratic	0.9794	0.9609	0.0125

Table 2: Performance metrics of ANN model

	Fit type	r	R-square	RMSE
ANN	Feed forward backpropagation	0.99	0.9804	0.0784

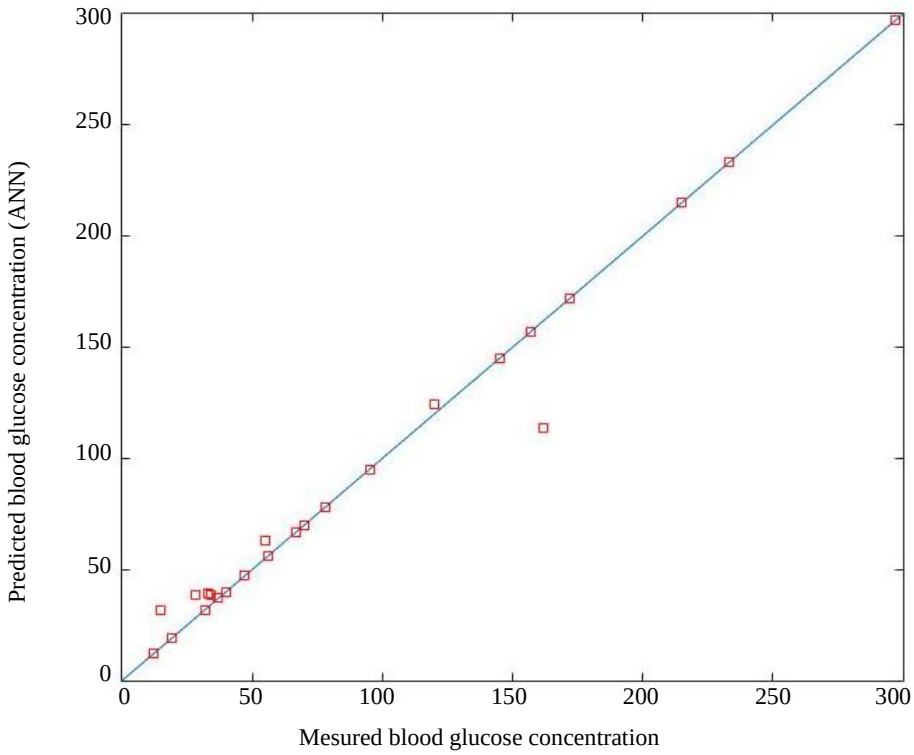


Fig. 5: Comparison of predicted BGC using ANN regression model with measured BGC using invasive device

