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Development of Blood Glucose Monitoring System using Image Processing and Machine Learning Techniques

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***Abstract*—Glucose concentration measurement is essential for diagnosis, monitoring and treatment of various medical conditions like diabetes mellitus, hypoglycemia, etc. This paper presents a novel image-processing and machine learning based approach for glucose concentration measurement. Experimentation based on Glucose oxidase - peroxidase (GOD/POD) method has been performed to create the database. Glucose in the sample reacts with the reagent wherein the concentration of glucose is detected using colorimetric principle. Colour intensity thus produced, is proportional to the glucose concentration and varies at different levels. Existing clinical chemistry analyzers use spectrophotometry to estimate the glucose level of the sample. Instead, this developed system uses simplified hardware arrangement and estimates glucose concentration by capturing the image of the sample. After further processing, its Saturation (S) and Luminance (Y) values are extracted from the captured image. Linear regression based machine learning algorithm is used for training the dataset consists of saturation and luminance values of images at different concentration levels. Integration of machine learning provides the benefit of improved accuracy and predictability in determining glucose level. The detection of glucose concentrations in the range of 10–400 mg/dl has been evaluated. The results of the developed system were verified with the currently used spectrophotometry based Trace40 clinical chemistry analyzer. The deviation of the estimated values from the actual values was found to be around 2-3%.**

***Keywords*—glucose; image processing; machine learning; colorimetry**

I. Introduction

ONE of the most common and essential biochemical assay is glucose concentration measurement. It is necessary for diagnosis and monitoring of diabetes mellitus, a major health problem around the world. This disease is becoming common day by day and a number of lifestyle factors such as urbanization, diet, stress, physical activity or lack of exercise are known to have contribution in the development of diabetes. Diabetes is a chronic disease which is caused due to completely or partially insufficient insulin production in the body or ineffective utilization of insulin by the body [1], [2]. Insulin is the blood sugar regulating hormone. In 2014, WHO reported an increase of 314 million diabetes patients in a period of 30 years [3]. In 2019, 1.5 million deaths were claimed to have been directly caused due to diabetes. When prolonged and left uncontrolled, diabetes can cause serious health conditions like cardiovascular diseases, neuropathy, nephropathy, and retinopathy [4]–[7]. It can be treated and its consequences can be avoided or delayed by proper monitoring of blood glucose. Inaccurate measurement of blood glucose can lead to improper diagnosis or treatment. It may even lead to hypoglycemia due to over dosage of insulin. Therefore, quality of glucose monitoring should be high in terms of the accuracy of the results. Accurate monitoring using quality glucose monitoring systems certainly helps regulate diabetes and avoid its ill-effects [8], [9].

Several devices employing various techniques for glucose assay are available. Some of these techniques are spectrophotometric [10], electrochemical [11], [12], polarometric [13], amperometric [14], and so on. One of the methods for analyte detection is colorimetry which is popularly used method due to simplicity, low cost, and quick implementation to perform [15]. Glucose concentration measurement using colorimetric approach is performed using in vitro method, in which a sample is taken from the human body and analysed based on interactions with certain enzymes [16]. For glucose assay, hexokinase, glucose oxidase, or glucose dehydrogenase enzymes are used [17]. Out of these, glucose oxidase enzyme is widely utilized because it is cheap and easily available, and shows greater selectivity for glucose compared to many other enzymes [18]. So, in colorimetry, the enzyme reacts with the analyte, in our case glucose sample, and a coloured solution is obtained. The colour change post reaction occurs with regard to the concentration of analyte present in the sample. So, for different glucose concentrations, different colour intensities can be observed.

