Pain-Free Blood Glucose Monitoring Using Wearable Sensors: Recent Advancements and Future Prospects

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***Abstract*—Keeping track of blood glucose levels noninvasively is now possible due to diverse breakthroughs in wearable sensors technology coupled with advanced biomedical signal processing. However, each user might have different requirements and priorities when it comes to selecting a self-monitoring solution. After extensive research and careful selection, we have presented a comprehensive survey on noninvasive/pain-free blood glucose monitoring methods from the recent five years (2012–2016). Several techniques, from bioinformatics, computer science, chemical engineering, microwave technology, etc., are discussed in order to cover a wide variety of solutions available for different scales and preferences. We categorize the noninvasive techniques into nonsample- and sample-based techniques, which we further grouped into optical, nonoptical, intermittent, and continuous. The devices manufactured or being manufactured for noninvasive monitoring are also compared in this paper. These techniques are then analyzed based on certain constraints, which include time efficiency, comfort, cost, portability, power consumption, etc., a user might experience. Recalibration, time, and power efficiency are the biggest challenges that require further research in order to satisfy a large number of users. In order to solve these challenges, artificial intelligence (AI) has been employed by many researchers. AI-based estimation and decision models hold the future of noninvasive glucose monitoring in terms of accuracy, cost effectiveness, portability, efficiency, etc. The significance of this paper is twofold: first, to bridge the gap between IT and medical field; and second, to bridge the gap between end users and the solutions (hardware and software).**

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I. Introduction

BASIC HUMAN body vitals such as heart rate, blood pressure, blood glucose, and oxygen saturation need to be monitored regularly to ensure a healthy life and to avoid complications that can occur due to the disturbance in the levels of these vitals [1]–[4].

Diabetes is one of the most common chronic diseases that occurs due to an imbalance in the glucose levels of the body [5]–[10]. It has two major categories: type 1 and type 2 [11]. In type 1 diabetes, the pancreas does not produce enough insulin, whereas in type 2, the body is unable to properly utilize the produced insulin [12]–[14]. Research is being done on the development of an artificial pancreas to benefit type 1 diabetes patients to help control the glucose concentration [15]. However, more than 90% of diabetes patients are categorized as type 2 [16]–[18]. According to a prediction by the International Diabetes Federation, the rate of the people affected by diabetes will increase greatly and by 2035: 592 million people will be diagnosed with diabetes [19]. The rapid growth in the number of diabetics can be seen in Fig. 1, created by using the information published in [20]–[22]. There is no cure for diabetes so far but monitoring the glucose levels regularly helps keep diabetes in control [23]–[25]. Self-management is one of the most feasible, helpful, and usable solutions to control diabetes.

Hyperglycemia and hypoglycemia are conditions caused by very high and very low blood glucose levels, respectively. Doctors advise frequent monitoring (four to five times a day) of glucose levels to reduce such conditions/events [26]. Complications arising from imbalanced glucose levels in diabetes patients include strokes, cardiovascular diseases, blindness, chronic kidney failure, amputations, etc. [27]–[29].

Blood glucose is measured in milligrams per unit deciliter (mg/dl) and different ranges of blood glucose levels are shown shown in Table I. The nature of the blood glucose monitoring techniques can be categorized as noninvasive, minimally invasive, and invasive.

Invasive devices are inconvenient as they cause pain while taking the blood sample and are costly as they require test strips for blood samples [30]. In the recent years, noninvasive devices

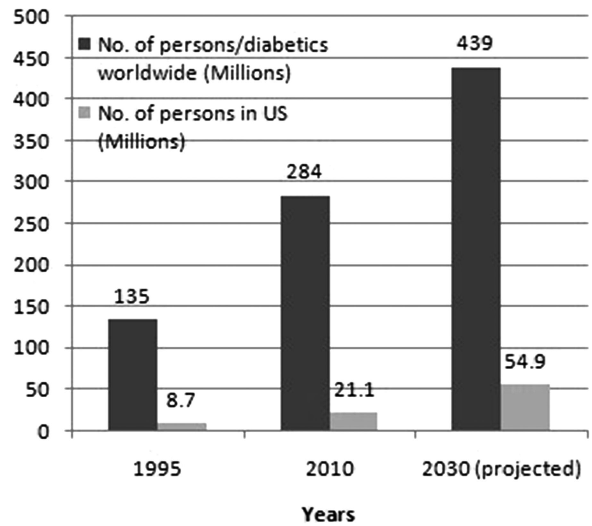

Fig. 1. Growth in the number of diabetics over the years.

TABLE I
DIFFERENT RANGES OF BLOOD GLUCOSE LEVELS [31], [32]

State	Range mg/dl
Normal (fasting)	70–130
Hypoglycemia	below 70
Hyperglycemia	above 180

are being developed by using wearable sensors, based on optics, biochemistry, microwave, saliva, tears, etc., to help diabetics avoid pain and infections.

In the past few years, researchers have reviewed the advancements of glucose monitoring from time to time [24], [33]. In [33], different techniques used for noninvasive glucose monitoring along with the devices are discussed, but the review covers the research only until early 2012. The work through 2014 is reviewed in [24], but it only discusses the glucose monitoring based on near-infrared (NIR) spectroscopy. Due to the advancement in biomedical signal processing and wearable sensors, many new methods are proposed every year, including methods other than NIR spectroscopy to estimate the glucose concentration that needs to be surveyed and analyzed.

After extensive research and careful selection, we present a comprehensive survey on noninvasive/pain-free blood glucose monitoring from the recent five years (2012–2016). The significance of this review is twofold: first, to bridge the gap between IT and the medical field; and second; to bridge the gap between end users and the solutions (hardware and software).

We searched five major databases: *IEEE Xplore*, ScienceDirect, PubMed, ACM Digital Library, and SpringerLink for noninvasive blood glucose monitoring from the recent five years, i.e., 2012–2016. After searching the databases for keywords (i.e., noninvasive blood glucose self-monitoring), about 2500 research articles were found but only a little over 300 were selected after screening their abstracts. Thorough full text screening of the related papers narrowed it down to 116 papers, and 84 papers were selected for discussion in the following sections.

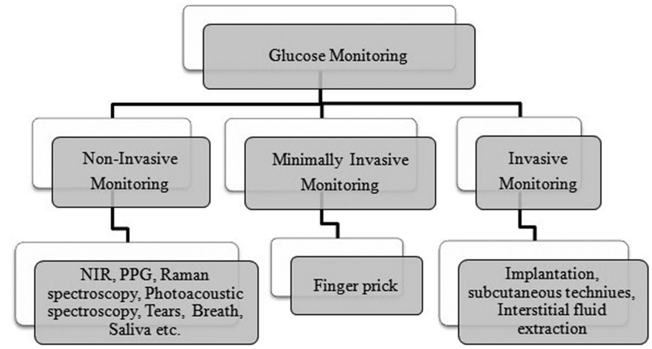

Fig. 2. Categories of glucose monitoring.

In this review, we categorize the noninvasive monitoring into nonsample- and sample-based techniques. Nonsample-based methods are grouped into optical and nonoptical techniques; sample-based techniques are grouped as intermittent and continuous monitoring methods. The advancements in the noninvasive/pain-free blood glucose monitoring are analyzed in the recent five years (2012–2016) based on cost effectiveness, portability, energy, and time efficiency of the methods along with a discussion on the devices available in the market for this task. With the advancement in technology, to develop robust systems for healthcare, the focus should be power/energy consumption, portability, response time, recalibration, cost, etc. Every research has different goals and to achieve those goals, tradeoffs need to be made. The users can select the systems according to their personal priority and requirements. This paper provides an overview of research in the healthcare monitoring domain using techniques from the computer sciences, biomedical, electrochemical, antenna propagation, and related fields.

The rest of this review is organized as follows. Section II discusses the noninvasive glucose monitoring devices. Sections III and IV analyze different nonsample- and sample-based techniques to monitor the blood glucose noninvasively, respectively. Section V sheds light on the major challenge and possible solutions. Section VI describes future prospects of the noninvasive blood glucose monitoring and Section VII concludes this paper.

II. NONINVASIVE GLUCOSE MONITORING DEVICES

As mentioned in Section I, the blood glucose monitoring techniques can be categorized as invasive, minimally invasive, and noninvasive, as shown in Fig. 2.

Invasive techniques can be painful at times and carry the risk of infections as they require sensors to be implanted subcutaneously or extraction of the interstitial fluids [34], [35]. The miniaturization and safety is very important to avoid severe injuries to the body [36]–[49].

Minimally invasive techniques require small blood samples to estimate the glucose concentration. They are more accurate than the noninvasive methods but can cause a little pain as a needle prick is required to take the sample, as shown in Fig. 3 [30], [50], [51]. Frequent testing can make the user uncomfortable and can result in poor management of diabetes [52]–[56].

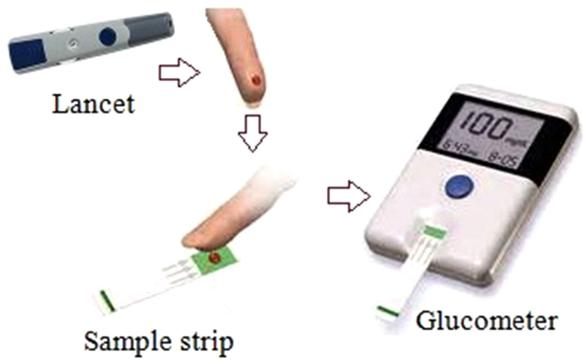

Fig. 3. Conventional blood glucose monitoring device.

Noninvasive techniques do not need any incision or implantation so they are pain-free and very convenient but less accurate, and there is a lag between the glucose levels in blood and other fluids, e.g., saliva, tears, etc. These methods often need to be calibrated for every individual.

Self-management tools help to calculate the glucose concentration over time, before and after food intake, etc., [9], [57]. These systems can also contain an insulin pump and insulin management modules for insulin infusion and management [58]. Most of the solutions available in the market are of invasive nature and use electrochemical biosensors to detect the glucose concentration in the blood sample.

