
IGLU 2.0: A NEW NON-INVASIVE, ACCURATE SERUM GLUCOMETER FOR SMART HEALTHCARE

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ABSTRACT

To best of authors knowledge, this article presents the first-ever non-invasive glucometer that takes into account serum glucose for high accuracy. In case of blood glucose measurement, serum glucose value has always been considered precise blood glucose value during prandial modes. Serum glucose can be measured in laboratory and more stable glucose level compare to capillary glucose. However, this invasive approach is not convenient for frequent measurement. Sometimes, Conventional invasive blood glucose measurement may be responsible for cause of trauma and chance of blood related infections. To overcome this issue, in the current paper, we propose a novel Internet-of-Medical (IoMT) enabled glucometer for non-invasive precise serum glucose measurement. In this work, a near-infrared (NIR) spectroscopic technique has been used for glucose measurement. The novel device called iGLU 2.0 is based on optical detection and precise machine learning (ML) regression models. The optimal multiple polynomial regression and deep neural network models have been presented to analyze the precise measurement. The glucose values of serum are saved on cloud through open IoT platform for endocrinologist at remote location. To validate iGLU 2.0, Mean Absolute Relative Difference (mARD) and Average Error (AvgE) are obtained 6.07% and 6.09%, respectively from predicted blood glucose values for capillary glucose. For serum glucose, mARD and AvgE are found 4.86% and 4.88%, respectively. These results represent that proposed non-invasive glucose measurement device is more precise for serum glucose compared to capillary glucose.

Keywords Smart healthcare, Healthcare Cyber-Physical System (CPS), Internet-of-Medical-Things (IoMT), Continous glucose measurement, Non-invasive glucose measurement, Capillary glucoes, Serum glucose, Regression model, Kernel based calibration

1 Introduction

Remote connectivity of doctors and patients is the key solution in providing better and advanced medical facilities to the patients [1, 2]. As the healthcare technologies are being advanced, there is an increment and consciousness of consumers for their health. In particular scenario, the demand for remote healthcare is more promoted than ever. Present Internet-of-Medical-Things (IoMT) solution for smart healthcare encourages hospitals to ameliorate the care quality with focusing on overall expenses reduction. The basic requirement of our Smart Healthcare solution comprises of sensors that collect patient data, cloud to store, analyze and process the data, web services and mobile applications for patients and doctors. In a big picture IoMT enabled healthcare Cyber-Physical System (CPS) makes smart healthcare possible [3].

The non-invasive, precise and rapid diagnosis of diabetes is of great demand worldwide due to low-cost, painless, and easy of usage [4, 5, 6, 7]. Instant non-invasive serum glucose measurement is not being possible at present to overcome the cause of trauma. Hence, the instant measurement of serum glucose with continuous monitoring is being recent challenge in the smart healthcare system. Proposed serum glucose measurement device is a handheld, IoMT enabled end-device which provides rapid and continuous monitoring. It interacts with an endocrinologist to the remote located

diabetic patients. The process flow of blood glucose diagnosis in smart health care system is shown in Figure 1, which represents the smart healthcare system for diabetic patients at remote location.

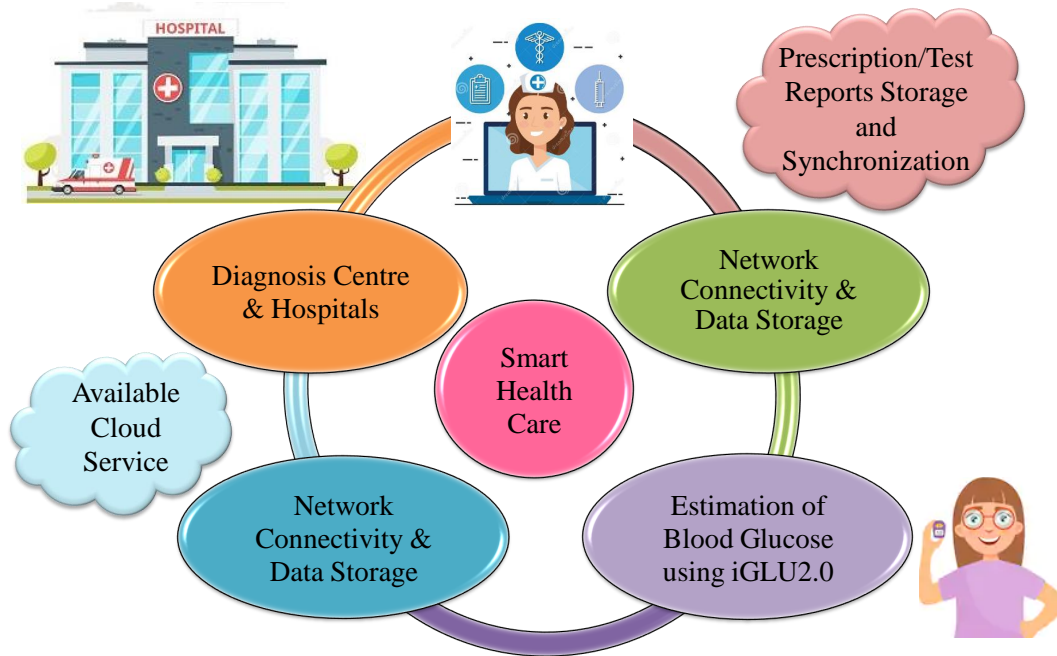


Figure 1: Blood glucose diagnosis in smart health care system.

In proposed non-invasive serum glucose measurement, optical detection approach is involved. The collected data is processed for acquisition and glucose is predicted by the regression model. The process flow is shown in Figure 2. According to this process, patients measure their serum glucose without pricking blood and store directly to the cloud where nearby endocrinologist can analyze the serum glucose data of particular patient. The prescription would also be sent by endocrinologist to particular patient for further treatment. Traditionally, blood glucose is being measured in the form of serum and capillary glucose of diabetic patients. The serum glucose test is a laboratory test where serum (centrifuged blood) is extracted from blood to measure the glucose level, whereas capillary glucose is being measured by commercially available glucometer. In this process, a drop of blood is pricked through lancet from finger and blood drop is taken on strip which has to be connected to the glucometer. For accurate blood glucose value, diabetic patients are always recommended for the serum glucose test. But, the whole process takes 1-2 hours for serum glucose value. Hence, it is necessary to develop the device which can measure the serum glucose without puncturing the finger instantly. People will be more conscious for blood glucose continuous monitoring. Such a device is advisable for smart healthcare. Designing a non-invasive serum glucose monitoring device comprises of spectroscopy techniques. Spectroscopy is the interaction between optical radiation and any molecules. This technique is used to measure the resultant light after interaction with molecules at the specific resonance frequency.

The rest of the paper is composed in the following manner. The prior related work is described in Section 2. Novel contribution of this paper is represented in Section 3. Section 4 discusses analytical modelling and calibration details of the sensor for serum and capillary glucose. The proposed device is presented with mechanism of serum glucose detection in Section 5. Experiments and analytical modelling with error analysis have been elaborated in Section 6.

2 The State-of-Art in Glucose Measurement and its Advancement through the Current Paper

2.1 Prior Research on Glucose Level Monitoring

Research on glucose level monitoring is being undertaken for a long time and also ongoing. Related prior research work can be classified as invasive, minimally invasive, and non-invasive blood glucose monitoring as represented in Figure 3.

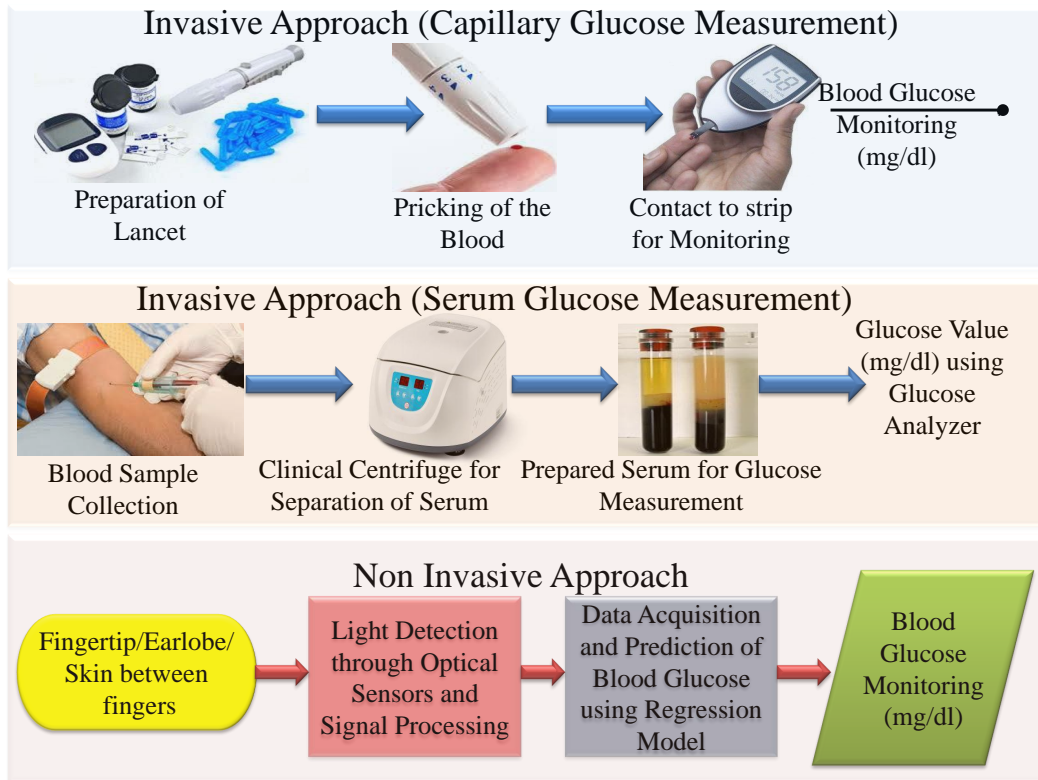


Figure 2: Processing steps of non invasive blood glucose measurement device.