The most commonly used pathology device for glucose concentration evaluation is spectrophotometric biochemistry analyser [19], [20]. The biochemical assay for spectrophotometric readouts depends on the colorimetric reaction which shows a visible change in colour. Spectrophotometry technique is based on the Beer-Lambert Law which states that the amount of light absorbed is proportionate to the concentration of the solute in the solution and the thickness of the solution being analysed. The clinical biochemical analyser system pipets out the sample and the reagent which are mixed in a cuvette and incubation of the assayed volume takes place. After the incubation, light emitted by a halogen lamp is directed as a straight beam by a collimator which splits it into several component wavelengths. A wavelength selector is used to allow only the wavelength

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specific for a particular assay to pass. The incident light passes through the cuvette containing the sample and the reagent solution. Depending of the concentration, certain amount of photons are absorbed by the sample-reagent solution while the transmitted light is measured by a detector at the other end. Based on this absorbance, concentration of the biochemical is measured. These devices have their specific precision and accuracy, different instruments require use of different reagents and these devices have much hardware complexity. Also, errors of 5 to 20% are not uncommon in these devices [21].

Instead of using spectrophotometry, simply an image of solution containing glucose sample mixed with reagent post incubation can be captured. Since colorimetric method is used, different colour intensities will be observed for different concentrations. Therefore, certain features from the image can be extracted that give relation with changing concentration. For this, various image processing techniques can be applied for instance, segmentation, cropping, averaging, etc.

N. Demitri et. al. proposed an invasive photometric measurement technique for glucose measurement comprising of a framework with the ability to deal with small blood samples, while ensuring the required accuracy [22]. The presented framework consisted of two major parts, namely image segmentation and convergence detection. Image segmentation part was based on iterative mode-seeking methods for estimation of the intensity value of the region of interest. This approach was capable of dealing with variation in the number and position of clusters without any prior knowledge. Furthermore, it incorporated sparse approximation based method which decreased the computational load, while maintaining accuracy. Convergence detection was achieved using temporal tracking and prediction, thereby decreasing the measurement time and improving usability.

Another algorithm has been proposed by S. Piramanayagam et al. [23] which used an image of the glucose spot captured at a particular wavelength for glucose concentration determination. The algorithm incorporated of a training phase and a testing phase. Training datasets comprised images at different concentration levels to which segmentation image processing technique has been applied and then a parameter relating to the intensity of the spot has been calculated. The image intensity has been used as the parameter to determine the glucose concentration. Thereafter, a mathematical model giving a relation between the extracted parameter values and the given concentrations has been obtained. During the testing phase, extraction of same parameters using image processing has been performed. Finally, the algorithm used the model (feature vs. concentration) to predict the unknown concentration.

These features extracted from the image need to demonstrate a significant relation with the glucose concentration. Any colour image is a representation of RGB colour model in which primary spectral colours red, green and blue are added together to reproduce each pixel within a broad array of colours. A. Fatoni et al., J. Kim et al. and R. Domniguez et al. [24]–[26] in their work made use of RGB values as the parameters relating to the concentration of glucose. But these RGB values cannot be directly used instead need to be converted into another parameter that has some correlation with the concentration. A colour image has three characteristics specifying its visual information. These are luminance or brightness that is the amount of light intensity as perceived by the eye irrespective of the colour, hue or tint that is the predominant spectral colour and saturation that is the colour's spectral purity [27]. Regardless of the change in concentration, hue will not change but luminance and saturation will be affected. A.Sivanantha Raja et al. in their paper compared traditional colorimeter for glucose measurement with glucose measurement based on RGB data of the colour image of the assay. Here, RGB values of the obtained colour image were converted into luminance value and relation between luminance and glucose concentration was obtained. This relation was also compared with the absorbance values. In another work, A.Sivanantha Raja et al. obtained hue and saturation values from the RGB data using chromaticity diagram and then established a relation between glucose concentration and saturation [28]. In this paper, both luminance (Y) as well as saturation (S) values have been employed to establish a mathematical model which forms an equation involving both S and Y values to estimate concentration.

The paper titled "Smartphone-based Colorimetric Detection to Measure Blood Glucose Levels" by S. Singhal et. al. provided a medical image processing system based on colorimetric detection wherein the RGB image was converted into HSV and LAB colour models [29]. Here, some of the imaging factors which limit the proposed technique were also highlighted. Firstly, the illumination factor that is the amount of light incident during capturing the image. Second imaging anomaly is the shadow. Lastly, the camera quality comprising of megapixel count, aperture, focus, etc. also plays a key role. Thus, this paper suggested suitable controlled environment with proper light illumination, good camera quality and positioning of sample reservoir with respect to the camera and lighting arrangement in such a way that shadow effect can be avoided.