During the past decade, developing noninvasive blood monitoring devices has been of great interest for researchers as well as medical equipment manufacturing companies. The accuracy of these devices plays an important role in calculating the insulin dosage, if the glucose level measured by the device deviates largely from the original glucose levels, the patient can end up taking a high dosage of insulin, which can be very harmful [59]–[62]. Some of the noninvasive blood glucose monitoring devices are discussed in this section and summarized later in Table II.

A. Nonsample Based: Optical Monitoring

Techniques that are not dependent on samples for estimating the glucose concentration, measure the concentration through the skin by utilizing light, electric current, electrocardiograph (ECG), etc., and are grouped as optical and nonoptical techniques based on the use of light.

Optical techniques use different wavelengths of light as the main component to measure the glucose concentration. It includes NIR spectroscopy, photoplethysmography (PPG), photoacoustic spectroscopy, etc. The optical techniques are cost effective and comfortable for the users but they are susceptible to the environmental conditions, e.g., temperature, pressure, skin hydration, humidity, etc.

1) TensorTip Combo Glucometer: TensorTip COG is one of the noninvasive tissue photography based CE certified glucose monitoring solutions. Users need to calibrate the device for a couple of weeks by using blood samples but after that the device can be used to monitor the glucose levels painlessly and conveniently by putting the finger inside the device, as shown in Fig. 4(a). The device has a smartphone interface and is also able to manage the history of glucose monitoring [63]. Calibration based on an individual's blood sample allows for personalization that offers more accuracy. The device is portable and uses rechargeable battery making the device a cost-effective solution. Rechargeable batteries can also come as a disadvantage as they have a self-discharge issue and recharging is time consuming.

2) Grove's Device: Grove Instruments designed a noninvasive glucose meter based on NIR spectroscopy that can measure the glucose concentration from the fingertip or earlobe within 20 s. The device is battery operated, portable, and accurate as it takes the readings from the blood on the capillary level instead of skin. Real-time estimation makes it a time-efficient solution, whereas the lack of individual-based calibration can affect the accuracy for certain users [64].

B. Nonsample Based: Nonoptical Monitoring

The nonoptical techniques use a small amount of current, electrocardiogram signals, microwave technology, etc., and are painless but are less portable and can be a little uncomfortable for the user.

1) Glucosense: Glucosense, based on photonic technology, is a noninvasive blood glucose monitoring device under development [65]. The device shown in Fig. 4(b) is claimed to be pain-free, easy to use, affordable, portable, and generates alerts for hypoglycemia. The user needs to touch the device to know about the glucose levels. The device consists of a silica glass that has ions sensitive to the infrared light and when the user touches the glass, the reflected spectrum changes according to the glucose concentration. The laser used to acquire the readings is low-powered that makes the device a power-efficient solution. The device takes about 30 s to estimate glucose levels, which makes it less time efficient as compared to other devices.

2) GlucoWise: GlucoWise is one of the devices based on radio wave technology that can be used for self-monitoring of the blood glucose levels noninvasively, i.e., without taking any blood samples for type 1 diabetics. The device provides intermittent monitoring by taking glucose readings from the area between the thumb and the forefinger, as shown in Fig. 4(c). The device measures glucose concentration on the capillary level, which makes it more accurate than the devices measuring glucose from the skin. It is claimed that the device is pain-free, cost efficient, convenient, and is compatible with smartphones and insulin pumps. The shape and the size of the device are also very efficient and the device also has bluetooth to transmit data and alerts [62], [66], [67].

The device is time efficient as it takes about 10 s to estimate the glucose concentration. The device is portable and easy to use so it can be used while driving, sleeping, exercising, etc. From the user's perspective, comfort, ease of use, cost, portability, and an above average accuracy are priorities. There might be harmful effects due to the use of localized energy but this can only be evaluated once the device is ready for the market after the clinical trial.

3) GlucoTrack: GlucoTrack merges the electromagnetic, ultrasound, and thermal technology to estimate blood glucose

TABLE II
SUMMARY OF NONINVASIVE BLOOD GLUCOSE DEVICES

Device	Company	Technique	Sample	Intermittent/ Continuous	Usage	Advantages/Characteristics
TensorTip Combo Glucometer	Cnoga Medical, Or Akiva, Israel	Tissue photography/ Photometric techniques	No sample	Intermittent	Fingertip	Painless, ease of use, Individual based calibration for high accuracy, PC and a Smartphone interface, rechargeable batteries, can manage history.
Groves's Device	Grove Instruments Inc., Worcester, MA, USA	NIR spectroscopy	No sample	Intermittent	Finger/earlobe	Portable, fast results, compact, battery operated
Glucosense	Glucosense Diagnostics Ltd., Buckinghamshire, UK	Photonics technology/ Fluorescence spectroscopy	No sample	Intermittent	Finger	Pain-free, compact, portable, ease of use, cost effective.
GlucoWise	MediWise, London, UK	Radio wave	No sample	Intermittent	Between forefinger and the thumb	Pain-free, compact, comfortable, cost effective, time efficient, increased penetration, Bluetooth to transmit data or alerts, compatibility with insulin pumps.
GlucoTrack	Integrity Applications, Ashdod, Israel	Electromagnetic, ultrasound and thermal technology	No sample	Intermittent	Earlobe	Pain-free, No frequent calibration, cost effective, comfortable, earlobe has very little fat and a lot of capillary vessels.
iQuickIt Saliva Analyzer	Quick LLC, Farmington, CT, USA	Salivary analysis	Sample	Intermittent	Mouth saliva	Pain-free, ease of use, portability.
Smart contact lens	Novartis, Basel, Switzerland & Google, Mountain View, CA, USA	Tear analysis	Sample	Continuous	Eye	Low power, comfortable, pain-free.
NovioSense	Noviosense, Nijmegen, Netherlands	Tear analysis	Sample	Continuous	Lower eye lid	Painless, wireless power, smartphone compatibility, compact, flexible/bendable.


(a) (b) (c) (d) (e) (f) (g)

Fig. 4. Noninvasive blood glucose monitoring devices: (a) TensorTip combo glucometer. (b) Glucosense. (c) GlucoWise. (d) GlucoTrack. (e) iQuickIt saliva analyzer. (f) Smart contact lens. (g) Noviosense.

levels measuring at the earlobe. The device is claimed to be painless, cost effective, comfortable and does not need frequent calibrations. Using the earlobe as the measuring site helps with the accuracy of the device as there are no bones and less fat in the earlobe. The device has two main components, an ear clip that measures the blood glucose from the earlobe and the main unit is where the results are displayed, as shown in Fig. 4(d) [68]–[70]. GlucoTrack received U.S. Food and Drug Administration (FDA) approval and a final CE mark in 2015 and 2014, respectively. Using three different techniques to measure glucose levels can improve the accuracy but make the device processing complex, resulting less power and a less time-efficient solution.

C. Sample Based: Intermittent Monitoring

Sample-based devices are dependent on fluid samples, e.g., saliva, tears, breath, etc., for glucose concentration estimation. These methods are accurate, convenient, portable, etc., but there is a lag between the change in glucose concentration in blood and other fluids. Sample-based devices are grouped into intermittent and continuous monitoring devices based on the frequency of the vitals information acquisition and monitoring.

Intermittent monitoring is when the samples are acquired periodically to estimate the glucose concentration. It is a cost-effective method for patients having rather stable glucose levels but the abnormal changes in the vitals in between the monitoring cannot be predicted/detected. Every single measurement requires a new sample.

1) iQuickIt Saliva Analyzer: iQuickIt Saliva analysis is under development and uses saliva samples instead of blood samples to measure glucose levels [71]. It uses disposable draw wick sticks for the samples and can transmit the readings to other smart devices. It is claimed that the device measures glucose levels painlessly and accurately and that it is easy to use. The device is shown in Fig. 4(e). Since the device is still under clinical trials, nothing can be said for sure but it has been designed to provide the results in real time making the device time efficient. The information regarding the processing or power consumption aspect has not been discussed yet. More can be known after the clinical trials and FDA's approval, when the device is available in the market.

D. Sample Based: Continuous Monitoring

In continuous monitoring, the vitals are monitored regularly, which is a better fit for patients having a history of severe hypo- or hyperglycemia, i.e., unstable glucose levels. This kind of monitoring can help in predicting and avoiding severe hypo- or hyperglycemia episodes but it can be a little expensive and a little uncomfortable in some cases.

1) Contact Lens: Smart contact lens shown in Fig. 4(f) uses tears to monitor the glucose concentration. It consists of a wireless transmitter to send glucose readings and uses a static electrical charge for power [72], [73]. It provides continuous monitoring of glucose levels, is portable, low power, easy to use, etc., but can make the user uncomfortable and overheat causing possible damage to the eye. The device/product is under development, proper analysis will be possible after the clinical trials, FDA's approval and availability in the market.

2) Noviosense: Noviosence, a device under development, uses tears to measure the glucose levels using electrochemical means [74]. The device is a 2 cm long and flexible spring, as shown in Fig. 4(g). The device is claimed to have a wireless module to transmit data and to power the device. The sensor is low power, painless, portable, sensitive, etc., but can cause a little discomfort for the users since eyes are a sensitive part of the body.

III. Noninvasive Nonsample Based Glucose Monitoring

Noninvasive techniques are pain-free, convenient, and no incision or injury needed but they are not as accurate as the conventional invasive techniques. The ubiquitous use of computer sciences in healthcare gives birth to designing noninvasive methods for basic vital monitoring such as heart rate, blood pressure, and blood glucose [75]–[78]. Computer science and data processing have played a vital role in medicine and healthcare inventions by helping in diagnosis improvement, disease prediction, etc., [79], [80].

Several techniques have been used over the years to measure/monitor the blood glucose noninvasively. We have categorized these techniques into sample- and nonsample-based glucose monitoring. The nonsample-based methods are further grouped into optical and nonoptical monitoring. Fig. 5 describes the general flow of nonsample-based optical monitoring systems, whereas Fig. 6 describes a state-of-the-art system model for nonsample-based optical monitoring.