Various invasive and non-invasive approaches have been explored for glucose measurement [8]. Demitri, et al. represented the photometric approach for glucose measurement using small blood volumes [9]. To mitigate the issue of frequent pricking blood, one-time wearable sensor is proposed in terms of a semi-invasive approach. This wearable sensor has advantages of rapid diagnosis and continuous monitoring. But, this has to be changed after a certain period. Hence, this will be irritating and may be the cause of trauma. Wang, et al. represented wearable minimally invasive microsystem for glucose monitoring [7]. This wearable microsystem is a neither painless nor cost-effective solution. Acciaroli, et al. discussed the new method to reduce the frequency of calibration of minimally invasive Dexcom sensor [10]. To make the painless system, Pai, et al. designed the prototype setup of photoacoustic spectroscopy for non-invasive glucose measurement [11]. But, implementation of corresponding components yield the setup costly and also occupies large area. However, the solution will not be portable. Yin, et al. proposed a DiabDeep framework that merge wearable sensors and neural networks for pervasive diagnosis of diabetes. They achieved classification accuracy to classify the healthy and diabetic patients. They considered various environmental and physiological parameters to justify the diabetic patients. However, accuracy has not been identified in terms of blood glucose measurement [12]. The work did not represent any kind of error analysis. Prasad, et. al. presented nanoparticles on alkali anodized steel (AS) electrode for glucose measurement through saliva [13]. Singh, et al. represented optical biosensor for glucose measurement using saliva [14]. Glucose measurement has also been done using IMPS spectroscopy through the skin [15, 16]. Electrical properties of skin, sweat and saliva vary according to person. So, this approach will not be reliable for glucose measurement. Non-invasive glucose measurement approach through retina has also been represented for precise glucose detection [17]. Such non-invasive approach is not desirable for frequent monitoring [18]. Raman spectroscopy has been preented for precise glucose measurement [19]. The implemented setup occupied a large area and will not be portable.

2.2 Commercial Products on Glucose Level Monitoring

Various products such as glucometer from Labiotech [20], GlucoTrack[®], and so on have limitations in terms of precision. The cost of these products is also high which varies in the range of 300-400 USD. Therefore, the cost effective device for precise non-invasive blood glucose measurement is presented. The Medical Training Initiative (MTI) is developing a non-invasive glucose monitoring device glucowise[™]. 2M Engineering is also actively

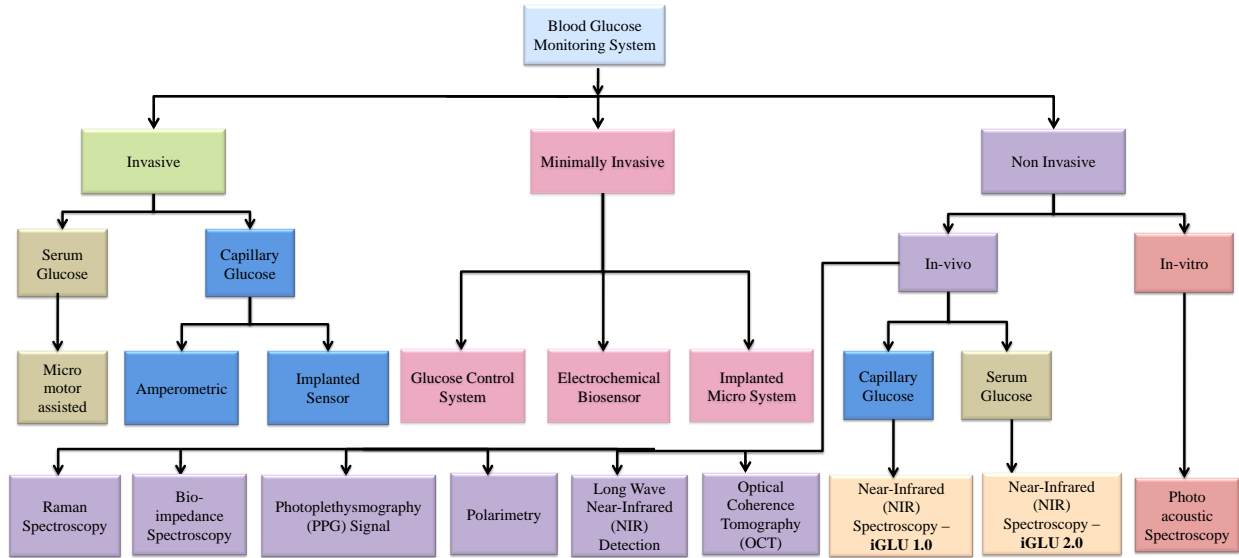


Figure 3: An overview of the related prior works.

developing solution for non-invasive glucose monitoring [21]. The device is based on Raman scattering spectroscopy technique with the use of laser technology. However, this is not cost effective solution. These devices are not available in the market for medication. In this way Freestyle Libre sensor, SugarBEAT from Nemaura medical are available in the market for medication [22]. These products are adhesive and skin-patch which are regularly disposable. These devices support the continuous glucose monitoring. These are minimally invasive devices. Omelon B-2 is one of the non-invasive stripless devices for continuous glucose monitoring which is available in the market for medication [23]. The device is bulky and is not wearable device for continuous glucose level monitoring and the precision in measurement has also not been achieved according to the users remarks.

2.3 Why NIR over other Non-Invasive Approaches?

Glucose measurement has been done using various non-invasive approaches such as impedance spectroscopy, NIR light spectroscopy, PPG signal analysis and so on. But, apart from optical detection, other techniques have constraints in terms of precise measurement. Desirable accuracy is not possible from measurement through sweat and saliva as properties always vary for each person. PPG signal analysis is based on extracted features of logged signal which is not based on principle of glucose molecular detection [24, 25]. The methodology of glucose measurement through PPG signal and NIRS are represented in Figure 4.

To overcome these limitations, Sharma, et al. also discussed about optical detection using long NIR wave which is not capable to detect the glucose molecules beneath the skin as it has shallow penetration [26]. Therefore, small NIR wave has been chosen for real-time glucose detection [27, 28].

2.4 Why Serum Glucose over Capillary Glucose?

In the case of invasive approaches, serum glucose and capillary glucose level are being analyzed for precise blood glucose values. Capillary glucose can be estimated instantly but serum glucose couldn't be identified instantly due to certain processes. However, it is clinically observed that the capillary glucose level is always higher than serum glucose which is not being considered actual blood glucose ever. Hence, there is a trade-off between both approaches. But, serum glucose has always been recommended for diagnosis as an accuracy point of view. Therefore, serum glucose is always being reliable compared to capillary glucose for medication.

The serum glucose measurement is explored through NIR light as presented in Figure 5. The incident light is passed through blood vessels and blood glucose molecules are detected in flowing concentration. During capillary glucose measurement, the drop of blood is pricked from epidermis layer of skin. The precise value of glucose may not be possible always through capillary blood glucose measurement. Therefore, serum glucose measurement is advisable through diabetologist generally for precise measurement.