To improve accuracy and predictability in determining glucose level, machine learning (ML) has been incorporated into the system [30]. This can be done using various machine learning algorithms, to name a few; linear predictor, decision tree, nearest neighbour, support vector machine, and so on [31].

Various researches have been carried out which signify how incorporation of machine learning to the glucose monitoring system can be of benefit. One such work carried out by Y. Marcus, et al. indicates how ML can improve accuracy and predictability in determining glucose level [30].

Another work by E. Monte-Moreno et al. presented a system for a simultaneous non-invasive estimate of the blood glucose level and the systolic and diastolic blood pressure, using a photoplethysmograph and machine learning techniques [32]. Ridge linear regression, a multilayer perceptron neural network, support vector machines and random forests techniques were tested and the random forest technique was employed.

Y. N. R. Reddy, et al. proposed a non-invasive blood glucose measurement method based on microwave transmission integrated with machine learning technique [33]. ML technique was applied to the system to facilitate a real-time processing capable of alerting the patients during hyperglycemia conditions, and suggest a precise insulin dose.

Spectrophotometric biochemistry analyser used in pathology laboratory use colorimetry and estimate concentration of glucose in the sample based on the absorbance of monochromatic light by the sample solution. It has been found that errors of 5 to 20% are common in these devices due to the use of monochromatic source. These devices have their specific

precision and accuracy. Also, these devices have much hardware complexity. To overcome these drawbacks, image processing based system was proposed. Image processing based systems discussed earlier help to extract data from the image of the sample but suffer from the drawbacks caused due to improper lighting conditions, non-linearity of the camera. Thus, this paper suggested suitable controlled environment with proper light illumination, good camera quality and positioning of sample reservoir with respect to the camera and lighting arrangement in such a way that shadow effect can be avoided. Further, instead of the complex ML algorithms employed in the papers discussed earlier, linear regression algorithm can be used which is very simple. Using ML, there is no need of any further explicit programming once the algorithm has been applied to the system to train it.

Therefore, in this work, we propose a glucose analyser with comparatively simple hardware setup that is integrated with image processing and machine learning. Some techniques to process the image of the glucose sample essential for extraction of data that gives some correlation to the concentration of glucose in the sample, have been proposed. Also, this work proposes integration with machine learning which provides an algorithm to train the system using dataset obtained from image processing to predict the concentration of unknown sample. Machine learning is used to improve accuracy and predictability.

II. Material and Methods

A. Chemicals and Material used

Trace40 clinical chemistry analyser glucose detection kit was used which contains glucose standard and reagent. The reagent was ready to use and consisted of 15ku/L Glucose oxidase (GOD), 1.0ku/L Peroxidase (POD), 0.3mmol/L p-hydroxybenzoic acid (Phenol), 2.6mmol/L 4-aminoantipyrine (4-AP), 92mmol/L Buffer pH 7.55 and Stabilizers and activators in given proportion. Glucose standard had a concentration of 100mg/dL.

Components used included Raspberry Pi 4 microcontroller board, raspberry pi noir camera module v2 which was used as the image sensor, a 15mm x 10mm x 10mm glass reservoir to carry the sample, a white box with LED strip arrangement, an LCD display and a keyboard.

B. Sample Preparation

Firstly, for glucose analysis Glucose oxidase and Peroxidase (GOD - POD) method [30] was taken into account. The principle equations involved are as mentioned in equation 1 and equation 2.

$$\text{D-glucose} + \text{O}\rightleftarrows_2 + \text{H}_2\text{O} \xrightarrow{\text{glucose oxidase}} \text{D-Gluconate} + \text{H}_2O_2 \quad (1)$$

$$2\text{H}_2O_2 + \text{p-hydroxybenzoic acid} + \text{4-aminoantipirine} \xrightarrow{\text{peroxidase}} \text{Quinoneimine dye} + 4\,\text{H}_2O \quad (2)$$

Equation 1 represents glucose oxidase formation (GOD) while equation 2 represents glucose oxidase formation (POD).