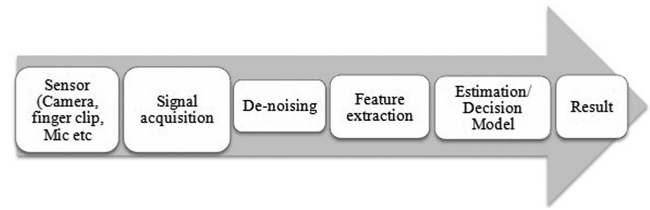

Fig. 5. Nonsample-based optical monitoring system general flow.

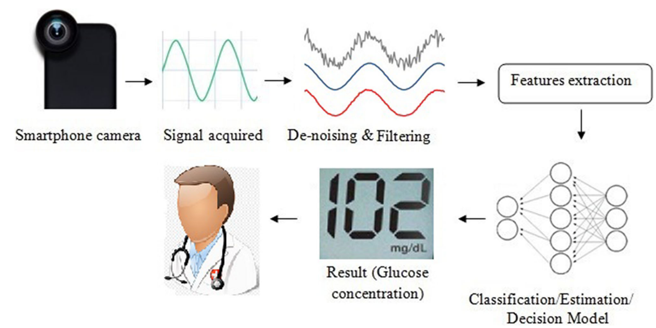

Fig. 6. Generic state-of-the-art noninvasive blood glucose monitoring system model.

Nonsample-based monitoring techniques utilize light, current, etc., instead of fluid samples to measure the glucose concentration.

A. Optical Monitoring

The methods based on light as the main component to estimate are known as optical methods. Table III summarizes the optical techniques for glucose monitoring.

1) NIR Spectroscopy: NIR spectroscopy is one of the most widely used noninvasive techniques in which the spectrum from the part of the body is acquired when light from the NIR range falls on it. This technique is simple and harmless but factors such as thickness of the skin, fatty tissues, blood altering illness, medication, and thermal properties of the skin affect the accuracy/performance by affecting the light absorbance.

In [81], Dantu *et al.* propose an NIR spectroscopy based blood glucose monitoring system using a smartphone. The data were acquired by capturing the laser light transmitted by the fingertip with a smartphone camera. The transmitted light intensity was found to be inversely proportional to the glucose concentration as more light is absorbed with higher glucose concentration. An application was developed to extract the intensity of red-green-blue (RGB) pixels from every frame. The concentration of glucose is determined by using the blue and green component intensities in the modified Beer–Lambert law and it was found that the glucose concentration measured by the smartphone is linearly proportional to the actual glucose concentration. The experiments were performed with both the glucose solution and then blood. The glucose levels were examined 15 and 45 min after drinking cola. The application utilizes android platform and is sensitive but needs a powerful processor in order to avoid slowing down other applications. The experiment results were calculated using MATLAB. The overall solution proposed is

TABLE III
SUMMARY OF OPTICAL NONINVASIVE TECHNIQUES FOR BLOOD GLUCOSE MONITORING

Ref.	Year	Technique	Equipment/site	Advantages	Disadvantages	Purpose
[84]	2015	PPG, NIR, ANN	Finger clip with an LED and a photo-diaode	Cost effective, FPGA helps in making hardware implementation fast.	Adaptive filters need to be applied which adds to the processing, FPGA ANN are challenging, PPG is susceptible to noise.	Blood glucose sensing
[81]	2014	NIR spectroscopy	Laser, HTC X Smart-phone	Cost effective, portable, easy to use, can be used frequently because it is convenient, sensitive to changes, easy calibration	A lot of factors e.g. medication etc. can affect the absorption of light and in turn the results.	Blood glucose monitoring
[85]	2012	PPG, NIR spectroscopy	Modified pulse oximeter	Pain-free, frequent monitoring, no chance of infections, no contact with pointed objects	It is dependent on the environment, also the angle of the incident light.	Glucose measurement
[28]	2014	NIR, LSSVM	Optical fiber probe, Human tongue, NIR Quest512 Spectrometer, tungsten halogen lamp	High vascularity, fatty tissues are less, the tongue has no skin so no thickness issues Environmental conditions affect the acquisition.	Susceptible to noise	Blood glucose concentration and diabetes identification
[87]	2016	NIR and MEMS technology, photoacoustic spectroscopy, Regression model	NIR sensor, MEMS sensor, Ear lobe	Pain-free, comfortable, less interference in the data, Calibration approach, using the two technologies together make it more accurate and sensitive, compact size, power efficient, earlobe skin is not very thick so deep penetration also no bones.	Environment e.g. temperature, humidity, pressure etc. dependent, performance is surface and surface area dependent.	Blood glucose monitoring system
[34]	2016	Skin oxygen saturation and partial oxygen pressure	CCD camera, thermal camera	Pain-free, oxygen distribution image	Light conditions affect	Glucose evaluation
[88]	2015	Photoacoustic, optical and thermal spectroscopy	Laser diode, Mic	Reliable, pain-free, improved sensitivity, compact size	Temperature and pressure dependent	Glucose monitoring
[89]	2015	Photoacoustic spectroscopy, NIR	Pulsed laser diodes, piezoelectric transducer	Painless, Sensitive, harmless, less optical scattering	Absorption behavior can be non-uniform	Glucose measurement
[82]	2015	NIR spectroscopy	Laser, spectroscope, thermal sensors	Pain-free, user friendly, cost effective	Not very accurate due to the limited data	Glucose concentration measurement
[90]	2015	Optical coherence tomography	Not clearly mentioned/Light source, coupler, interferometer	High resolution images, deep penetration and better SNR.	Trade-off between the depth and the transverse resolution, temperature and pressure dependent	Blood glucose monitoring

cost effective but highly dependent on light conditions and different skin area exposure for every user. The performance can also be affected if the user is suffering from other chronic illnesses.

In [28], NIR spectra were acquired using the fiber probe on the tongue and after the denoising and reconstruction of the spectra, least square support vector machine (LSSVM) was used to build the calibration and the prediction model for the diabetes classification with a reasonable accuracy. Nonlinear calibration models are designed for better accuracy and LSSVM is utilized because of its capability in nonlinear models. The diabetes classification model was found to yield better results than the glucose concentration estimation. For the experimental setup, the probe was used on user's tongue and the reflected signals were collected from the tip of the tongue. Acquiring data from the tongue rules out the difference in user's skin thickness, the fats, and offers a high signal-to-noise ratio (SNR). The environmental conditions, e.g., pressure, temperature, humidity, etc., can affect the system performance.

Light beam with a wavelength of 1310 nm has been used in [82] to detect the glucose concentration in aqueous solution. The light beam was split into two beams, one beam was passed through the solution, whereas the other was captured directly. Absorbance and optical distance changes the transmitted light intensity. The measurement is done by deriving a relationship between the power outputs of the light beams against different glucose concentrations in the solution. The power output was found to be inversely proportional to the glucose concentration. Thickness of the skin and fatty tissues can also affect the transmittance of light. The experiment was conducted on aqueous solutions with different concentrations of glucose. The proposed method is energy consuming, not portable, or accurate enough and testing on real blood is necessary to prove the effectiveness of the system.

PPG is used to measure the flow of blood volume in a certain part of the body. Light falls on the surface of the body part and a portion of that light is absorbed by the blood and the other portion is reflected back or traversed through the body part and represents the volume of blood, i.e., it can be used to acquire the PPG signal. The PPG is cost effective, painless, and convenient [83]. This data can be termed as BigData if the data are gathered from a large number of subjects for a long period of time.

In [84], transmission PPG acquired by an LED and a photodiode embedded finger clip was used to estimate the blood glucose levels based on difference in optical intensity. The PPG waveform reflects the cardiac cycles and according to the authors, the transmittance of light is inversely proportional to the glucose concentration in the blood. The acquired signals were converted to electrical signals, filtered for noise removal using a series of filter, e.g., a high-pass filter, amplifier, and a fourth-order low-pass filter to finally get the PPG signal. The PPG signal was then filtered using an adaptive ADALINE neural network filter to remove motion artifacts. An invasive glucometer was used to collect the actual glucose levels of the subjects, which were used along with the filtered PPG signals to predict the glucose levels using artificial neural networks for field programmable gate arrays (FPGA). The data were collected from 50 individuals for 3 different wavelengths. The model was trained and tested using MATLAB toolbox for neural networks and the accuracy in the estimation was found to be 95.38%. Fatty tissues and motion artifacts can affect the system performance. The signal acquisition is simple, portable, and convenient but the processing is complex and time consuming besides adding processing load.

Paul *et al.* [85] discuss transmission PPG based blood glucose monitoring system that uses a modified pulse oximeter to acquire the PPG signals. According to the authors, with an increase in the glucose concentration, the absorbance of the light in the blood decreases. The acquired signals were in the form of photo current, which was converted to measurable voltage values before being filtered. The filtered signals then use labVIEW for processing and the ac component of the PPG has been used to estimate the glucose levels. The experiments were performed on five individuals before and 2 h after the food intake. The results were validated by comparing with the glucose measurements of an invasive glucometer. The proposed method requires proper equipment to acquire the PPG signals, which makes the simple and convenient acquisition method costly and less portable. The signals need to be transferred to a computer for further processing that makes it time consuming.

When light falls on the skin, a part of it is absorbed and the remaining portion is reflected and can be used to measure the oxygen saturation level by taking the difference of oxyhemoglobin and deoxyhemoglobin. Glucose concentration and the oxygen saturation are linearly dependent and inversely proportional to each other, i.e., the more the calculated oxygen saturation, the less the glucose concentration. NIR light is used to measure the skin oxygen saturation in [34] as the wavelength of the light affects the penetration depth, the lower the wavelength, the further it goes and the better results are yielded. The data are acquired in the form of skin tissue images and the temperature distribution on the skin and transferred to a computer for further processing. The environmental conditions, e.g., temperature, humidity, etc., can affect the data acquisition process and hence the system performance. The relation between the oxygen saturation level of the skin and the glucose concentration in the blood is derived and applied on the acquired data to estimate the glucose levels of subjects from different age groups and genders. The experiments were performed to examine the fluctuations in the glucose concentrations before and after meal. The equipment required for data collection makes it less portable and costly. The processing is simple but the procedure is a little time consuming since the data needs to be transferred to a computer and then processed.