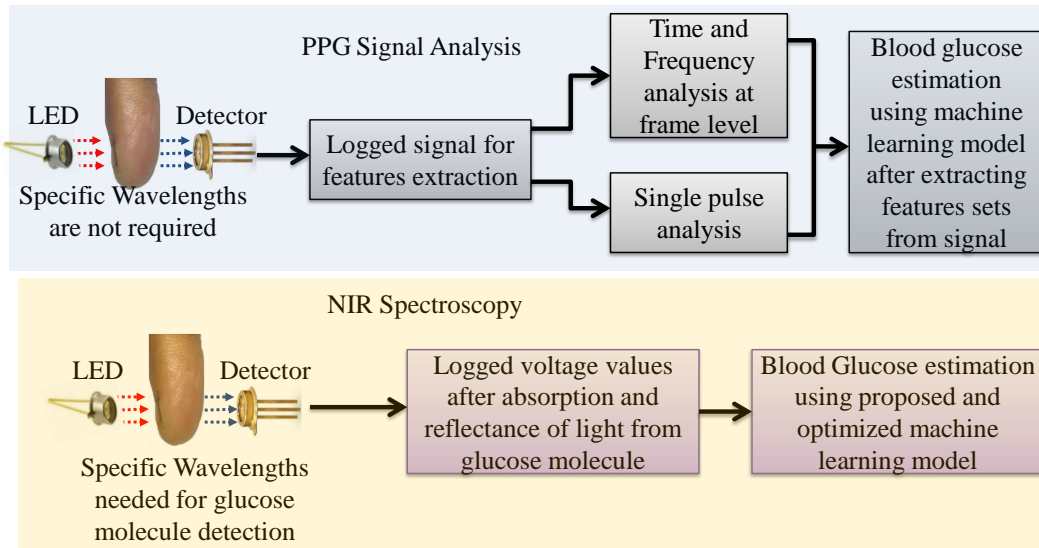


Figure 4: Mechanism of Serum and Capillary Glucose Measurement.

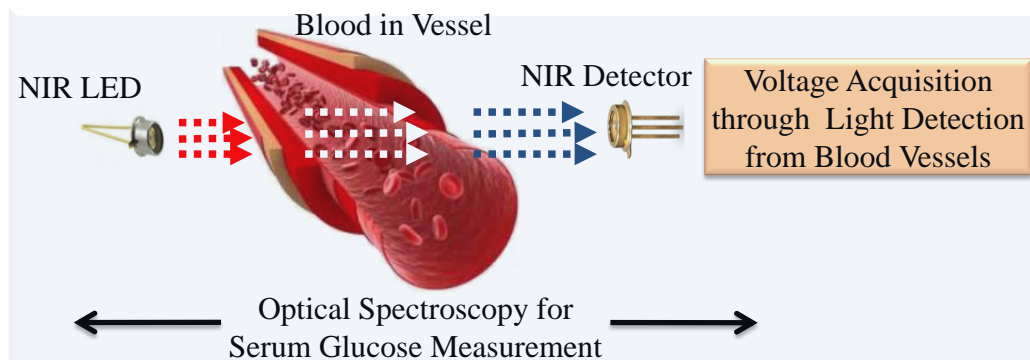


Figure 5: NIR Spectroscopy Mechanism of Serum Glucose Measurement.

2.5 Advancement over our Previous work iGLU

The works related to non-invasive blood glucose measurement have been proposed using multiple techniques. Non-invasive detection reduces the chance of being blood-related infections during measurement. But, these measurement techniques have some limitations. Hence, the device iGLU 1.0 has been represented for non-invasive capillary glucose measurement [4]. Serum glucose has always been considered more precise compared to capillary blood glucose as per medical aspects. Therefore, it is required to design a portable device for non-invasive serum glucose measurement which would have better accuracy. In current paper, iGLU 2.0 is proposed for serum glucose monitoring using short-wave NIR spectroscopy technique with calibration and validation [29].

3 Novel Contributions of the Current Paper to the State-of-Art

Research Questions Addressed in the current Paper: For serum glucose measurement, it is necessary to prick the blood and it takes more time to measure the glucose. The well equipped laboratory is required for processes to extract the serum and storage at specific (frozen) temperature. Hence, the laboratory needs a large space with frozen facility of serum. Hence, this process is neither being a cost-effective nor time-saving solution in terms of instant diagnosis. The questions which are addressed in the current paper for the advancement of smart healthcare: (1) How can we have a device that can measure serum glucose without pricking the blood at the user and stores the data in cloud for future use by the patient and healthcare providers? (2) Can we have a device that can provide the facility of continuous serum glucose monitoring at the user-end so that it can function even if the Internet connectivity is not available all the time?

(3) Can we have a device that can measure automatically serum glucose frequently all the time? (4) Can we have a device that can measure the serum glucose of all types of patients precisely?

Challenges in Addressing the Research Problem and Questions: The solution of various challenges for the research questions to obtain precise serum glucose measurement include the following: (1) Analyzing and validation of specific wavelengths for glucose detection are required for precise measurement. (2) Optimization in circuit level design of data acquisition module is required to improve the performance of proposed device for CGM. (3) Acquiring of voltages and serially transfer for data logging will be possible with synchronization for frequent measurement. (4) Analysis of optimized regression model with calibration and validation using healthy and diabetic samples to measure serum glucose of all patients precisely.

Proposed Solution of this Paper: To address the above research questions, we proposed an edge-device called iGLU 2.0 in the current paper that measures serum glucose of patient and stores the data at the cloud. We have proposed the non-invasive serum glucose measurement device which is a comparatively precise and low-cost solution. The proposed device is also integrated with IoMT framework for data storage on the cloud. The risk factor of blood-related diseases has been mitigated through proposed device. The device can be used to measure the serum glucose of every person at anytime. iGLU 2.0 is an advancement in the non-invasive device era. This device measures the serum glucose instantly with continuous monitoring. Flow of proposed work is represented in Figure 6.

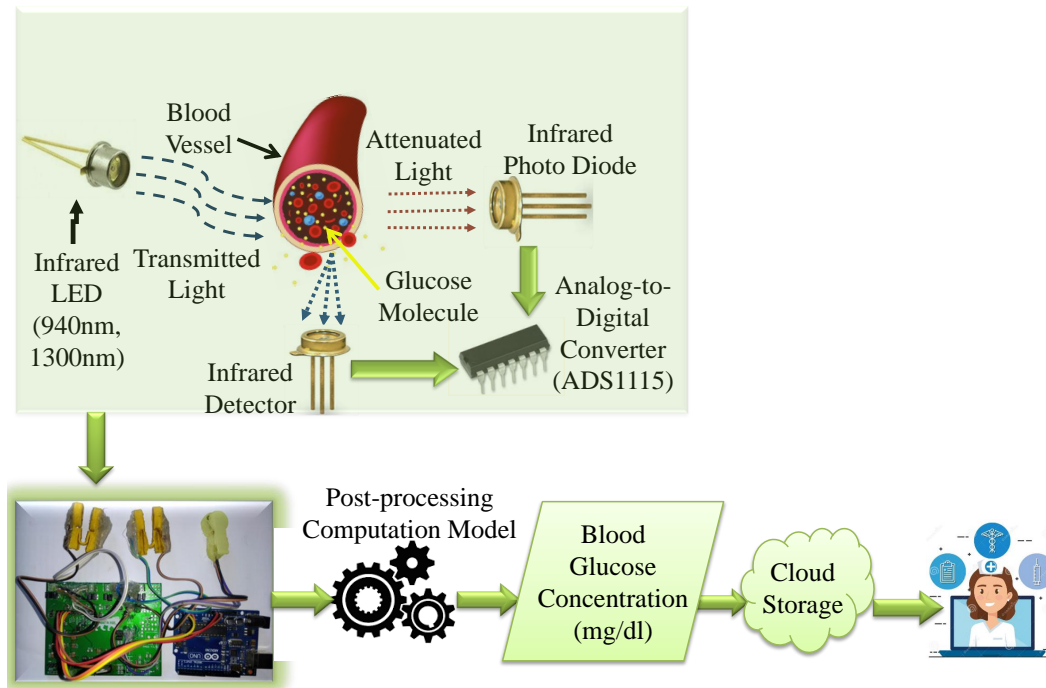


Figure 6: Top level representation of proposed device (iGLU 2.0).

Novel contribution in current paper include the following:

1. A precise non-invasive serum glucometer called iGLU 2.0 using absorption and reflectance of light with two short NIR waves using specific wavelengths (940 nm and 1300 nm) has been introduced.
2. An optimized kernel based regression model for serum glucose sensor calibration has been presented.
3. A serum glucose monitoring device has been formed with optimized circuital biasing of sensors for calibration using precise and optimized regression model to validate and test the subjects.
4. With the active support from diabetic center and hospital, real-life experimental validation has been done directly from human blood.
5. The proposed device has been integrated in IoMT framework for data (serum glucose values) storage, patient monitoring and treatment on proper time with cloud access by both the patient and doctor.

4 Machine Learning (ML) Models for Blood Glucose Level Calculation from the NIR Signal

Optimized computation model is analyzed after calibration of regression models (RM) for serum and capillary glucose estimation. In current work, the detector's outputs from three channels are logged as input vectors for prediction of glucose. The calibrated models are used to predict the blood glucose concentrations for validation. The logged data from each sample is essential to convert in predicted glucose values. Hence, it is required to calibrate an appropriate kernel for precise measurement. 113 samples of capillary glucose and 74 samples of serum glucose are taken for device calibration which includes prediabetic, diabetic and healthy samples. The baseline characteristics of the samples are shown in Table 1.

Table 1: Baseline characteristics of collected samples for calibration, validation and testing.