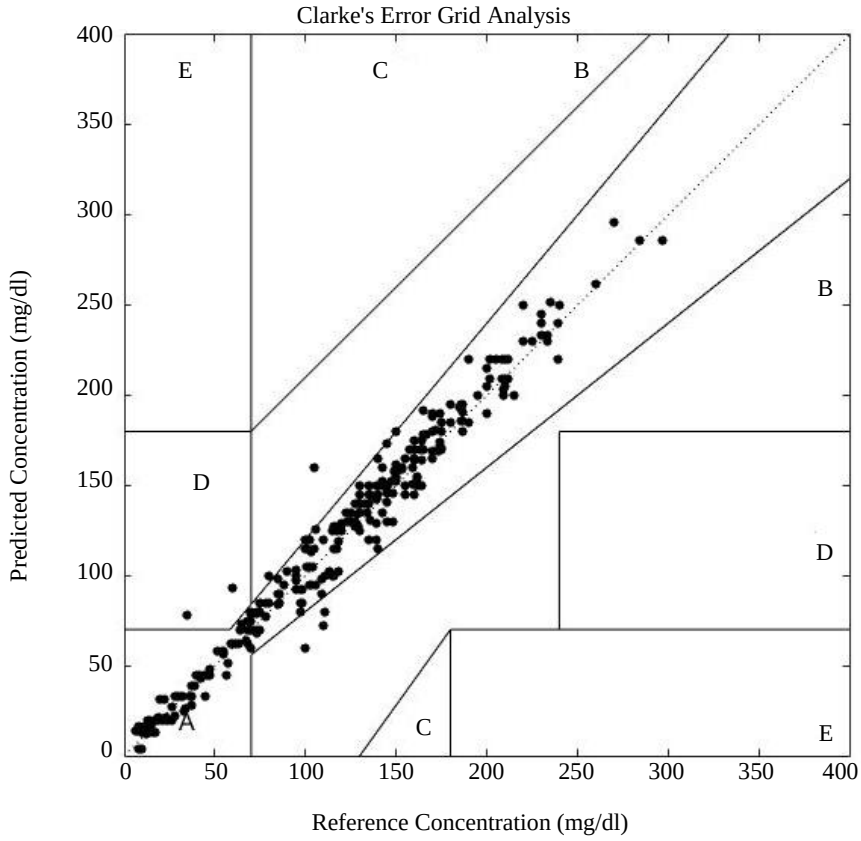


Fig. 6: Clarke error grid analysis

Finally, based on all accuracy metrics, we deduce that the best result is accomplished by using the feedforward backpropagation neural network despite its higher RMSE compared to Poly-PLS. That is why; we will continue the validation step with the ANN regression model.

For validation, 300 samples are used. A Clarke Error Grid based on the ANN regression model is shown in Fig. 6 where 97.33% of the results fall into the clinically acceptable zone A. The results show that artificial neural networks have a high predictive capacity for blood glucose concentration measurement. Furthermore, validation results show that the designed device based on NIR infrared spectroscopy and ANN regression model allows the monitoring of blood glucose concentrations non-invasively with high clinical accuracy.

To summarize, this study indicates the potential use of our designed device as a non-invasive sensor for continuous blood glucose monitoring. In addition to showing acceptable accuracy, results demonstrate that this method has a high classification accuracy rate for the rediction of glucose concentration with 0.99 for the correlation coefficient.

Our model provides the chance of detecting blood glucose concentration in real time. This is useful for all diabetics people since the sensor was tested in human serum collected from different populations.

Moreover, the choice of a good technique for the glucometer design affects the quality of results. To achieve the best results, numerous glucometer are developed and improved in several researches. Section 1 presents the best results in the literature. Our experimental results prove that our chosen technique as well as the regression model are better than the other methods (Parab *et al*., 2010; Uwadaira *et al*., 2015; Mougiakakou *et al*., 2006; Perez-Gandia *et al*., 2010; Robertson *et al*., 2011; Pappada *et al*., 2011; Zecchin *et al*., 2012; Ming and Raveendran, 2009; Zhua *et al*., 2019; Wu *et al*., 2017).

Conclusion

In this study, a new approach is proposed for non-intrusive glucose measurement based on NIR spectroscopy. In this sense, three regression models are used to predict blood glucose concentration non-invasively. The purpose of our study is the high predictive capacity of the

designed device with 0.98 for R-Squared, 0.99 for correlation coefficient and 0.0784 for RMSE. Furthermore, 97% of the measured fall within the clinically acceptable regions. This paper led us to deduce that the non-invasive designed device coupled with ANN regression model provides an auxiliary tool for the early diagnosis of diabetes complications.

Future efforts will be focused on architecture, performance and displayed results in our designed device.

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Competing Interests

Authors declare that they have no competing interests.

Availability of Data and Materials

The datasets used and analyzed during the current study is available from the corresponding author upon reasonable request.

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References

ADA, 2011. Standards of medical care in diabetes. American Diabetes Association, Diabetes Care.

Al-Mbaudeen, A.A., T. Rahman and M. Benaissa, 2010. Determination of glucose concentration from near-infrared spectra using principle component regression coupled with digital bandpass filter. Proceedings of the IEEE Workshop On Signal Processing Systems, Oct. 6-8, IEEE Xplore Press, San Francisco, CA, USA, pp: 243-248. DOI: 10.1109/SIPS.2010.5624795

Anas, M.N., A. Syafirah, A.N. Norali and M. Normahira, 2012. Non-invasive blood glucose measurement Application of near infrared optical measurement. Proceedings of the IEEE Conference on Sustainable Utilization and Development in Engineering and Technology, Oct. 6-9, IEEE Xplore Press, Kuala Lumpur, Malaysia, pp: 258-261. DOI: 10.1109/STUDENT.2012.6408415

Benhamou, P.Y., B. Catargi, B. Delenne, B. Guerci and H. Hanaire, 2012. Real-time Continuous Glucose Monitoring (CGM) integrated into the treatment of type 1 diabetes: Consensus of experts from SFD, EVADIAC and SFE. Diabetes Metabolism, 38: 67-83. DOI: 10.1016/S1262-3636(12)71538-0