2) Photo Acoustic Spectroscopy: The change in the media/medium pressure caused by the ultrasonic/sound waves can be used to measure the blood glucose concentration with high sensitivity and is known as the photo acoustic spectroscopy [86], [87]. It can be combined with other techniques such as NIR spectroscopy to yield better results. In [88], the photoacoustic signals were obtained after optical to thermal conversion of the incident light. Glucose concentration in aqueous solution was estimated based on the change in optical absorption coefficient and the change in pressure. The photoacoustic signal samples were acquired using a 1550-nm laser light and a microphone in a photoacoustic cell. Photoacoustic signals for different glucose concentration were collected and a linear relationship was found between these signals and the glucose concentration. The signal acquisition process is independent of light scattering in tissues but sensitive to pressure and temperature variations. The overall procedure is costly in terms of energy and time.

In [89], the sensor uses the measured change in the pressure of the body part, i.e., finger, earlobe, etc., caused by the sound waves generated by them. Two pulsed laser diodes and piezoelectric transducer were used to gather the photoacoustic signals. It was found that the higher the glucose concentration, the stronger the response photoacoustic signals. The signals were amplified, averaged to improve SNR and reduce noise before transferring to a computer for further processing. Features were extracted from the signals and the glucose concentration was estimated by the photoacoustic amplitude. Regression analyses were used for calibration and the system was validated by an invasive glucose meter. The solution lacks time and energy efficiency and also the temperature and pressure can affect the performance along with nonuniform absorbance.

3) Optical Coherence Tomography (OCT): In OCT, high resolution optical imaging using the reflected or the scattered light is utilized. It is quite similar to the ultrasound technique where sound is used instead of light. Microscopic characteristics can be examined and analyzed noninvasively using OCT. In [90], the glucose concentration is estimated by acquiring two-dimensional OCT images using an interferometer. The correlation coefficient between the OCT and the skin depth is optimized on the basis of the tissue scattering coefficient. The relation between the OCT slope and the blood glucose concentration is utilized to estimate the glucose concentration. The calibration of the OCT noninvasive system is done by using the invasive techniques to measure blood glucose level. The technique is temperature- and pressure-dependent, i.e., the environmental conditions can affect the performance. The calculation for estimating the glucose concentration is time consuming and the process assumes there are no other affecting parameters.

B. Nonoptical Monitoring

The techniques that are not dependent on light are called the nonoptical techniques. Table IV summarizes the nonoptical techniques for glucose monitoring.

1) ECG Signals: ECG signals are used to monitor the working of one's heart and any abnormalities in the functioning of the

TABLE IV
SUMMARY OF NONINVASIVE NONOPTICAL TECHNIQUES FOR BLOOD GLUCOSE MONITORING

Ref.	Year	Technique	Equipment/site	Advantages	Disadvantages	Purpose
[23]	2014	ECG, ANN	Compumedics ECG device	Pain-free, no need for frequent calibration	No portability, accuracy is not good, too many input parameters makes it complex and put a load on the processor	Hyperglycemia detection
[91]	2016	ECG, ELM (extreme machine learning)	ECG	Fast convergence and scalable computations	The ECG parameters used for estimation can be affected by any other heart conditions.	Hypoglycemia monitoring
[92]	2012	Reverse Iontophoresis	Forearm, skin-gel electrodes	High sensitivity, use of potassium improved the correlation	Use of electric current can be uncomfortable for certain individuals, analyte correlation dependant, frequent calibration is required, not accurate enough for clinical use	Glucose measurement
[93]	2016	Microwave technology	Microwave sensor (microstrip ring patch antenna)	Compact, cost effective, painless, more accurate because it uses resonant method	They can be affected by the environmental conditions.	Measurement of the dielectric properties of the aqueous glucose
[94]	2016	Microwave technology	Microwave sensor (microstrip spiral patch antenna)	Compact, cost effective, pain-free, high quality	Atmospheric conditions can introduce noise	Blood glucose monitoring
[95]	2016	Microwave technology	microstrip two faced patch antenna	high penetration, high sensitivity, ease of use	VNA effects the miniaturization of the system also the convenience, Atmospheric conditions affects the working.	Glucose sensing
[62]	2016	Millimeter wave/Antenna	Glucowise (2 sensor patch antennas)	Painless, convenient, portability, less interference.	Localized energy can cause harmful effects	Glucose sensing
[96]	2016	Wireless technology	Wearable wireless sensor	User friendly, portable, pain-free, high accuracy, low power consumption, cost effective	Wireless technology is prone to the interference	Blood glucose measurement
[97]	2015	Microwave	Microstrip triangular patch antenna	Affordable, small size, linearity	Low power handling	Glucose measurement
[98]	2014	Dielectric spectroscopy/ Microwave technology	Patch resonator	Small size, high sensitivity	High error rate on higher frequencies	Monitoring of blood glucose levels
[99]	2012	Optical, Dielectric spectroscopy	Optical, temperature, humidity, movement, dielectric sensor, upper right arm	No physiological and environmental perturbation problems due to unfavorable conditions	Results are not yet comparable to the enzymatic needle sensors	Continuous glucose monitoring
[100]	2014	Antenna, Cole-Cole model	Antenna, network analyzer, wrist	accurate calibration model	Environmental conditions can affect the results, individual based calibration is needed	Blood glucose level estimation

heart are reflected on the ECG signals. An ECG signal happens to paint a good picture about high and low glucose levels so it can be used to check one's blood glucose levels [23].

Nquyen *et al.* in [23] uses 16 parameters from the ECG signal and ANN to detect hyperglycemia/normoglycemia events, i.e., if the glucose level is greater than 150 mg/dl, it is hyperglycemia and if it falls between 60–150 mg/dl, it is a normoglycemia event. Among the 16 parameters, 5 ECG intervals, e.g., heart rate, QT interval, etc., are utilized as main variables. The ECG data are acquired using the Compumedics device, the extracted parameters are fed into an ANN and the output of the model indicates normo- or hyperstate. The experiments were performed on ten individuals (T1) and a geometric mean accuracy of 67.94% was obtained. In [91], EML is used with ECG signals to detect hypoglycemia and hyperglycemia. EML has a fast learning property that makes the system time efficient and its ability to deal with the problem of overfitting makes it a better fit solution. Heart rate and QT interval are the main variables used in the proposed model as hyperglycemia causes the heart rate and QT internval to increase. The experiments were performed for 10 h overnight on 16 children (T1) with a 70% sensitivity in results. Using ECG is pain-free but any kind of heart condition, e.g., arrhythmia, etc., and the medications will affect ECG signals and that might end up affecting the accuracy of the measured glucose concentration.

2) Reverse Iontophoresis: Reverse iontophoresis is when a small current is applied to the skin, the glucose molecules move closer toward the skin and makes it easier to measure the glucose concentration [101].

In [92], two skin-gel electrodes are used with a small current by constantly reversing the polarity and the glucose concentration in the gel is measured using standard glucose monitoring devices such as Gluco Pap. The accuracy of the technique is greatly dependent on the calibration and the correlation between the glucose level of the blood and the extracted analyte. The technique is quite close as to taking a blood sample with-

TABLE V
SUMMARY OF SAMPLE-BASED NONINVASIVE TECHNIQUES FOR BLOOD GLUCOSE MONITORING

Ref.	Year	Technique	Equipment/site	Advantages	Disadvantages	Purpose
[19]	2015	Salivary analysis	On-chip Saliva biosensor	Sensitivity, pain-free, convenient, fast.	Saliva viscosity is affected by environment, the correlation can vary for different persons.	continuous salivary glucose monitoring
[106]	2012	Breath analysis, regression analysis (SVOR-support vector ordinal regression)	12 metal-oxide semiconducting sensors, e-nose	Independent of environmental conditions (temperature, humidity etc.), low cost sensors	The setup is complex and can be performed in a laboratory with specific equipment	Blood glucose monitoring
[102]	2015	Salivary analysis	Optical biosensor, paper strip	Cost effective, affordable	Not sensitive to low glucose levels, prone to interference	Glucose sensing
[103]	2015	Salivary and tear analysis	Biosensor	Painless, high sensitivity	More sample volume is needed for better signals, complicated process to remove proteins from the samples	Glucose detection
[104]	2015	Saliva Analysis	Disposable biosensor	Painless, simple, high accuracy, sensitive, ease of use, cost effective	Prone to motion artifacts, possibility of data noise	Glucose sensing
[105]	2015	Salivary analysis	Cavitous sensors	Pain-free, continuous, wireless module for telemetry, customized mouth piece	Can be a little uncomfortable to use	Glucose monitoring
[109]	2012	Tear analysis	Contact lens, Glucose sensor, wireless transmitter	High sensitivity, reduced chances of infection, time efficient	Increase in eye temperature, visionary issues, harmful effects of the equipment on the eye	Tear glucose monitoring
[107]	2014	Breath analysis	E-nose	Improved accuracy, convenient, pain-free	Not fit for clinical use	Blood glucose prediction
[108]	2014	Breath analysis	E-nose	Individual based prediction model, takes into account the humidity and alveolar air, cost effective, portable	The prediction model is not accurate enough for practical use.	Diabetes screening and blood glucose level prediction

out actually drawing any blood, which makes it pain-free and convenient. The limitation being the longer the process takes, the chances of getting skin burns due to the current gets higher. Also the current level is kept too small to be bearable for the skin, which limits the accuracy.