To create a dataset, samples with varying glucose concentrations in the range of 10mg/dL to 400mg/dL were created. For this purpose, Trace40 clinical chemistry analyser glucose detection kit was used which contains 100mg/dL glucose standard and reagent. The standard is equivalent to 100mg/dL glucose concentration in human blood. Therefore, this standard was used to form samples of varying glucose concentrations to form the dataset. To form 'x' mg/dL sample, 'x/10' uL standard is added to 1000uL as given in the formula below.

$$[(\text{x}/10)\mu\text{L standard}] + [1000\mu\text{L reagent}] = [(x)\ \text{mg/dL glucose sample}] \quad (3)$$

Some examples for proportion of standard and reagent to form samples with different concentrations are as shown in table 1. The concentration of the samples thus formed was cross verified on Trace40 clinical chemistry analyser.

TABLE I
PROPORTION OF STANDARD AND REAGENT TO FORM DIFFERENT CONCENTRATION SAMPLES

Glucose concentration (in mg/dL)	Reagent (in uL)	STD (in uL)
50	1000	5
100	1000	10
150	1000	15
200	1000	20

After mixing the standard and the reagent, the solution is incubated at 37°C for 5 min or at room temperature for 10 min. When a sample containing glucose reacts with the reagent, a red coloured solution is formed. This intensity of colour is proportional to the concentration of glucose in the sample. The colour of the solution remains stable for about 15 to 30 minutes. Hence, the procedure for detection needs to be carried out within this duration. The image of each glucose sample was captured in the white box.

C. Experimental setup

The experimental setup developed for glucose concentration estimation is shown in figure 1. The setup included a white box within which the images were captured. To capture the image under proper lighting conditions, an arrangement containing LED strips was embedded within the box. Raspberry pi noir camera module v2 was used as the image sensor to capture the images. A small glass reservoir with dimensions of 15mm x 10mm x 10mm was used to carry the solution of sample and reagent while capturing the images. Camera module was interfaced with Raspberry pi 4 microcontroller board which was programmed to capture image of the sample, process it and create a dataset. A machine learning algorithm was also applied to raspberry pi to predict the glucose concentration of unknown sample based on the training dataset. An LCD display and a keyboard were provided for user interactions.

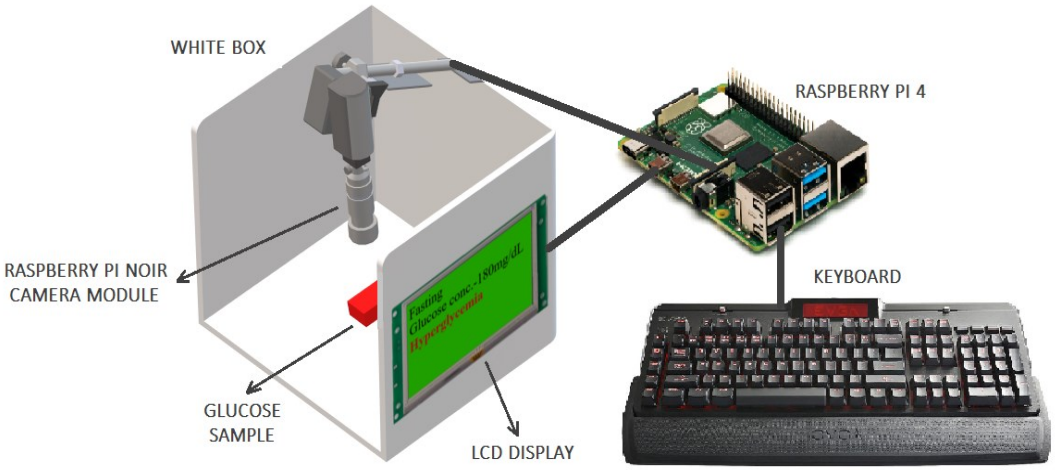


Fig. 1. Experimental setup.