Samples Basic Characteristics	Capillary Glucose	Serum Glucose	Capillary Glucose	Serum Glucose
Calibration		Validation and Testing		
Prediabetic Samples				
Age (Years)				
Male:-18-80	Male:-23	Male:-13	Male:-18	Male:-10
Female:-17-75	Female:-20	Female:-16	Female:-16	Female:-09
Diabetic Samples				
Age (Years)				
Male:-18-80	Male:-30	Male:-18	Male:-14	Male:-15
Female:-17-75	Female:-19	Female:-12	Female:-12	Female:-12
Healthy Samples				
Age (Years)				
Male:-18-80	Male:-09	Male:-08	Male:-07	Male:-05
Female:-17-75	Female:-12	Female:-07	Female:-07	Female:-08
Total Samples				
Age (Years)				
Male:-18-80	Male:-62	Male:-39	Male:-39	Male:-30
Female:-17-75	Female:-51	Female:-35	Female:-35	Female:-29

The proposed process flow of calibration and validation is shown in Figure 7. Mean absolute deviation (MAD), AvgE, mARD, and Root Mean Square Error (RMSE) are calculated to analyze the performance of proposed device.

4.1 Proposed Deep Neural Network (DNN) and Other Models for Glucose Sensor Calibration

Several machine learning-based computation models have been examined to get optimized regression method in terms of precise measurement. Support vector regression with multiple Gaussian kernels is used to analyze the optimized model. In case of blood glucose estimation, a margin of tolerance (epsilon) is set in approximation as per the independent variables. To reduce the error, a kernel (medium gaussian kernel) scale value is also set to the square root of number of predictors. This customized kernel scale is used to remove the outlier from data. The cubic kernel (kernel with polynomial degree 3) based model is customized to remove the outliers. This customized kernel scale is used for precise measurement. Kernel (fine gaussian kernel) scale value is also set to the square root of predictors which is divided by 4 ($\frac{\sqrt{P}}{4}$). The fitting model of DNN has also been analyzed for capillary and serum glucose prediction in the current work [16]. Sigmoid activation functions have been used in the proposed DNN models and have been trained through Levenberg-Marquardt backpropagation algorithm [30]. In proposed models, 10 hidden layers have been analyzed to predict precise glucose values. The error analysis is graphically represented in Figure 8. These optimized models have been used to predict the glucose values from logged data. Here, the responses (voltages) from three channels are taken as inputs of the proposed DNN models. The predicted blood glucose values corresponding to capillary and serum glucose are formed through the modelling of three channels voltage values. Weights of the voltage values correlate predicted glucose values to the channels data. Overall accuracy through DNN is better using 10 hidden layers. The block diagram of DNN model is given in Figure 9.

4.2 Proposed Method: Multiple Polynomial Regression (MPR) model of Glucose Concentration with Voltage

Multiple polynomial regression with polynomial degree 3 based model (MPR 3) is applied to analyze the optimized model for capillary and serum glucose prediction. Using multiple polynomial regression, proposed model represents the relationship between three channels detector's outputs and corresponding referenced glucose values (serum glucose

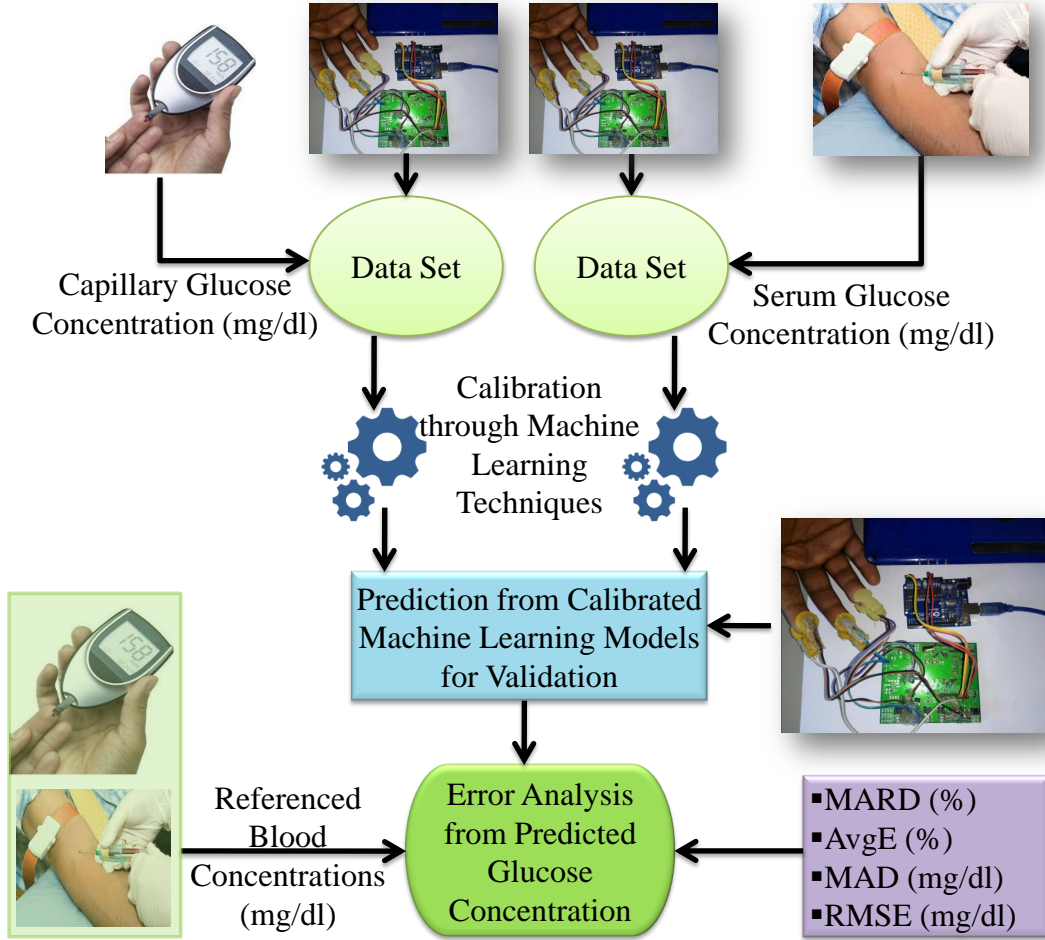


Figure 7: The process flow of calibration and validation of proposed device (iGLU 2.0).

or capillary glucose) by fitting a cubic kernel based regression model which is represented as follows:

$$\begin{aligned}
 y = & a_1x_1^3 + a_2x_2^3 + a_3x_3^3 + a_4x_1^2x_2 + a_5x_1^2x_3 + a_6x_1x_2^2 + a_7x_1x_3^2 + a_8x_2^2x_3 \\
 & + a_9x_2x_3^2 + a_{10}x_1^2 + a_{11}x_2^2 + a_{12}x_3^2 + a_{13}x_1x_2x_3 + a_{14}x_1x_2 + a_{15}x_1x_3 \\
 & + a_{16}x_2x_3 + a_{17}x_1 + a_{18}x_2 + a_{19}x_3 + \epsilon,
 \end{aligned} \tag{1}$$

where, a_1 - a_{19} are regression coefficients and ϵ is residual of errors. The model is used to observe the predicted glucose value from iGLU. The values of these regression coefficients and residual of error depend upon the predictors and corresponding response of calibrated model. In the proposed model, three channels voltage values are represented as x_1 , x_2 and x_3 as independent variables (predictors) and estimated glucose (mg/dl) is the dependent variable y . Each value of detector's output voltage value is associated with reference glucose value. Proposed multiple polynomial regression model (MPR 3) kernel for calibration is represented in Figure 10.

Proposed MPR is a complex multivariable interaction approach based regression model. 19 customized interacted variables combinations based kernel is an optimized model which is represented in eq. 10. The maximum polynomial degree 3 of terms (interactions of multiple variables) have been analyzed for precise model. The correlation plots between predicted glucose concentration and reference glucose concentration for regression models are represented in Figure 11(a)- Figure 11(h). The error analysis of calibrated machine learning regression models is also represented in Table 2.

Proposed MPR 3 model represents better results of calibration and validation compared to DNN based model and other regression models because of its complexity and polynomial interaction-based approach with polynomial degree 3. During analysis, prediction of serum glucose is found more precise compared to prediction of capillary glucose using MPR 3.