3) Microwave/Antenna: Resonance frequency can be used to estimate the blood permittivity, which can be used to measure the blood glucose levels. A microstrip patch antenna can be used to measure the blood glucose levels based on the frequency shift. When microwaves falls on a part of the body, a part of them is absorbed/transmitted and the other part is reflected. Any of the part can be used to study the details about the part of the body, e.g., the glucose concentration, etc. In [97], a microwave antenna is designed to estimate glucose concentration. A finger is placed on the patch of the antenna and the change in the resonance frequency is measured. Ansoft HFSS (Pittsburgh, PA, USA) is used to simulate the antennas [98]. The operating frequency and the shape of the antenna patch can be different, e.g., a ring [93], a spiral [94], rectangular [95], and triangular [97]. In [100], an antenna was used for real-time estimation of blood glucose levels noninvasively. A shunt capacitor circuit was utilized to track the change in glucose concentration using the Cole–Cole model. An antenna and a network analyzer were utilized to collect readings from the wrist of an individual every 15 s. The difference in resonant frequency for both the diabetic and nondiabetic individuals was measured over time after food intake. It was found that individual-based calibrations are required for blood glucose estimation. A calibration technique based on the shift in resonant frequency was proposed. The results were validated by comparing to the results of a standard glucometer and Clarke grid analysis. The results yielded proved to be in good correlation with the results of a glucometer. The environmental conditions, e.g., temperature, sweat, and blood pressure can introduce noise and affect the performance of the antennas.

4) Miscellaneous: Different sensors can be used to measure the glucose concentration in the blood noninvasively by processing the light reflected by the skin. The wavelength of the source light varies, i.e., infrared, fluorescence, or ultrasound and so the penetration depth of the light. The relation between the measured reflected light and the actual glucose levels is different for different individuals because of different body structures and conditions. Accurate mathematical relations can be derived between the two using differential equations to have an accurate estimation of the blood glucose concentration [96]. The skin and tissue dielectric properties change due to physiological factors such as variations in blood glucose and temperature. A combination of optical, humidity, temperature, and dielectric sensors was used to estimate blood glucose levels. Identification models using variety of techniques such as least absolute shrinkage and selection operator (LASSO) were utilized for linear regression. The data were acquired in 150 channels from the upper right arm of 6 T1DM subjects. The data were preprocessed, the first 75 min recording was removed and the signals were filtered to remove spikes. It was found that though the accuracy is not yet comparable to the currently used enzymatic technique, the LASSO method improves the glucose concentration estimation accuracy of the multisensor [99].

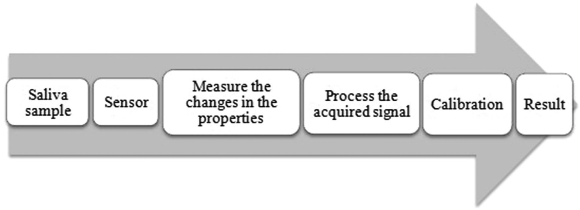

Fig. 7. Sample-based monitoring system general flow.

IV. Noninvasive Sample Based Glucose Monitoring

There are techniques that require a sample, e.g., saliva, tears, urine, breath, etc., to estimate the glucose concentration in the blood and are termed as sample-based techniques. Sample-based glucose monitoring is further categorized as intermittent and continuous monitoring. Table V summarizes the sample-based techniques for glucose monitoring, whereas Fig. 7 describes the general flow of sample-based monitoring systems.

A. Intermittent Monitoring

If the samples are taken to measure the glucose concentration periodically over the time, it is called as intermittent monitoring. Intermittent monitoring is cost effective and is a better fit for the patients in a stable condition.

1) Salivary Analysis: The biochemical markers found in saliva are believed to represent the human body as well as a mirror. Using saliva for diagnostic or monitoring purposes has a lot of advantages such as convenience, cost effectiveness, accuracy, sensitivity, and portability, but the correlation varies for every individual, the saliva viscosity is affected by the environment, also there is lag in the glucose concentration changes between the blood and the saliva [19], [102]–[104]. In [19], a disposable biosensor for measuring the saliva glucose levels is proposed that can act as a standalone electrochemical device for glucose monitoring. The saliva sample is taken and amperometric measurements are carried out to measure the glucose level. Though the clinical trials were carried out accurately, the sample acquisition procedure is a bit complex and time consuming. The overall procedure is costly, energy consuming, and will take about 90 s to measure the glucose concentration. The work in[102] uses a scanner to record the color changes in a filter paper when the saliva is placed on it. The glucose concentration is calculated by analyzing the RGB components of the scanned paper strip. The whole procedure takes atleast 50 s, 3–5 s for sample acquisition and then color scanning after 45 s, i.e., the sensor's response time. Among the three colors, the blue color was found to be the most sensitive. The process is convenient for the user and simpler as compared to the centrifugation process but it is time consuming and requires proper equipment to estimate the glucose concentration, which affects the energy consumption and portability of the process.

Arakawa *et al.* [105] utilize sensitive cavitous sensors with a customized mouthpiece to measure the salivary glucose concentration. The glucose concentration is estimated by amperometric measurements with an interval of 180 s. The mouthpiece also includes an embedded wireless module to a setup for telemedicine. The use of microelectromechanical systems (MEMS) technology in the proposed system offers portability, telemetry, and reduced power consumption but it is time consuming and the mouthpiece can be a little inconvenient for the users. In [104], Zhang *et al.* propose a glucose monitoring system that uses a disposable glucose sensor and amperometric measurements at an interval of 18, 20, and 21 s. Different sizes of the sensor were compared with respect to the sensitivity. The correlation found in the fasting state seems quite promising. It is claimed that the proposed glucose sensor is cost effective, easy to use, and has a high accuracy and sensitivity but is prone to motion artifacts and the complex process is time consuming as well as affects the portability.

2) Breath Analysis: The amount of acetone in one's breath is directly proportional to the blood glucose concentration, which means breath analysis can be used to estimate blood glucose levels [106]. The change in the conductivity of a set of sensors sensitive to different components/elements in the breath can be used for signal acquisition. The data are labeled with four levels according to the glucose concentration. The same data signals were processed using support vector machine and sparse-representation-based classification to compare the performance and accuracy of SVOR. SVOR was found to be the most accurate among the three. The sample acquisition method used is fast, simple, and relatively low in cost as compared to the alternate/conventional method but transmitting data first to a computer for further processing is very time consuming. The processing algorithm is better suited for such classification but it does not work very well with the dataset outliers and is a bit complicated as compared to alternate machine learning algorithms; thus, consume more resources [106]. In [107], ten sensors are used to acquire the breath samples, which are then digitized and processed. Local and global regression models have been fused together to improve the accuracy of the prediction and to reduce the variant interference caused by individuals but the system is still not fit for clinical use. The data acquisition is convenient but the process is time consuming since the signals are extracted from the samples and are then transferred to a computer to further process for estimating glucose concentration. In [108], Yan and Zhang utilized e-nose to acquire the breath samples and designs the individual-based prediction models for blood glucose monitoring since the correlation between the blood glucose and the breath components can be different for different individuals. The authors claim that using the individual-based design makes the prediction more accurate but the procedure is a bit complex and time consuming since it requires the samples to be collected and then converted to signals to be able to be used for prediction models. The prediction models still need improvements to be able to use for practical use.

3) Tear Analysis: Tears can be used to measure the blood glucose concentration as they have prominent biomarkers same as in the blood. In [103], both saliva and onion induced tears are used to estimate the blood glucose levels by centrifugation process. The results from the tear samples were found to be more accurate as compared to the saliva samples. The proposed method uses a complicated procedure to remove proteins from the collected samples also the volume of the samples were found to be directly proportional to the accuracy of the proposed method. The procedure to get to the final results is time consuming and complex.

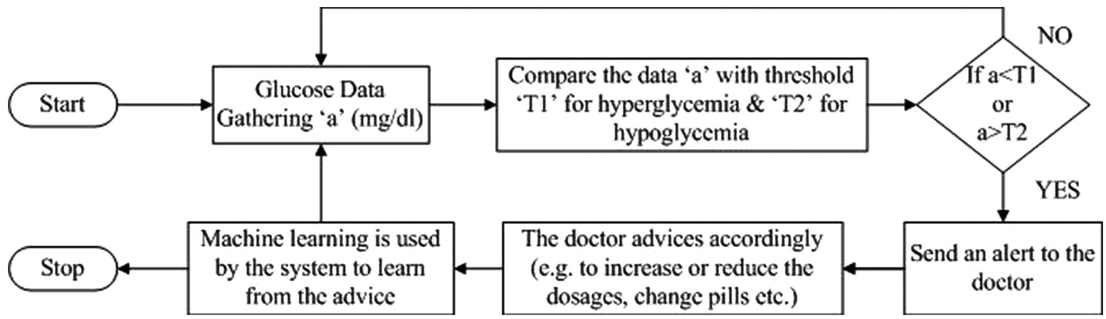

Fig. 8. State-of-the-art AI-based blood glucose monitoring system.

B. Continuous Monitoring

If the samples are collected to estimate the vitals round the clock, it is termed as continuous monitoring. For the patients having unstable vitals, continuous monitoring is more suitable to predict hyper- or hypoglycemia episodes.

1) Tear Analysis: In [109], Liao *et al.* propose a tear analysis based continuous glucose monitoring system. The glucose sensor mounted contact lens has been used to get the tear samples and a wireless transmitter on the lens is then used to transfer the information to a reader wirelessly connected to the lens. The glucose levels are estimated in real time making the proposed system time efficient. The lens are designed in a way that the mounted modules do not get in the way of vision and utilize RF power. The time to get the results was found to be about 35 s while testing the proposed contact lens. The solution presented is portable, time efficient, and can provide a better control on glucose levels but the temperature increase because of the equipment can have harmful effects on the eye.

V. Major Challenge and Possible Solutions

To provide convenient and pain-free blood glucose monitoring, noninvasive blood glucose monitoring systems are being designed, most of which are based on optically acquired signals. The accuracy of existing noninvasive glucose monitoring systems has been a great challenge for developers and researchers but is still far less than that of the invasive systems, which makes them not fit for clinical and patient use [110].

Individual-based calibration helps in improving the accuracy of such systems limiting the number of users to one as the user is required to calibrate the device once and later provides accurate results for that specific user.

In order to develop accurate systems without the need for individual-based calibration, a larger dataset and a larger feature set is required so that the data from a large number of individuals can be studied to train a vast variety of parameters.