D. Image processing for data extraction

Fig. 2 shows the steps involved in the image processing flow for data extraction needed for glucose concentration quantification.

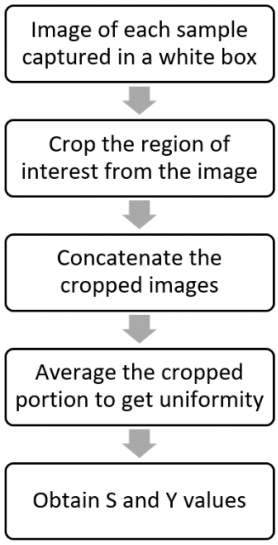
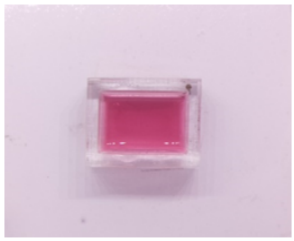


Fig. 2. Image processing flow data extraction.

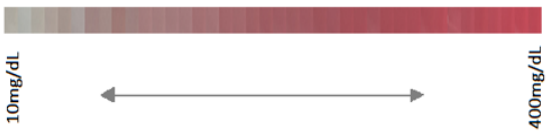
First, this entire process has been illustrated with the help of an example of a glucose sample with a known concentration of 340 mg/dL. The image of the sample was captured in the white box as shown in figure.3 (a).

Further, it was cropped to obtain the area of interest i.e. the coloured glucose spot as shown in figure 3(b). These two steps were followed for all the samples in the dataset. Figure 3(c) shows the concatenation of all the cropped images and it can be observed that with increase in the concentration of glucose from 10mg/dL to 400mg/dL, the colour intensity increases. Further, an average of each cropped image was taken to have uniformity over every pixel in the image. Then HSV (Hue, Saturation, Value) and YCbCr (Luminance, Chroma blue, Chroma red) values of the averaged image for each sample was obtained. Out of all the values, only saturation and luminance values change with changing concentration. Thus, a data set was obtained containing saturation and luminance values for different glucose concentrations. This procedure was repeated to verify consistency of readings for same glucose concentrations recorded at different times.



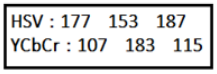
(a) Image of each sample was captured in the white box

(b) Cropped image of the sample



(c) Concatenated cropped images in the order of increasing concentration

(d) Averaged cropped image



(e) Obtained HSV and YCbCr values

Fig. 3. Stepwise flow for image processing of a glucose sample.

E. Estimation of glucose sample concentration using machine learning

Once data set was obtained, the system was trained to predict glucose concentration of any unknown sample using machine learning [31], [32]. For this, linear regression algorithm was applied. The algorithm took the saturation and luminance values from the data set that were provided as input and then used statistical techniques to predict output that fits this data. The algorithm formed a relation between the dependent variables and formed an equation using the intercept and coefficient values obtained from the relation. The equation formed is as shown below.

$$\text{Concentration} = (-318.265 + (\text{float}(S) * 3.245) + (\text{float}(Y) * 1.652)) \quad (4)$$

Thus, when values from any unknown concentration sample were given as input, the algorithm predicts the value of glucose concentration for that sample.

III. Result and Discussion

Colorimetric technique was used to form dataset of samples containing glucose concentration in the range of 10 mg/dL to 400 mg/dL. Images of these samples was captured and processed to extract HSV and YCbCr values.

It was observed that out of all the obtained values, i.e. HSV and YCbCr, saturation (S) and luminance (L) values varied the most over the range as concentration increased. This can be observed in fig. 4 which depicts relation between glucose concentration with saturation and luminance values respectively.