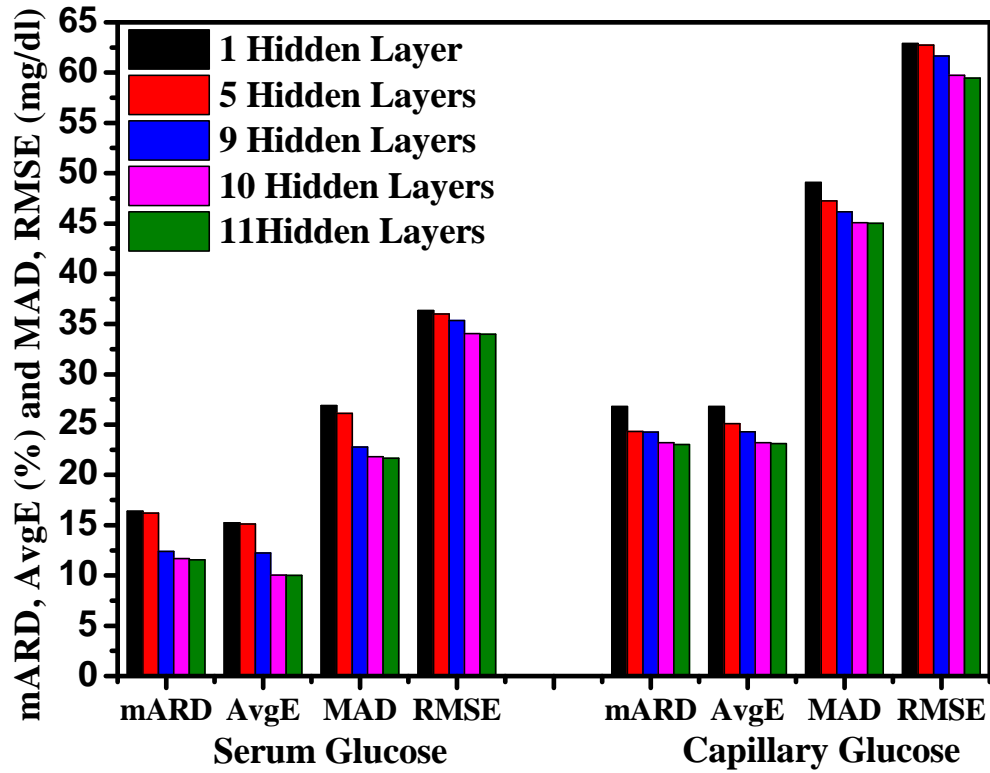


Figure 8: Error analysis of DNN models using different hidden layers

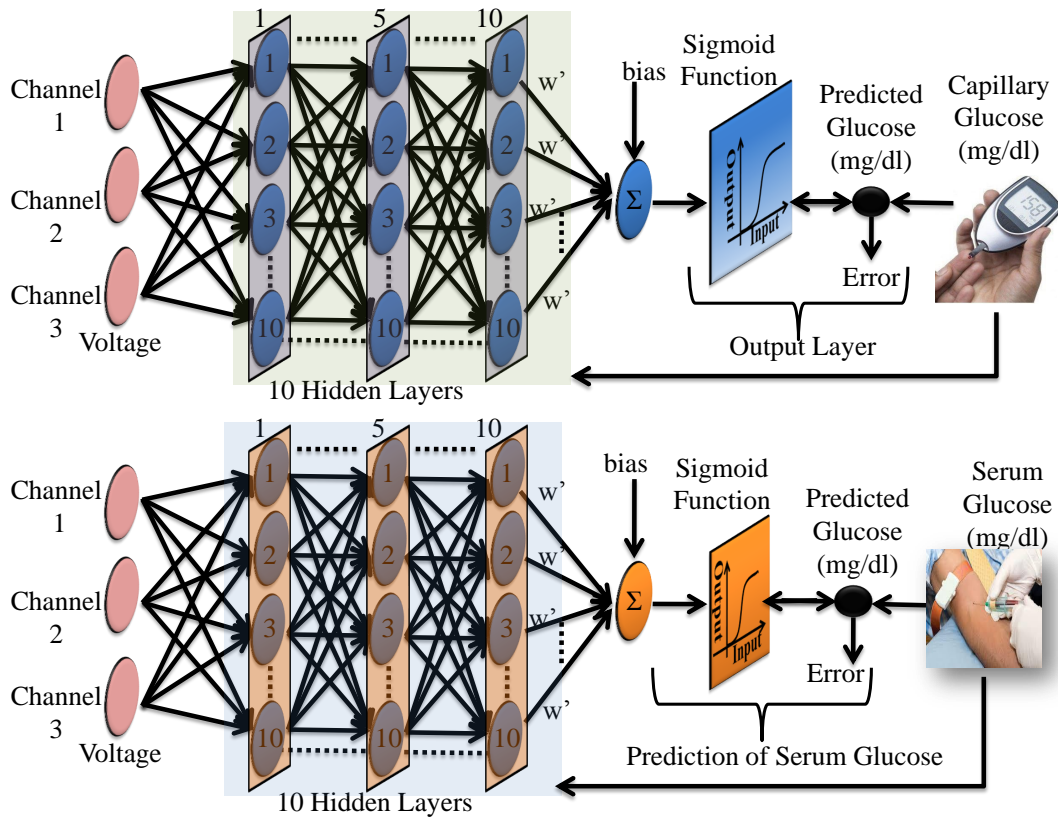


Figure 9: The Deep Neural Network (DNN) for proposed work

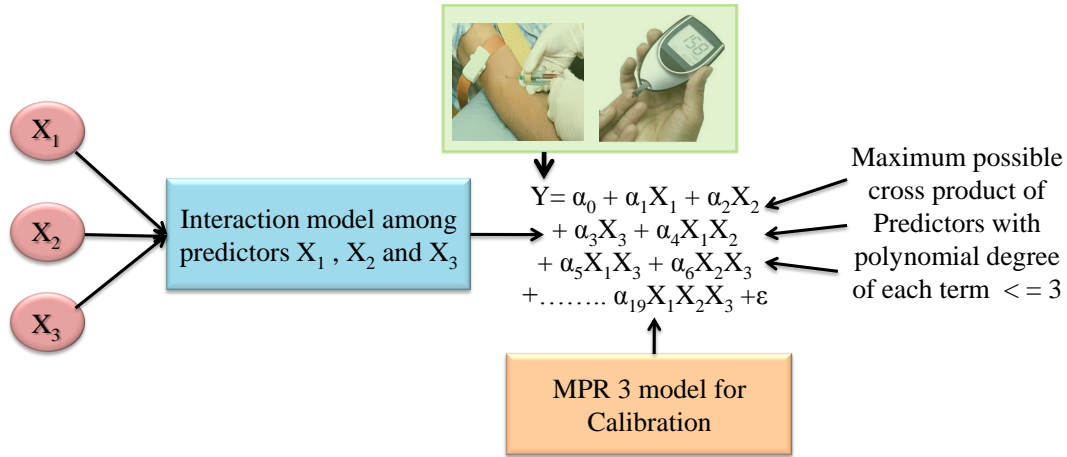


Figure 10: MPR 3 model representation for calibration.

Table 2: Statistical Analysis of calibration of proposed model and existing techniques.

Regression Model	mARD %	AvgE %	MAD mg/dl	RMSE mg/dl
Linear SVR (Capillary)	34.40	31.27	65.64	83.50
Serum	39.24	36.21	70.59	83.21
Cubic SVR (Capillary)	31.85	27.32	59.42	79.66
Serum	26.69	32.55	51.92	73.32
Quadratic SVR (Capillary)	33.43	29.73	63.59	81.38
Serum	33.42	10.86	61.35	83.47
Medium Gaussian SVR (Capillary)	31.36	26.82	58.43	77.83
Serum	26.50	24.66	47.75	66.01
Coarse Gaussian SVR (Capillary)	33.71	30.74	64.58	82.10
Serum	40.09	34.75	70.37	81.05
Fine Gaussian SVR (Capillary)	14.31	12.49	27.36	45.06
Serum	12.31	10.45	20.96	31.09
DNN (Capillary)	29.06	22.14	46.47	62.51
Serum	9.11	8.95	19.47	27.95
MPR3 (Capillary)	6.07	6.09	13.28	19.71
Serum	4.86	4.88	9.42	13.57

5 Design of the Proposed Novel Glucometer for Serum Glucose Monitoring - The iGLU 2.0

The proposed device is based on short wave NIR spectroscopy using wavelengths (940 and 1300 nm) and implemented using three channels. Each channel contains emitter and detector of a particular wavelength for glucose detection. The flow of proposed work is represented in Figure 6.

5.1 The Proposed Approach for Data Acquisition

The pseudocode of data acquisition for proposed iGLU 2.0 is represented in process flow which is shown in Figure 12. The data is collected and serially logged by 16 bit ADC with sample rate of 128 samples/sec. The logged data is calibrated and validated through an optimized model of existing regression techniques for precise measurement.

Independent samples of person aged 24-50 have also been taken for testing and validation of iGLU 2.0. The serum glucose values have been stored on the cloud using open IoT platform. The data can be accessed by patients and doctor. On the basis of serum glucose values, the treatment can be provided at a remote location. A 2 layer PCB is designed and system is developed to embed NIR LEDs and detectors.