The mathematical models used for signal analysis sometimes fail to develop precise relation between the acquired input signal and the variations in blood glucose levels [111]. Choosing better data acquisition (procedure and equipment), noise canceling, signal processing, and analysis systems will also help develop an accurate noninvasive blood glucose monitoring system.

VI. Future Prospects

The rapid increase in the number of diabetics gave birth to the need to develop reliable noninvasive self-monitoring solutions. The ultimate target of all the research being done in the field of glucose monitoring is to develop tools beneficial for diabetes patients. The monitoring systems need to utilize the concepts of artificial intelligence (AI) and expert systems to develop state-of-the-art monitoring systems, as shown in Fig. 8.

Since the main focus of this manuscript is to discuss the glucose level estimation so we will mainly talk about the glucometers being designed for self-monitoring the blood glucose concentration. Accuracy of a glucometer is very important as the dosage of the insulin is dependent on the results acquired from the glucometer. An overdose of insulin can be very harmful for the patients and can cause an increase in the heart rate, seizures, unconsciousness, etc. A good glucometer is the one that meets the maximum allowed error standards set by International Organization for Standardization and possess all or most of the following features/qualities.

A. Affordability

The self-monitoring tools should be cost effective in order for everyone to be able to benefit from them. The invasive solutions available in the market these days can be a bit costly since they need a one-time use test strip every time they use the glucose meter to measure glucose concentration. The strips are expensive and make it an expensive solution. Noninvasive solutions that have a low cost of operation and low total cost of ownership need to be designed for all kinds of target customers. More research needs to be done to be able to use devices such as smartphones as a glucometer, which will save the cost of buying a dedicated device for monitoring blood glucose.

B. Time Efficient

The doctors advise the patients to check their vitals (glucose levels) about four to five times a day. If the glucose meter has more delay to display the results, it discourages the patients to measure the glucose concentration frequently as it wastes time and is inconvenient. So one of the most important qualities a glucose meter should have is that it should take the least possible time for processing and displaying the results. The least delay offered by noninvasive devices discussed in earlier sections is about 10 s. Future research should focus on reducing this delay up to maximum 3–5 s.

C. Portability

Portability is another important feature; the users should be able to use the devices anywhere anytime. The devices should be small sized and convenient to carry around. If the functionality of a glucometer is embedded into smartphones, the solutions will become portable besides being cost effective.

D. Power Efficient

With portability comes the need for power efficiency. If the system consumes less power and has convenient recharge options, it adds to the portability. Usually for making the systems more time efficient, more resources are utilized that end up consuming more power making the solution, less power efficient. Sometimes a tradeoff is needed between time and power. Systems that are adaptive to the user requirements are needed to be investigated in future research in order to tradeoff between time and power according to user preference or the circumstances.

E. Recalibration

The devices need to be recalibrated in order to perform accurately over time for different individuals. Frequent recalibrations are painful as they require invasive methods. The purpose of choosing noninvasive methods is to avoid pain and risk of infection, so the recalibrations should be kept to longest possible period of time. The devices having individual calibrations seem to perform better and they do not require frequent recalibrations. Future research should focus on developing noninvasive solutions that do not require recalibration or the least possible recalibration.

Secondary features to enhance the functionality, efficiency, and user experience that need to be focused on are usability, safety, record storage, and history management, record/data transfer to computer, verbal instructions, etc. Multifunctional solutions are required and components interoperability is a must in order to provide users with these features. The proposed solutions need to be evaluated on the basis of user satisfaction. Large-scale clinical evaluations need to be carried out and more feasible error models are needed to be designed.

For serious/unstable cases, there should be solutions available, e.g., to detect the level of waste materials/products built up so they can know when an emergency dialysis is needed, etc. Methods for early detection of organ failure due to diabetes are also needed to be investigated in depth in future research.

VII. Conclusion

Portable, time efficient, compact, cost-effective, accurate, easy to use, and power-efficient methods to monitor blood glucose levels are needed in order to keep diabetes in control. Besides having the aforementioned qualities, if the technique is also comfortable and pain-free, it will be very convenient for the users to manage their glucose levels. Moreover, factors such as blood altering illnesses, medication, and dehydration should be kept in consideration while designing noninvasive models. Much research is being done in the field of medicine in collaboration with several other fields such as computer sciences, biology, chemistry, physics, and electrical engineering over recent years to develop more reliable and stable implantable sensors for invasive monitoring. Minimally invasive techniques with reduced processing time and sample volume are introduced, whereas pain-free, sensitive, and portable noninvasive monitoring methods are being further developed to have a better control of glucose levels.

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References

[1] S. A. Siddiqui, Y. Zhang, Z. Feng, and A. Kos, “A pulse rate estimation algorithm using PPG and smartphone camera,” *J. Med. Syst.*, vol. 40, no. 5, pp. 1–6, 2016.
[2] S. N. Shukla *et al.*, “Noninvasive cuffless blood pressure measurement by vascular transit time,” in *Proc. 28th Int. Conf. VLSI Des.*, 2015, pp. 535–540.
[3] K. Shafqat, R. Langford, S. Pal, and P. Kyriacou, “Estimation of venous oxygenation saturation using the finger photoplethysmograph (PPG) waveform,” in *Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2012, pp. 2905–2908.
[4] J. Tomas, J. Lloret, D. Bri, and S. Sendra, “Sensors and their application for disabled and elderly people,” in *Handbook of Research on Personal Autonomy Technologies and Disability Informatics*. Hershey, PA, USA: IGI Global, 2010, pp. 311–330.
[5] S. El-Sappagh, M. Elmogy, and A. M. Riad, “A fuzzy-ontology-oriented case-based reasoning framework for semantic diabetes diagnosis,” *Artif. Intell. Med.*, vol. 65, no. 3, pp. 179–208, 2015.
[6] A. Karahoca and M. A. Tunga, “Dosage planning for type 2 diabetes mellitus patients using indexing HDMR,” *Expert Syst. Appl.*, vol. 39, no. 8, pp. 7207–7215, 2012.
[7] A. Militaru, M. Frandes, and D. Lungeanu, “Smart wristbands as inexpensive and reliable non-dedicated solution for self-managing type 2 diabetes,” in *Proc. E-Health Bioeng. Conf.*, 2015, pp. 1–4.
[8] M. W. Aslam, Z. Zhu, and A. K. Nandi, “Feature generation using genetic programming with comparative partner selection for diabetes classification,” *Expert Syst. Appl.*, vol. 40, no. 13, pp. 5402–5412, 2013.
[9] K. Zarkogianni *et al.*, “Comparative assessment of glucose prediction models for patients with type 1 diabetes mellitus applying sensors for glucose and physical activity monitoring,” *Med. Biol. Eng. Comput.*, vol. 53, no. 12, pp. 1333–1343, 2015.
[10] S. Perveen, M. Shahbaz, A. Guergachi, and K. Keshavjee, “Performance analysis of data mining classification techniques to predict diabetes,” *Procedia Comput. Sci.*, vol. 82, pp. 115–121, 2016.
[11] O. Vahidi, K. E. Kwok, R. B. Gopaluni, and F. K. Knop, “A comprehensive compartmental model of blood glucose regulation for healthy and type 2 diabetic subjects,” *Med. Biol. EngComput.*, vol. 54, no. 9, pp. 1383–1398, 2016.
[12] F. Beloufa and M. A. Chikh, “Design of fuzzy classifier for diabetes disease using modified artificial bee colony algorithm,” *Comput. Methods Programs Biomed.*, vol. 112, no. 1, pp. 92–103, 2013.
[13] N. Ozana *et al.*, “Noncontact speckle-based optical sensor for detection of glucose concentration using magneto-optic effect,” *J. Biomed. Opt.*, vol. 21, no. 6, pp. 9721–9728, 2016.
[14] U. R. Acharya, O. Faust, N. Adib Kadri, J. S. Suri, and Y. Wenwei, “Automated identification of normal and diabetes heart rate signals using nonlinear measures,” *Comput. Biol. Med.*, vol. 43, no. 10, pp. 1523–1529, 2013.
[15] P. Li, L. Yu, Q. Fang, and S. Y. Lee, “A simplification of cobelli’s glucose-insulin model for type 1 diabetes mellitus and its FPGA implementation,” *Med. Biol. Eng. Comput.*, vol. 54, no. 10, pp. 1–15, 2015.
[16] H. R. Marateb, M. Mansourian, E. Faghihimani, M. Amini, and D. Farina, “A hybrid intelligent system for diagnosing microalbuminuria in type 2 diabetes patients without having to measure urinary albumin,” *Comput. Biol. Med.*, vol. 45, no. 1, pp. 34–42, 2014.
[17] S. Luo *et al.*, “Exploring the effects of intervention for those at high risk of developing type 2 diabetes using a computer simulation–Computers in biology and medicine,” *Comput. Biol. Med.*, vol. 53, pp. 105–114, 2014.
[18] S. Kang, P. Kang, T. Ko, S. Cho, S. J. Rhee, and K. S. Yu, “An efficient and effective ensemble of support vector machines for anti-diabetic drug failure prediction,” *Expert Syst. Appl.*, vol. 42, no. 9, pp. 4265–4273, 2015.

[19] W. Zhang, Y. Du, and M. L. Wang, "Noninvasive glucose monitoring using saliva nano-biosensor," *Sens. Biosens. Res.*, vol. 4, pp. 23–29, 2015.

[20] [Online]. Available: http://static.cdn-seekingalpha.com/uploads/2013/3/14/1149932-13632481066428409-Daniel-Lauchheimer.jpg

[21] [Online]. Available: http://www.altfutures.org/pubs/diabetes2030/UNITEDSTATES-Data-Sheet.pdf

[22] [Online]. Available: http://www.cdc.gov/diabetes/statistics/prev/national/fig-persons.htm

[23] L. L. Nguyen, S. Su, and H. T. Nguyen, "Neural network approach for non-invasive detection of hyperglycemia using electrocardiographic signals," in *Proc. 36th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2014, pp. 4475–4478.