Bunescu, R., N. Struble, C. Marling and J. Shubrook, 2013. Blood glucose level prediction using physiological models and support vector regression. Proceedings of the 12th International Conference on Machine Learning and Applications, Dec. 4-7, IEEE Xplore press, Miami, FL, USA, pp: 135-140. DOI: 10.1109/ICMLA.2013.30

Clarke, W., D. Cox, L. Gonder-Frederick, W. Carter and S. Pohl, 1987. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care, 10: 622-628. DOI: 10.2337/diacare.10.5.622

Djakouré-Platonoff, C., R. Radermercker, G. Reach, G. Slama and J. Selam, 2003. Accuracy of the continuous glucose monitoring system in inpatient and outpatient conditions. Diabetes Metabolism, 28: 159-162. DOI: 10.1016/S1262-3636(07)70023-X

Eleni, G., P. Vasilios, P. Demosthenes and F. Dimitrios, 2015. Evaluation of short-term predictors of glucose concentration in type 1 diabetes combining feature ranking with regression models. Medical Biol. Eng., 53: 1305-1318. DOI: 10.1007/s11517-015-1263-1

Eleni, I.G., C.P. Vasilios, A. Diego, M. Michela and Z. Ivana *et al*., 2013. Multivariate prediction of subcutaneous glucose concentration in type 1 diabetes patients based on support vector regression. IEEE J. Biomed. Health Inform., 17: 71-81. DOI: 10.1109/TITB.2012.2219876

Falco, I.D., A.D. Cioppa, A. Giugliano, A. Marcelli and T. Koutny *et al*., 2019. A genetic programming-based regression for extrapolating a blood glucose-dynamics model from interstitial glucose measurements and their first derivatives. Applied Soft Comput. J., 77: 316-328. DOI: 10.1016/j.asoc.2019.01.020

Goodarzi, M., S. Sharma, H. Ramon and W. Saeys, 2015. Multivariate calibration of NIR spectroscopic sensors for continuous glucose monitoring. Trac-Trends Anal. Chem., 67: 147-158. DOI: 10.1016/j.trac.2014.12.005

Hamdi, T., J.B. Ali, V.D. Costanzo, F. Fnaiech and E. Moreau *et al*., 2018. Accurate prediction of continuous blood glucose based on support vector regression and differential evolution algorithm. Biocybernet. Biomed. Eng., 38: 362-372. DOI: 10.1016/j.bbe.2018.02.005

Hidalgo, J.I., J.M. Colmenar, G. Kronberger, S.M. Winkler and O. Garnica *et al*., 2017. Data based prediction of blood glucose concentrations using evolutionary methods. J. Medical Syst., 142: 1-20. DOI: 10.1007/s10916-017-0788-2

Islam, M.N., 2015. Near-infrared lasers for non-invasive monitoring of glucose, Ketones, HBA1C and other blood constituents. US 2015/0305658 A1.

Jensen, M.H., T.F. Christensen, L. Tarnow, E. Seto and M.D. Johansen., 2013. Real-time hypoglycemia detection from continuous glucose monitoring data of subjects with type 1 diabetes. Diabetes Technol. Therapeut., 15: 538-543. DOI: 10.1089/dia.2013.0069

Joseph, J.J. and S.H. Golden, 2014. Type 2 diabetes and cardiovascular disease: What next? Curr. Opin. Endocrinol. Diabetes Obesity, 21: 109-20.

Kamuran, T., S.B. Elif, Q. Lauretta, L. Elizabeth and R. Derrick., 20137.035. Hypoglycemia early alarm systems based on multivariable models. Industrial Eng. Chem. Res., 52: 12329-12336. DOI: 10.1021/ie3034015

Khalil, O.S., 1999. Spectroscopic and clinical aspects of noninvasive glucose measurement. Clin. Chem., 45: 165-177.