The circuit is designed to implement the setup for optical detection [4]. Emitters, detectors and ADS 1115 are embedded with optimized biasing with 5 V DC supply. Passive components have been chosen for better efficiency

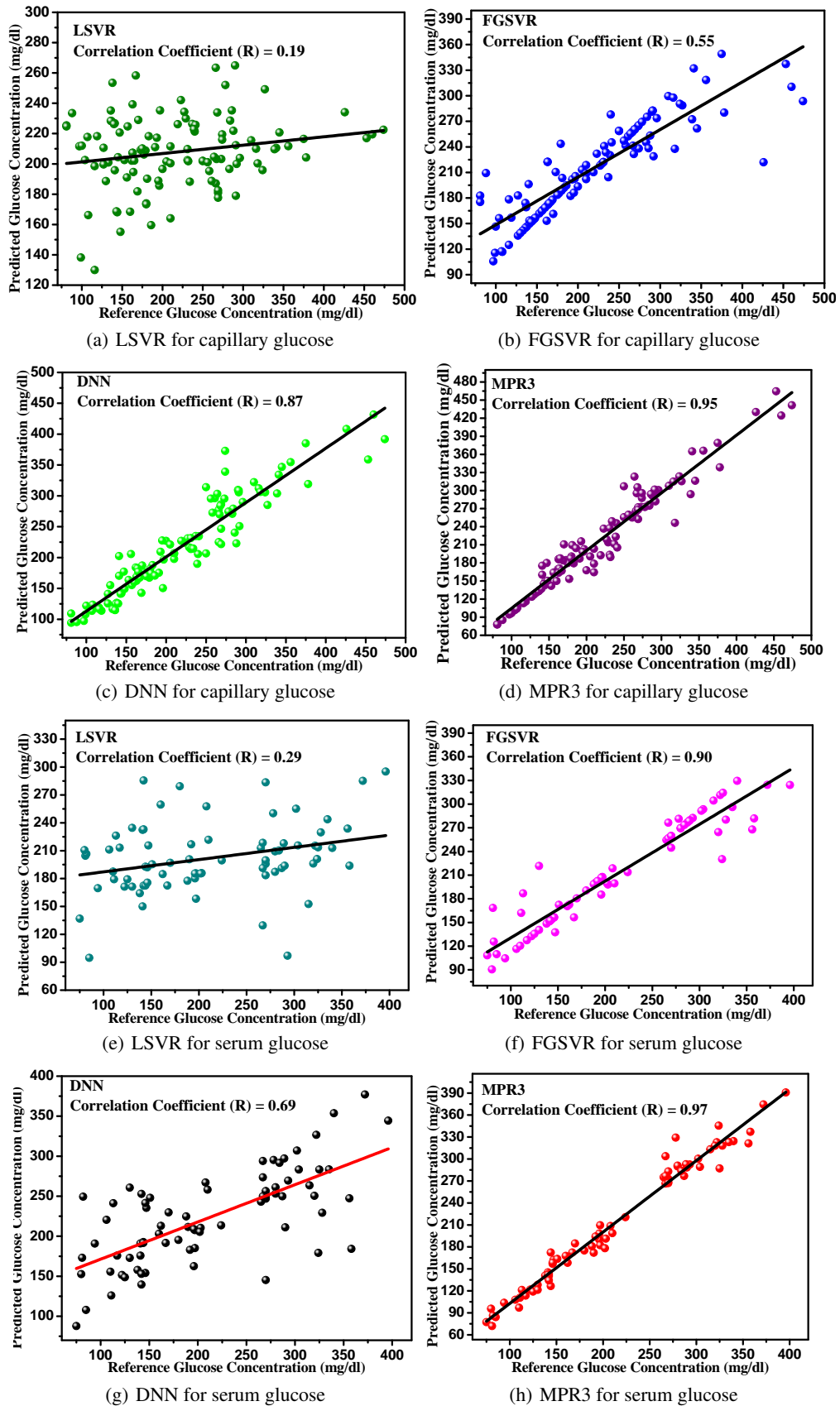


Figure 11: Correlation plot of predicted and referenced blood glucose concentration model during calibration.

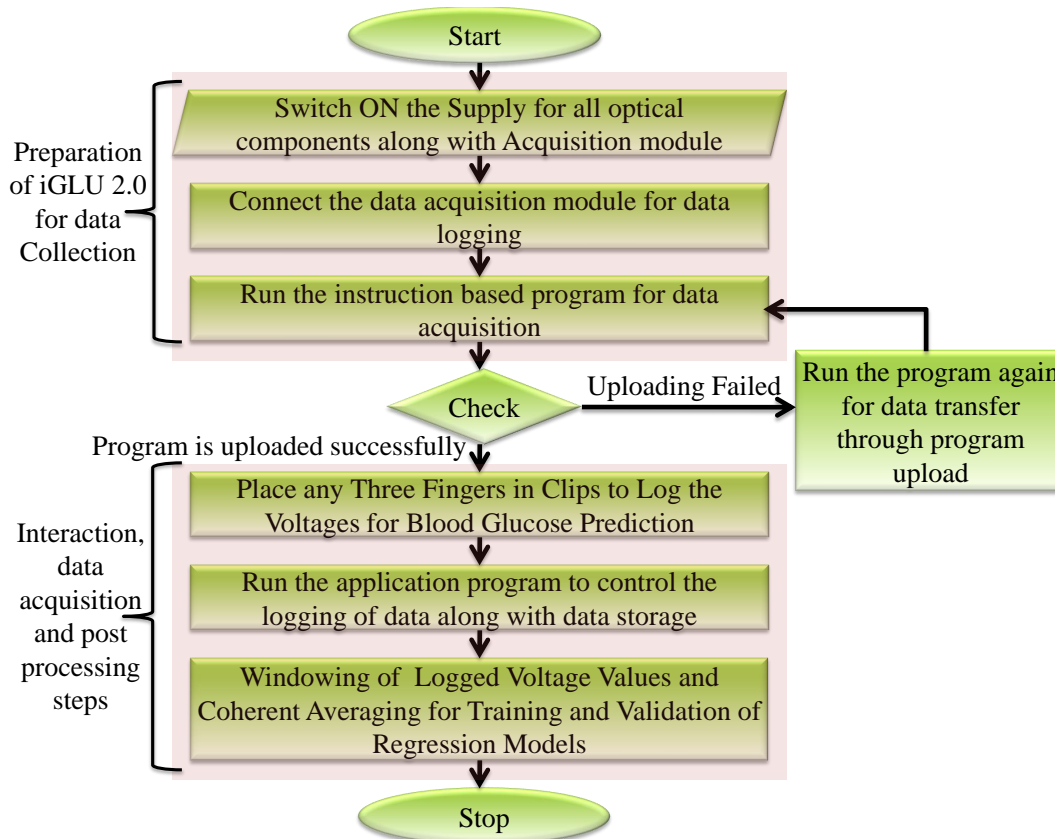


Figure 12: Process flow data acquisition for proposed device (iGLU 2.0).

of NIR LEDs and detectors. All NIR LEDs and detectors are connected with proper biasing. The detectors are used in photoconductive mode. All detectors have specifications of daylight blocking filters [4]. ADS 1115 has been used to serially transfer the three channels data in decimal form. The ADS 1115 is controlled through microcontroller ATmega328P using arduino uno board.

5.2 The Proposed System of the Glucometer

In this paper, we implement optical detections using specific wavelengths for absorptions and reflection. Concentration of glucose molecules depends upon the change in light intensity. The logged voltage values from the detectors depend on received light intensity. During placing the object (fingertip or earlobe) between NIR LED and detector, the voltages (data) are logged. The coherent averaging of voltage samples is done to improve the measurement error. For calibration and validation, the averaging of 1024 samples has been done in 8 seconds. Block representation of proposed iGLU is shown in Figure 13. During experimental analysis, serum glucose has been measured in laboratory and capillary glucose has been measured by invasive glucometer SD check gold device for validation [31]. The serum and capillary glucose values are taken as referenced glucose values (mg/dl). At that time, detector responses (in milivolts) have been collected through all channels simultaneously. During measurement process, the data has been logged through all channels in the form of voltages from detector of each channel using ADS 1115. These logged voltage values are corresponding to serum and capillary glucose values.