[24] J. Yadav, A. Rani, V. Singh, and B. M. Murari, "Prospects and limitations of non-invasive blood glucose monitoring using near-infrared spectroscopy," *Biomed. Signal Process. Control*, vol. 18, pp. 214–227, 2015.

[25] J. Shin, H. Park, S. Cho, H. Nam, and K. J. Lee, "A correction method using a support vector machine to minimize hematocrit interference in blood glucose measurements," *Comput. Biol. Med.*, vol. 52, no. 3, pp. 111–118, 2014.

[26] N. S. Virdi and J. J. Mahoney, "Importance of blood glucose meter and carbohydrate estimation accuracy," *J. Diabetes Sci. Technol.*, vol. 6, no. 4, pp. 921–926, 2012.

[27] P. Biswas, S. Bhaumik, and I. Patiyat, "Estimation of glucose and insulin concentration using nonlinear Gaussian filters," in *Proc. IEEE 1st Int. Conf. Control, Meas. Instrum.*, 2016, pp. 16–20.

[28] Z. Li, G. Li, W.-J. Yan, and L. Lin, "Classification of diabetes and measurement of blood glucose concentration noninvasively using near infrared spectroscopy," *Infrared Phys. Technol.*, vol. 67, pp. 574–582, 2014.

[29] C. Hui, T. Chao, L. Zan, and W. Tong, "The diagnostics of diabetes mellitus based on ensemble modeling and hair/urine element level analysis," *Comput. Biol. Med.*, vol. 50, no. 4, pp. 70–75, 2014.

[30] [Online]. Available: https://www.accu-chek.com/meters/aviva-meter

[31] H. Kirchsteiger, L. Zaccarian, E. Renard, and L. Del Re, "LMI-based approaches for the calibration of continuous glucose measurement sensors," *IEEE J. Biomed. Health Informat.*, vol. 19, no. 5, pp. 1697–1706, Sep. 2015.

[32] M. Vettoretti, A. Facchinetti, G. Sparacino, and C. Cobelli, "Patient decision-making of CGM sensor driven insulin therapies in type 1 diabetes: In silico assessment," in *Proc. 37th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2015, vol. 2015, pp. 2363–2366.

[33] S. K. Vashist, "Non-invasive glucose monitoring technology in diabetes management: A review," *Analytica Chimica Acta*, vol. 750, no. 11, pp. 16–27, 2012.

[34] T.-T. Wei, H.-Y. Tsai, C.-C. Yang, W.-T. Hsiao, and K.-C. Huang, "Non-invasive glucose evaluation by human skin oxygen saturation level," in *Proc. IEEE Int. Instrum. Meas. Technol. Conf.*, 2016, pp. 1–5.

[35] A. Asaduzzaman, S. Samadarsinee, and K. K. Chidella, "Simulating multisensor noninvasive blood glucose monitoring systems," in *Proc. SoutheastCon*, 2016, pp. 1–7.

[36] A. Dehennis, S. Getzlaff, D. Grice, and M. Mailand, "An NFC enabled CMOS IC for a wireless, fully implantable glucose sensor," *IEEE J. Biomed. Health Informat.*, vol. 20, no. 1, pp. 18–28, Jan. 2016.

[37] X. Y. Liu, Z. T. Wu, Y. Fan, and M. Tentzeris, "A miniaturized CSRR loaded wide-beamwidth circularly polarized implantable antenna for subcutaneous real-time glucose monitoring," *IEEE Antennas Wireless Propag. Lett.*, vol. 16, pp. 577–580, 2016.

[38] N. Anabtawi, S. Freeman, and R. Ferzli, "A fully implantable, nfc enabled, continuous interstitial glucose monitor," in *Proc. IEEE EMBS Int. Conf. Biomed. Health Informat.*, 2016, pp. 612–615.

[39] B. Lu *et al.*, "Side-polished fiber SPR sensor with tempetrature self-compensation for continuous glucose monitoring," in *Proc. IEEE 29th Int. Conf. Micro Elect. Mech. Syst.*, 2016, pp. 411–414.

[40] X. Wang, C. Mdingi, A. Dehennis, and A. E. Colvin, "Algorithm for an implantable fluorescence based glucose sensor," in *Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2012, pp. 3492–3495.

[41] W. Shang *et al.*, "Detection and monitoring of microparticles under skin by optical coherence tomography as an approach to continuous glucose sensing using implanted retroreflectors," *IEEE Sensors J.*, vol. 13, no. 11, pp. 4534–4541, Nov. 2013.

[42] S. Wang *et al.*, "Detection and monitoring of microparticles under skin by optical coherence tomography as an approach to continuous glucose sensing using implanted retroreflectors," *IEEE Sensors J.*, vol. 13, no. 11, pp. 4534–4541, Nov. 2013.

[43] X. Huang, S. Li, E. Davis, D. Li, Q. Wang, and Q. Lin, "A MEMS dielectric affinity glucose biosensor," *J. Microelectromech. Syst.*, vol. 23, no. 1, pp. 14–20, 2013.

[44] E. Ghafar-Zadeh, B. Gholamzadeh, F. Awwad, and M. Sawan, "Toward implantable glucometer: Design, modeling and experimental results," in *Proc. 35th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2013, vol. 2013, pp. 5658–5661.

[45] P. Dardano, A. Calio, J. Politi, and I. Rea, "Diagnostic and therapeutic devices based on polymeric microneedles: Fabrication and preliminary results," in *Proc. 18th AISEM Annu. Conf.*, 2015, pp. 1–4.

[46] S. Guerra, A. Facchinetti, G. Sparacino, G. D. Nicolao, and C. Cobelli, "Enhancing the accuracy of subcutaneous glucose sensors: A real-time deconvolution-based approach," *IEEE Trans. Biomed. Eng.*, vol. 59, no. 6, pp. 1658–1669, Jun. 2012.

[47] H. Yu, D. Li, R. C. Roberts, and K. Xu, "An interstitial fluid transdermal extraction system for continuous glucose monitoring," *J. Microelectromech. Syst.*, vol. 21, no. 21, pp. 917–925, 2012.

[48] X. Y. Liu, Z. T. Wu, Y. Fan, and M. Tentzeris, "A miniaturized CSRR loaded wide-beamwidth circularly polarized implantable antenna for subcutaneous real-time glucose monitoring," *IEEE Antennas Wireless Propag. Lett.*, vol. 16, pp. 577–580, 2016.

[49] "Semi-implantable glucose sensor based on dual-stacked polymeric film for wireless continuous monitoring," in *Proc. IEEE 29th Int. Conf. Micro Elect. Mech. Syst.*, 2016, pp. 407–410.

[50] T. Bailey *et al.*, "Accuracy and user performance evaluation of the contour; next link 2.4 blood glucose monitoring system," *Clinica Chimica Acta*, vol. 448, pp. 139–145, 2015.

[51] [Online]. Available: https://www.fora-shop.com/collections/blood-glucose-meter/products/fora-v30a-t alking-blood-glucose-meter

[52] A. K. Seifert, N. Demitri, and A. M. Zoubir, "Decreasing the measurement time of blood sugar tests using particle filtering," in *Proc. IEEE Int. Conf. Acoust., Speech, Signal Process.*, 2016, pp. 4433–4437.

[53] A. Sun, T. Wambach, A. G. Venkatesh, and D. A. Hall, "A multitechnique reconfigurable electrochemical biosensor for integration into mobile technologies," in *Proc. Biomed. Circuits Syst. Conf.*, 2015, pp. 1–4.

[54] Z. Darabi, S. Solgi, M. Fazel Zarandi, and I. Turksen, "An intelligent multi-agent system architecture for enhancing self-management of type 2 diabetic patients," in *Proc. IEEE Conf. Comput. Intell. Bioinformat. Comput. Biol.*, 2015, pp. 1–8.

[55] Z. Wang and R. Paranjape, "The self-aware diabetic patient software agent model," *Comput. Biol. Med.*, vol. 43, no. 11, pp. 1900–1909, 2013.

[56] N. Demitri and A. Zoubir, "Measuring blood glucose concentrations in photometric glucometers requiring very small sample volumes," *IEEE Trans. Biomed. Eng.*, vol. 64, no. 1, pp. 28–39, Jan. 2017.

[57] E. I. Georga, V. C. Protopappas, D. Polyzos, and D. I. Fotiadis, "Evaluation of short-term predictors of glucose concentration in type 1 diabetes combining feature ranking with regression models," *Med. Biol. Eng. Comput.*, vol. 53, no. 12, pp. 1305–1318, 2015.

[58] B. Nacht *et al.*, "Integrated catheter system for continuous glucose measurement and simultaneous insulin infusion," *Biosensors Bioelectron.*, vol. 64, pp. 102–110, 2015.

[59] O. El-Gayar, P. Timsina, N. Nawar, and W. Eid, "Mobile applications for diabetes self-management: Status and potential," *J. Diabetes Sci. Technol.*, vol. 7, no. 1, pp. 247–62, 2013.

[60] M. Frandes, B. Timar, A. Tole, S. Holban, and D. Lungeanu, "Mobile technology support for clinical decision in diabetic keto-acidosis emergency," *Stud. Health Technol. Informat.*, vol. 210, pp. 316–20, 2015.

[61] Z. Lu *et al.*, "A point of care electrochemical impedance spectroscopy device," in *Proc. 28th IEEE Int. Syst. Chip Conf.*, 2015, pp. 240–244.

[62] I. Gouzouasis *et al.*, "Detection of varying glucose concentrations in water solutions using a prototype biomedical device for millimeter-wave non-invasive glucose sensing," in *Proc. 10th Eur. Conf. Antennas Propag.*, 2016, pp. 1–4.

[63] Cnoga Medical. [Online]. Available: http://cnogacare.co/portfolio-item/combo-glucometer/

[64] University of Rhode Island. [Online]. Available: http://www.ele.uri.edu/courses/bme281/F12/JonathanI-2.pdf

[65] Glucosense Diagnostic Ltd. [Online]. Available: http://www.glucosense.net/

[66] Glucowise. [Online]. Available: http://www.gluco-wise.com/

[67] Desang. [Online]. Available: http://www.desang.net/2015/01/glucowise-non-invasive-blood-glucose-testing/

[68] I. Harmanboehm, A. Gal, A. M. Raykhman, E. Naidis, and Y. Mayzel, "Noninvasive glucose monitoring: Increasing accuracy by combination of multi-technology and multi-sensors," *J. Diabetes Sci. Technol.*, vol. 4, no. 3, pp. 583–595, 2010.