Lu, X.F., T.L. Zhang, F. Xiao, G. Li and Y. Wang, 2016. Noninvasive blood glucose analysis based on near-infrared reflectance spectroscopy. Spectroscopy Spectral Anal., 36: 2312-2317. DOI: 10.3964/j.issn.1000-0593(2016)07-2312-06

Ming, C.Z. and P. Raveendran, 2009. Comparison analysis between PLS and NN in noninvasive blood glucose concentration prediction. Proceedings of the International Conference for Technical Postgraduates, Dec. 14-15, IEEE Xplore Press, Kuala Lumpur, Malaysia, pp: 1-4. DOI: 10.1109/TECHPOS.2009.5412048

Mougiakakou, S.G., A. Prountzou, D. Iliopoulou, K.S. Nikita and A. Vazeou *et al*., 2006. Neural network based glucose-insulin metabolism models for children with type 1 diabetes. Proceedings of the 28th IEEE, EMBS Annual International Conference, Aug. 30-Sept. 3, IEEE Xplore Press, USA, pp: 3545-3548. DOI: 10.1109/IEMBS.2006.260640

Pappada, S.M., B.D. Cameron, P.M. Rosman, R.E. Bourey and T.J. Papadimos *et al*., 2011. Neural network-based real-time prediction of glucose in patients with insulin-dependent diabetes. Diabetes Technol. Therapeut., 13: 135-141. DOI: 10.1089/dia.2010.0104

Parab, J.S., R.S. Gad and G.M. Naik, 2010. Noninvasive glucometer model using partial least square regression technique for human blood matrix. J. Applied Phys., 107: 1-5. DOI: 10.1063/1.3380850

Perez-Gandia, C., A. Facchinetti, G. Sparacino, C. Cobelli and E.J. Gomez *et al*., 2010. Artificial neural network algorithm for online glucose prediction from continuous glucose monitoring. Diabetes Technol. Therapeut., 12: 81-88. DOI: 10.1089/dia.2009.0076

Robertson, G., E.D. Lehmann, W. Sandham and D. Hamilton, 2011. Blood glucose prediction using artificial neural networks trained with the Aida diabetes simulator: A proof-of-concept pilot study. J. Electrical Comput. Eng. DOI: 10.1155/2011/681786

Simon, F., M. Sabah, F. Jinan and K.K. Chee, 2013. Using causality modeling and fuzzy lattice reasoning algorithm for predicting blood glucose. Expert Syst. Applic., 40: 7354-7366. DOI: 10.1016/j.eswa.2013.0

Tronstad, C., O. Elvebakk, O.M. Staal, H. Kalvoy and J.O. Hogetveit., 2018. Non-invasive prediction of blood glucose trends during hypoglycemia. Analytica Chimica Acta, 1052: 37-48. DOI: 10.1016/j.aca.2018.12.009

Uwadaira, Y., A. Shimotori, A. Ikehata, K. Fujie and Y. Nakata *et al*., 2015. Logistic regression analysis for identifying the factors affecting development of non-invasive blood glucose calibration model by near-infrared spectroscopy. Chem. Intell. Lab. Syst., 148: 1-14. DOI: 10.1016/j.chemolab.2015.09.012

WHO, 2018. World Health Organization. Diabetes. https://www.who.int/news-room/fact-sheets/detail/diabetes/document

Wold, H., 1966. Estimation of principal components and related models by iterative least squres. In: Krishnajah, P.R. (Ed.), Multivariate Analysis pp: 391-420. NewYork: Academic Press.

Wu, H., S. Yang, Z. Huang, J. He and X. Wang, 2017. Type 2 diabetes mellitus prediction model based on data mining. Inform. Med. Unlocked, 10: 100-107. DOI: 10.1016/j.imu.2017.12.006

Xizhao, W. and H. Minghu, 1992. Fuzzy linear regression analysis. Fuzzy Sets Syst., 51: 179-188.

Xu, J., L. Ye, C. Li, M. Zhang and P. Li, 2018. Rapid and nondestructive measurement of glucose in a skin tissue phantom by near-infrared spectroscopy. Optik, 170: 30-36. DOI: 10.1016/j.ijleo.2018.05.050

Zecchin, C., A. Facchinetti, G. Sparacino, G.D. Nicolao and C. Cobelli, 2012. Neural network incorporating meal information improves accuracy of short-time prediction of glucose concentration. IEEE Trans. Biomed. Eng., 59: 1550-1560. DOI: 10.1109/TBME.2012.2188893

Zhua, C., C.U. Idemudia and W. Feng, 2019. Improved logistic regression model for diabetes prediction by integrating PCA and K-means techniques. Inform. Med. Unlocked. DOI: 10.1016/j.imu.2019.100179