6 Validation of the Proposed Device iGLU 2.0

6.1 Testing and Error Analysis

After calibration of iGLU 2.0, 50 different healthy, prediabetic and diabetic samples of capillary glucose and 37 samples of serum glucose have been taken to validate the device. During device validation, 26 males and 20 females

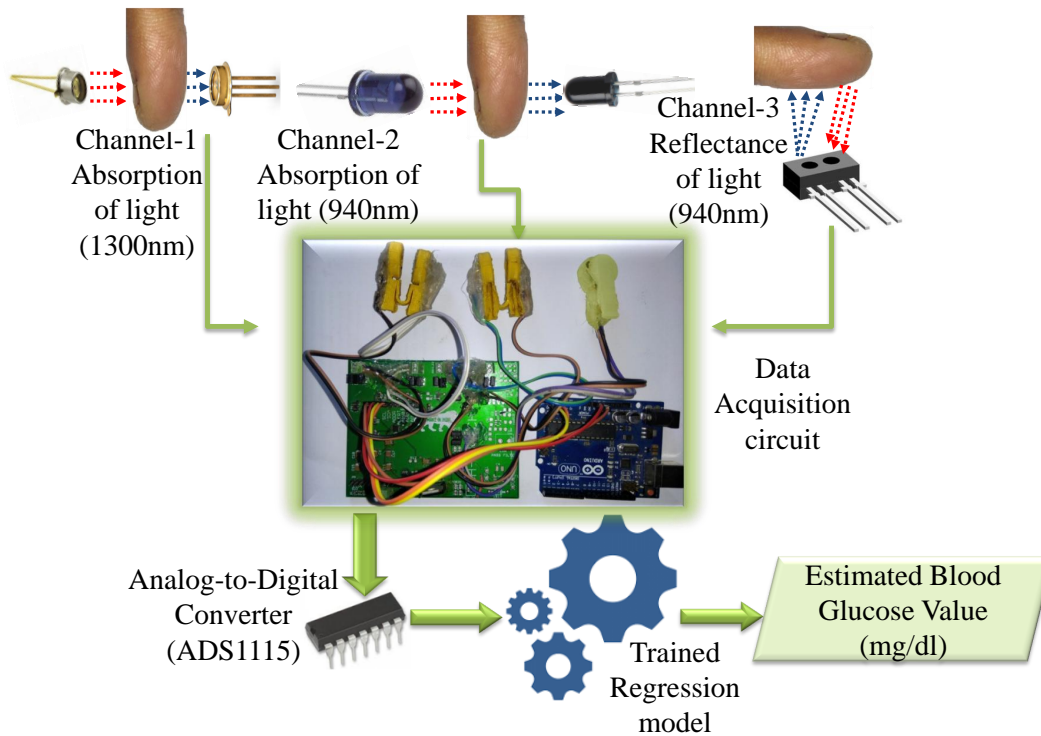


Figure 13: Block Representation of proposed device (iGLU 2.0).

samples are tested following medical protocols. The samples are taken in fasting, post-prandial and random modes for validation and testing. The baseline characteristics and error analysis is represented in Table 1 and 3.

Table 3: Statistical Analysis of validation of proposed model and existing techniques.

Regression Model	mARD %	AvgE %	MAD mg/dl	RMSE mg/dl
FGSVR (Capillary)	14.09	11.45	25.20	41.18
Serum	9.17	9.12	19.09	27.34
DNN (Capillary)	23.19	22.14	45.07	59.74
Serum	11.67	10.02	21.81	34.05
MPR3 (Capillary)	7.74	7.70	16.08	22.46
Serum	5.009	4.97	9.74	12.98

As per analysis of results, serum glucose measurement is found more accurate compared to capillary glucose measurement using MPR 3 model. To test the device stability, an experimental analysis has been done with multiple measurements of 2 volunteers. For this experimental work, each volunteer has been chosen for measurement of capillary and serum glucose through iGLU 2.0. The measurement has been done in fasting and post-prandial mode. Result analysis is shown in Figure 15.

6.2 Clarke Error Grid (CEG) Analysis

CEG analysis is explored by W. L. Clarke in 1970. This is used to analyze the accuracy of predicted blood glucose concentration values from proposed device. This error analysis has been presented to analyze the precision level of predicted blood glucose values from device iGLU 2.0 [32]. Clarke analysis explores the zones by the variation between referenced and predicted glucose concentration. All samples have been arranged gender-wise to confirm the accuracy of iGLU 2.0 for capillary and serum glucose measurement along with testing and validation which are represented in Figure 16 and 17 respectively. The proposed device is considered as desirable for clinical purpose. According to Table 4, proposed non-invasive device iGLU 2.0 is more precise compared to other glucose monitoring devices. During

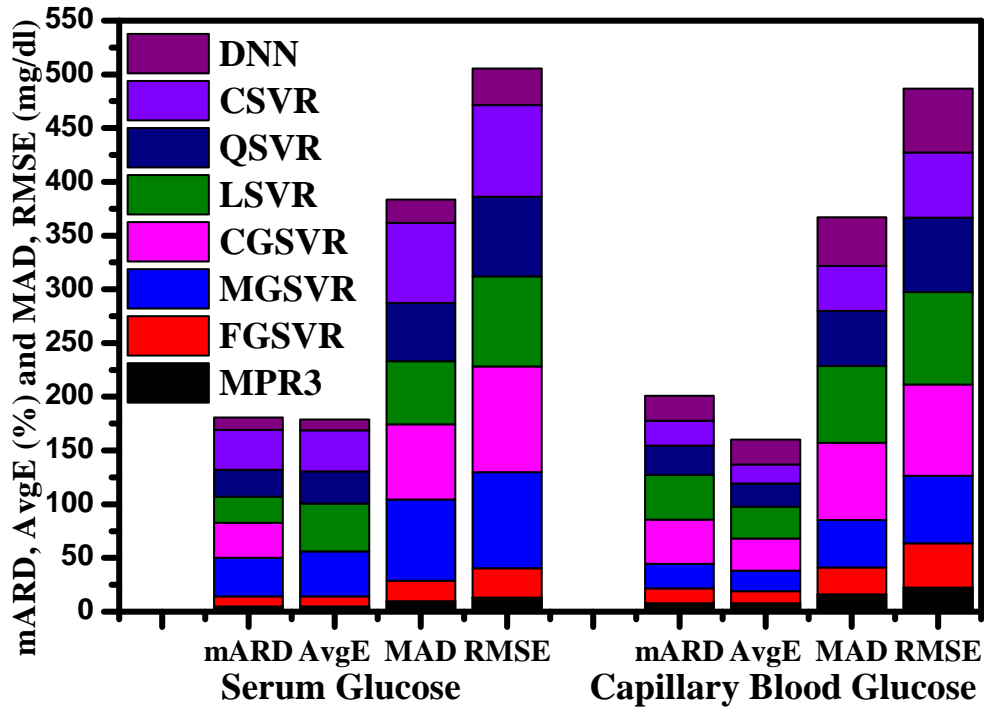


Figure 14: Error analysis of validation of data using existing regression techniques.

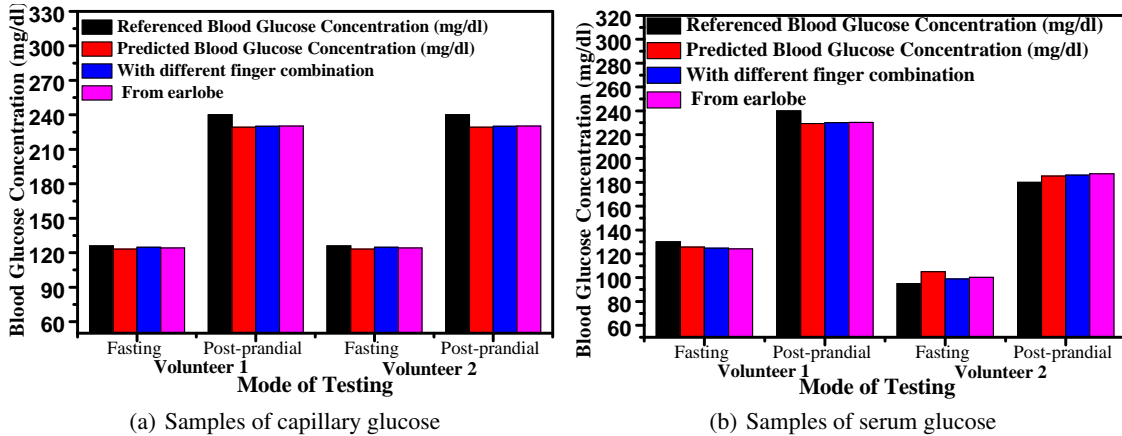


Figure 15: Predicted and reference blood glucose concentration for validation of iGLU 2.0 on 2 volunteers.

analysis, it has been observed that all samples of serum glucose exist in zone A and all samples of capillary glucose exist in zone A and zone B.

It has also been concluded that 4.86% *mARD* of serum glucose is better than 6.07% *mARD* of capillary glucose. The *AvgE* and *MAD* 4.88% and 9.42 mg/dl represent the precision level of the proposed device. Real-time analysis and cross validation have been performed for real-time applications [5].