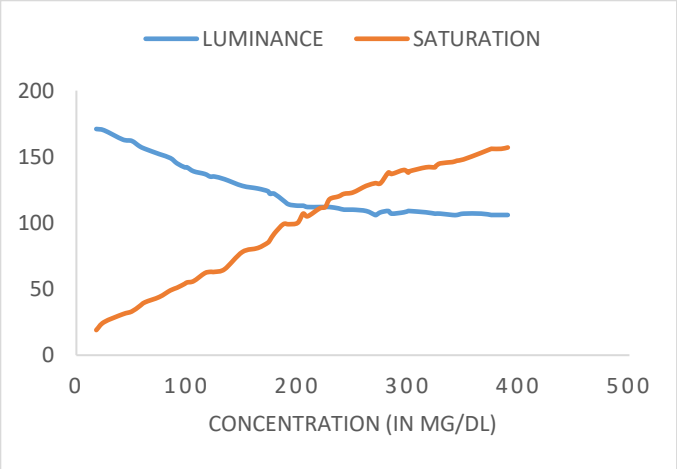


Fig. 4. Glucose concentration Vs Saturation and Luminance

As concentration increases from 1 mg/dL to 400 mg/dL, saturation also increases. On the other hand luminance component decreases with increasing concentration. It was observed that the rate of change of saturation and luminance values was not constant for the values closer to 400 mg/dL because the assay using the reagent used does not exhibit linearity for values approaching 400 mg/dL and above.

The system was tested using 5 test samples having random glucose concentrations within the range of 1 mg/dL to 400 mg/dL. The saturation and luminance values extracted for these test samples with unknown concentration were recorded as shown in table 2. It also depicts the deviation of concentration as estimated by the developed system from the existing device for the test samples.

Table II
Comparison of concentration estimated by the developed system and the existing device for various test samples

UNKNOWN TEST SAMPLE	SATURATION (S)	LUMINANCE (Y)	CONCENTRATION ESTIMATED BY THE DEVELOPED SYSTEM	CONCENTRATION ESTIMATED BY THE EXISTING SYSTEM	DEVIATION (%)
Test sample 1	35	157	50.09	50	0.18
Test sample 2	64	139	119.4	119	0.336
Test sample 3	65	134	127.775	127	0.610
Test sample 4	112	110	226.913	225	0.850
Test sample 5	144	108	327.468	321	2.015

After estimating the concentration values using the developed system, the same samples were tested on Trace40 clinical chemistry analyser and the concentration values were matched.

It was observed that for values closer to 400mg/dL, the deviation from actual value was greater while for values closer to 0mg/dL, the concentration value estimated by the system was nearly equal to the concentration value found using Trace40 clinical chemistry analyser. In general, it can be said that the deviation of concentration as estimated by the developed system from the existing spectrophotometric device was 2-3%.

Conclusion

Diabetes mellitus is a chronic disease which is becoming a global concern day by day due to the rate at which it is increasing. Glucose concentration measurement is vital and necessary for diagnosis and monitoring of diabetes mellitus.

Therefore, an image processing based glucose analyser integrated with machine learning was developed in this paper. It provides an approach for glucose concentration estimation based on image processing. The system used colorimetric method similar to existing spectrophotometric devices for preparation of sample and reagent solution. Sample and reagent solution was formed using GOD-POD method and then its image was captured. Further, the saturation and luminance values were extracted from the image of the sample solution by cropping and averaging the image and later extracting HSV and YCrCb parameter. Further, linear regression machine learning algorithm was applied to predict the concentration of glucose in any unknown sample. Using this device, the detection of glucose concentrations in the range of 10–400 mg/dl was evaluated. The deviation of concentration as estimated by the developed system from the existing spectrophotometric device was found to be 2-3%. Also, the developed system exhibited a simpler hardware compared to the existing spectrophotometric biochemical analyser.

Future work includes analysis of other biochemical such as proteins, lipids, enzymes, electrolytes, etc. into the system by altering the reagents. Also, an automated dispensing arrangement to aspirate and mix sample and reagent in the reservoir on-chip needs to be integrated. The system can further

be enhanced to provide future hypoglycemic and hyperglycemic alerts and suggest precise insulin dosage in hyperglycemic condition.

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