[69] Integrity Applications. [Online]. Available: http://www.integrity-app.com/
[70] Medgadget. [Online]. Available: http://www.medgadget.com/2007/06/navigator-continuous-glucose-monitoring-system-approved-in-europe.html?trendmd-shared=0
[71] Quick LLC. [Online]. Available: http://www.iquickitsalivaanalyzer.com/
[72] Digital Trends. [Online]. Available: http://www.digitaltrends.com/mobile/google-novartis-smart-contact-lens/
[73] Novartis. [Online]. Available: http://www.novartis.com/newsroom/media-releases/en/2014/1824836.shtml
[74] Noviosense. [Online]. Available: http://noviosense.com/
[75] Y. Zhang, L. Sun, H. Song, and X. Cao, "Ubiquitous WSN for healthcare: Recent advances and future prospects," *IEEE Int. Things J.*, vol. 1, no. 4, pp. 311–318, Aug. 2014.
[76] E. Monte-Moreno, "Non-invasive estimate of blood glucose and blood pressure from a photoplethysmograph by means of machine learning techniques," *Artif. Intell. Med.*, vol. 53, no. 2, pp. 127–138, 2011.
[77] G. Robertson, E. D. Lehmann, W. Sandham, and D. Hamilton, "Blood glucose prediction using artificial neural networks trained with the aida diabetes simulator: A proof-of-concept pilot study," *J. Elect. Comput. Eng.*, vol. 2011, 2011, Art. no. 681786.
[78] Y. Z. Hsieh, M. C. Su, C. H. Wang, and P. C. Wang, "Prediction of survival of ICU patients using computational intelligence." *Comput. Biol. Med.*, vol. 47, no. 1, pp. 13–19, 2014.
[79] M. Graña, D. Chyzhyk, C. Toro, and S. Rios, "Innovations in healthcare and medicine editorial," *Comput. Biol. Med.*, vol. 72, pp. 226–228, 2016.
[80] D. Gradolewski and G. Redlarski, "Wavelet-based denoising method for real phonocardiography signal recorded by mobile devices in noisy environment," *Comput. Biol. Med.*, vol. 52, no. 3, pp. 119–129, 2014.
[81] V. Dantu, J. Vempati, and S. Srivilliputhur, "Non-invasive blood glucose monitor based on spectroscopy using a smartphone," in *Proc. 36th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2014, pp. 3695–3698.
[82] X. Li and C. Li, "Research on non-invasive glucose concentration measurement by NIR transmission," in *Proc. IEEE Int. Conf. Comput. Commun.*, 2015, pp. 223–228.
[83] D. Grimaldi, Y. Kurylyak, F. Lamonaca, and A. Nastro, "Photoplethysmography detection by smartphone's videocamera," in *Proc. IEEE 6th Int. Conf. Intell. Data Acquisition Adv. Comput. Syst.*, 2011, vol. 1. pp. 488–491.
[84] S. Ramasahayam, L. Arora, S. R. Chowdhury, and M. Anumukonda, "FPGA based system for blood glucose sensing using photoplethysmography and online motion artifact correction using adaline," in *Proc. 9th Int. Conf. Sens. Technol.*, 2015, pp. 22–27.
[85] B. Paul, M. P. Manuel, and Z. C. Alex, "Design and development of non invasive glucose measurement system," in *Proc. 1st Int. Symp. Phys. Technol. Sensors*, 2012, pp. 43–46.
[86] J. Kottmann, U. Grob, J. M. Rey, and M. W. Sigrist, "Mid-infrared fiber-coupled photoacoustic sensor for biomedical applications," *Sensors*, vol. 13, no. 1, pp. 535–549, 2013.
[87] A. Asaduzzaman, S. Samadarsinee, and K. K. Chidella, "Simulating multisensor noninvasive blood glucose monitoring systems," in *Proc. SoutheastCon*, 2016, pp. 1–7.
[88] N. Wadamori, "Behavior of long-period measurements using a small-sized photoacoustic cell for aqueous glucose monitoring," in *Proc. 37th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2015, pp. 1267–1270.
[89] P. P. Pai, P. K. Sanki, A. De, and S. Banerjee, "Nir photoacoustic spectroscopy for non-invasive glucose measurement," in *Proc. 37th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2015, pp. 7978–7981.
[90] S. Amrane, N. Azami, and Y. Elboulqe, "Optimized algorithm of dermis detection for glucose blood monitoring based on optical coherence tomography," in *Proc. 10th Int. Conf. Intell. Syst., Theories Appl.*, 2015, pp. 1–5.
[91] S. H. Ling, P. P. San, and H. T. Nguyen, "Non-invasive hypoglycemia monitoring system using extreme learning machine for type 1 diabetes," *ISA Trans.*, vol. 64, pp. 440–446, 2016.
[92] C. McCormick, D. Heath, and P. Connolly, "Towards blood free measurement of glucose and potassium in humans using reverse iontophoresis," *Sensors Actuators B, Chem.*, vol. 166, pp. 593–600, 2012.
[93] V. V. Deshmukh and R. B. Ghongade, "Measurement of dielectric properties of aqueous glucose using planar ring resonator," in *Proc. Int. Conf. Microelectron., Comput. Commun.*, 2016, pp. 1–5.
[94] J. Shao, F. Yang, F. Xia, Q. Zhang, and Y. Chen, "A novel miniature spiral sensor for non-invasive blood glucose monitoring," in *Proc. 10th Eur. Conf. Antennas Propag.*, 2016, pp. 1–2.
[95] S. Saha *et al.*, "Evaluation of the sensitivity of transmission measurements at millimeter waves using patch antennas for non-invasive glucose sensing," in *Proc. 10th Eur. Conf. Antennas Propag.*, 2016, pp. 1–4.
[96] X. Zhang, J. Xiao, B. Ling, C. Li, and K. Tsang, "Accurate, wearable, wireless and pinless blood glucose measurement system modeled by a set of fractional differential equations," in *Proc. IEEE Int. Conf. Consum. Electron.*, 2016, pp. 595–597.
[97] R. Baghbani, M. A. Rad, and A. Pourziad, "Microwave sensor for non-invasive glucose measurements design and implementation of a novel linear," *IET Wireless Sensor Syst.*, vol. 5, no. 2, pp. 51–57, 2015.
[98] T. Yilmaz, R. Foster, and Y. Hao, "Broadband tissue mimicking phantoms and a patch resonator for evaluating noninvasive monitoring of blood glucose levels," *IEEE Trans. Antennas Propag.*, vol. 62, no. 6, pp. 3064–3075, Jun. 2014.
[99] M. Zanon *et al.*, "Non-invasive continuous glucose monitoring: Improved accuracy of point and trend estimates of the multisensor system," *Med. Biol. Eng. Comput.*, vol. 50, no. 10, pp. 1047–1057, 2012.
[100] A. Adhyapak, M. Sidley, and J. Venkataraman, "Analytical model for real time, noninvasive estimation of blood glucose level," in *Proc. 36th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2014, pp. 5020–5023.
[101] J. Liu, L. Jiang, H. Liu, and X. Cai, "A bifunctional biosensor for subcutaneous glucose monitoring by reverse iontophoresis," *J. Electroanal. Chem.*, vol. 660, no. 1, pp. 8–13, 2011.
[102] A. Soni and S. K. Jha, "A paper strip based non-invasive glucose biosensor for salivary analysis," *Biosensors Bioelectron.*, vol. 67, pp. 763–768, 2015.
[103] C. Liu *et al.*, "A glucose oxidase-coupled dnazyme sensor for glucose detection in tears and saliva," *Biosensors Bioelectron.*, vol. 70, pp. 455–461, 2015.
[104] W. Zhang, Y. Du, and M. L. Wang, "On-chip highly sensitive saliva glucose sensing using multilayer films composed of single-walled carbon nanotubes, gold nanoparticles, and glucose oxidase," *Sens. Bio-Sens. Res.*, vol. 4, pp. 96–102, 2015.
[105] T. Arakawa *et al.*, "Mouth guard type biosensor "cavitous sensor" for monitoring of saliva glucose with telemetry system," in *Proc. 9th Int. Conf. Sens. Technol.*, 2015, pp. 46–49.
[106] D. Guo, D. Zhang, L. Zhang, and G. Lu, "Non-invasive blood glucose monitoring for diabetics by means of breath signal analysis," *Sensors Actuators B, Chem.*, vol. 173, pp. 106–113, 2012.
[107] K. Yan and D. Zhang, "Blood glucose prediction by breath analysis system with feature selection and model fusion," in *Proc. 36th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2014, pp. 6406–6409.
[108] K. Yan, D. Zhang, D. Wu, H. Wei, and G. Lu, "Design of a breath analysis system for diabetes screening and blood glucose level prediction," *IEEE Trans. Biomed. Eng.*, vol. 61, no. 11, pp. 2787–2795, Nov. 2014.
[109] Y. T. Liao, H. Yao, A. Lingley, B. Parviz, and B. P. Otis, "A 3-μw CMOS glucose sensor for wireless contact-lens tear glucose monitoring," *IEEE J. Solid-State Circuits*, vol. 47, no. 1, pp. 335–344, Jan. 2012.
[110] A. Nawaz, P. Ohlckers, S. Saelid, M. Jacobsen, and M. Akram, "Review: Non-invasive continuous blood glucose measurement techniques," *J. Bioinformat. Diabetes*, vol. 1, pp. 1–27, 2016.
[111] W. Liu, A. Huang, and P. Wang, "BpMC: A novel algorithm retrieving multilayered tissue bio-optical properties for non-invasive blood glucose measurement," in *Proc. IEEE Int. Conf. Bioinformat. Biomed.*, 2017, pp. 451–456.

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