7 Conclusions and Future Directions of This Research

Non-invasive serum glucose measurement device is proposed which is based on short-wave NIR spectroscopy with two specific wavelengths (940 and 1300 nm). The device is validated and tested through healthy, prediabetic and diabetic patients. The combination of reflection and absorption of NIR light using MPR model based calibration is implemented for non-invasive serum glucose measurement. The proposed device is the combination of optical

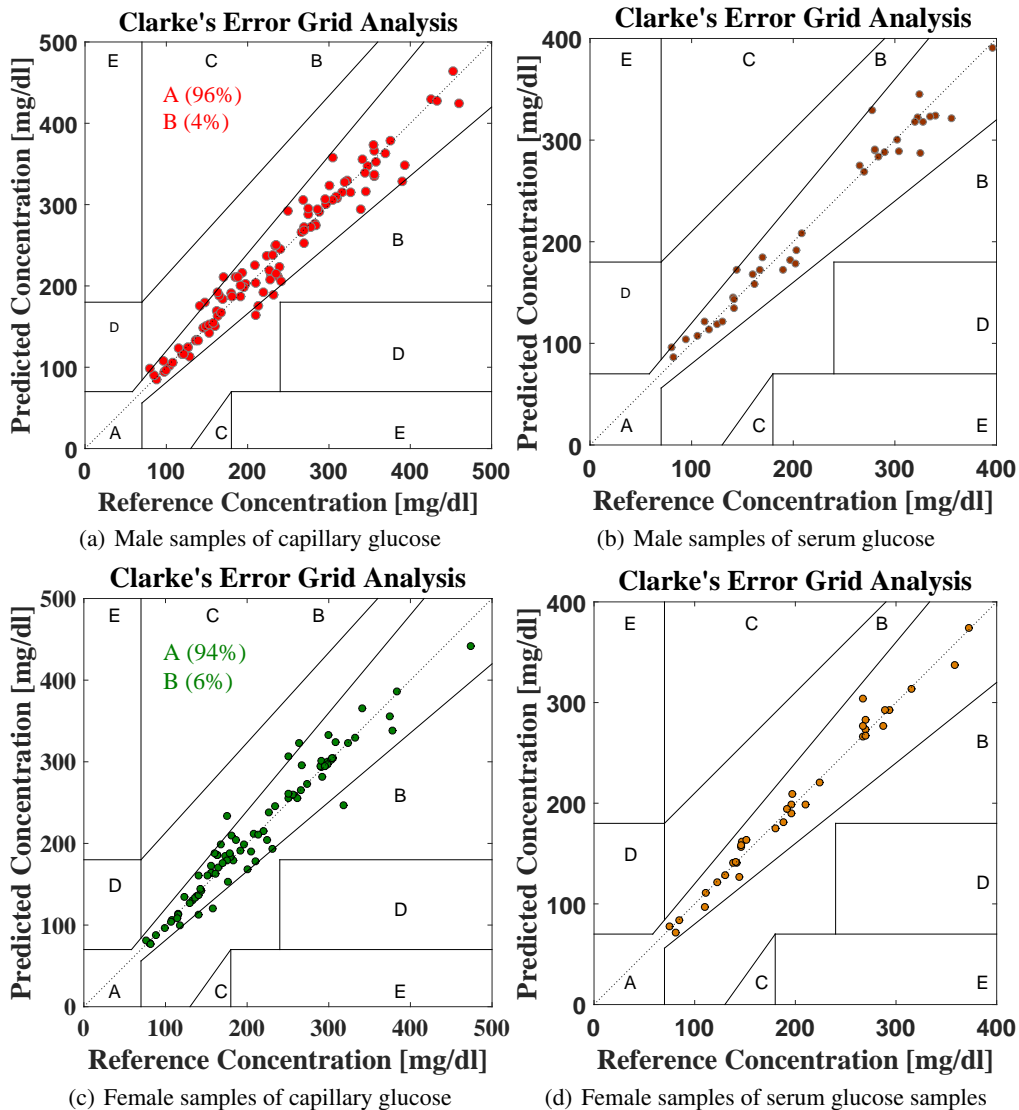


Figure 16: CEG analysis of predicted blood glucose concentration for validation of iGLU 2.0 device.

detection and optimized machine learning regression model which is an innovative approach for precise serum glucose measurement. For device validation, all samples have been taken from persons aged 17-80. During device calibration for serum glucose, the capillary glucose has also been calculated from the same samples for error analysis. During statistical analysis, 0.79 coefficient of determination is calculated for serum glucose calibration using MPR based model with polynomial degree 3 which shows a better result compared to capillary glucose calibration. It has been observed that *AvgE* and *mARD* represent better results of calibration and validation for serum glucose compared to capillary glucose. After analysis of predicted serum glucose values, 100% samples come in zone A.

In the future research, we will consider Internet-of-Medical-Things (IoMT) integration of the iGLU in healthcare CPS (H-CPS) so that the healthcare data can be securely stored in the cloud. We will also evaluate the options of edge-computing and IoT-computing paradigms for fast response as well as long-term storage of the user's records. This can be have significant impact on smart living component of smart healthcare for smart homes [33]. The long-term goal of iGLU project is an unified H-CPS for non-invasive glucose level monitoring and release of appropriate level of insulin with full-proof security arrangement [34].

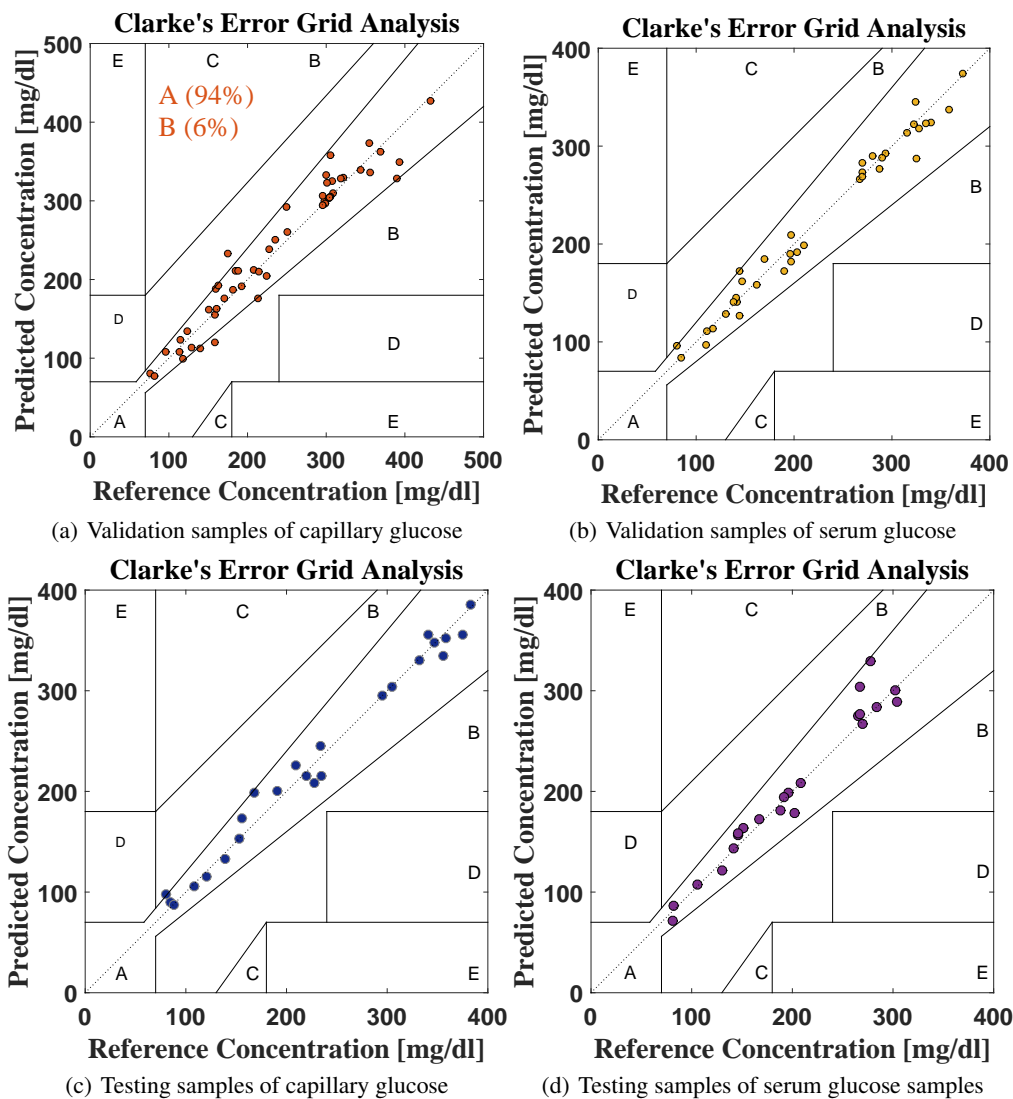


Figure 17: CEG analysis of predicted blood glucose concentration for validation of iGLU 2.0 device.

Table 4: Comparison with Non-invasive Works

Works	R value	mARD (%)	AvgE (%)	MAD (mg/dl)	RMSE (mg/dl)	Used model	Measurement sample	Device cost
Singh, et al. [14]	0.80	-	-	-	-	Human	Saliva	Cheaper
Song, et al. [16]	-	8.3	19	-	-	Human	Blood	Cheaper
Pai, et al. [11]	-	7.01	-	5.23	7.64	in-vitro	Blood	Costly
Dai, et al. [15]	-	5.99	5.58	-	-	in-vivo	Blood	Cheaper
Beach, et al. [8]	-	-	7.33	-	-	in-vitro	Solution	-
Ali, et al. [27]	-	8.0	-	-	-	Human	Blood	Cheaper
Haxha, et al. [28]	0.96	-	-	-	33.49	Human	Blood	Cheaper
Jain, et al. (iGLU) [4]	0.95	6.65	7.30	12.67	21.95	Human	Blood	Cheaper
Proposed Work (iGLU 2.0)	0.97	4.86	4.88	9.42	13.57	Human	Blood	Cheaper

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