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SURVEY

Non-Invasive Glucose Measurement Technologies: Recent Advancements and Future Challenges

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ABSTRACT Diabetes is a long-term condition in which a person's body cannot break down blood sugar adequately due to a shortage of insulin. The most crucial element of health care is continuously monitoring blood glucose (BG) levels. The main concern of effective glucose monitoring equipment is based on the blood-pricking technique. However, this may not be suggested for frequent glucose measurement. The paper presents various glucose-measuring technologies. The research discusses various non-invasive glucose measurement techniques and their management using advanced medical technologies. The configuration of the precise measuring device is essential to meet the blood glucose monitoring requirements that are not invasive systems. Non-invasive glucose monitoring devices solve the issue of frequently pricking patients for blood samples for clinical tests. For the goal of continuous health monitoring, a Smart Healthcare framework would be built on the Internet-of-Medical-Things (IoMT) and a Healthcare Cyber-Physical System (H-CPS) to estimate blood glucose. The study also discusses a few consumer devices and cutting-edge methods for measuring glucose. The paper also outlines the several difficulties and open challenges with glucose prediction.

INDEX TERMS Non-invasive intelligent system, glucose monitoring, healthcare, edge computing devices, diabetes, glucose controlling paradigm.

I. INTRODUCTION

The human body uses glucose as an effective origin of energy. The Normal blood glucose (BG) range (80-150 mg/dl) is required to perform daily activities by the human [1]. However, fluctuations in the normal blood glucose range might cause complications in the body. In addition, insulin is a vital hormone the body produces for glucose balance after food consumption. Food digestion produces glucose, which provides energy for routine work in daily life. If insulin is not produced properly, excessive glucose concentrations will build up in the blood. The controlling feedback system of glucose generation and utilization in the body is examined in Fig. 1 [2]. If the development of *alpha* cells is greater than that of *beta* cells, a persistently high blood glucose level may result. This disorder prevents the body from producing enough insulin to neutralize the glucose. Diabetes mellitus is a disease distinguished by increased blood glucose (beyond the normal range) in the body. The key contributing factor to diabetes is an irregular sugar profile [3].

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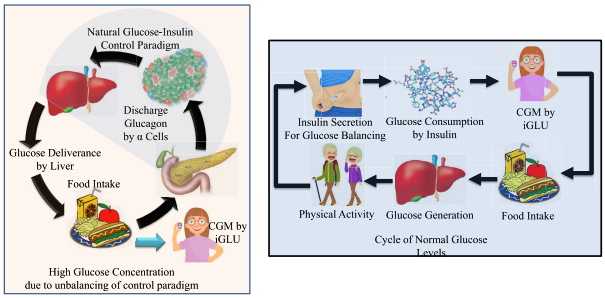

FIGURE 1. An example of the closed-loop production and consumption of glucose [2].

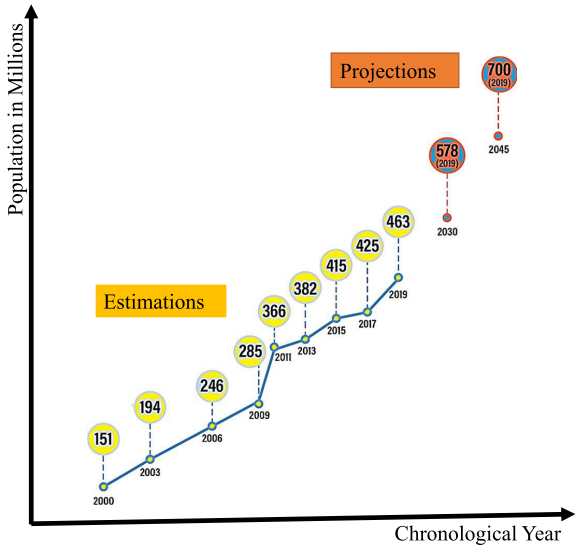

FIGURE 2. Global tendency of diabetes, assumed from [7].

Non-communicable disease (NCD) and chronic disease prevalence rates have multiplied during the past several years. An estimated 20 million deaths from cardiovascular disease are recorded yearly, and high blood sugar is a critical risk factor. Additionally, those with diabetes are particularly impacted by viral pandemic epidemics [4], [5], [6]. Diabetes patients have increased considerably over the past several years due to obesity, poor diet, an aging population, and sedentary lifestyles. Since the number of individuals living with diabetes has more than quadrupled over the past two decades, diabetes is one of the health issues with a rapidly increasing number of patients in the last decades (Refer Fig. 2) [7]. 2019 had a 9.3% global prevalence of diabetes, affecting over 463 million people. With a 10.2% prevalence rate, it is anticipated to increase to over 600 million people by the end of two decades and reach 700 million by the end of four decades. Prevalence is 10.8% in urban areas compared to 7.2% in rural areas. Almost half of diabetes patients are ignorant of their glycemic profile. Indeed, diabetes is on the rise globally, affecting roughly 1 in 10 individuals now. In the next ten years, more than 0.5 billion individuals are predicted to have diabetes [8]. According to research from the International Diabetes Federation (IDF), more people die from diabetes than from malaria (0.6 million), HIV/AIDS (1.5 million), and TB (1.5 million) combined [9]. Diabetes is one of the primary chronic diseases that has a long-term effect on a person's health and quality of life. Insufficient insulin, insulin resistance, or excessive glucagon production are all regarded to be the causes of diabetes mellitus (DM), which is characterized by physiological dysfunctions and high blood glucose levels [10]. It is the most important health concern of the 21^{st} century. Since a few years ago, Type 2 Diabetes (T2DM) has seen tremendous global expansion. Any form of diabetes can cause complications in the human body that may raise the risk of death. Hyperglycemia, also known as a high blood glucose level, causes blood vessels to harden, which can damage kidneys, cause vision problems, and, in rare cases, even cause these organs to fail. Diabetes is linked to cardiac disease, peripheral vascular disease, and amputation of limbs. Contrarily, Type 1 Diabetes Patients (T1DM) may have low blood sugar or hypoglycemia due to high insulin administration [11]. Dizziness, over-sweating, and tiredness are the most typical signs of hypoglycemia in patients, and in the worst cases, it can result in coma and death. The diseases caused by diabetes in a picture is represented in Fig. 3

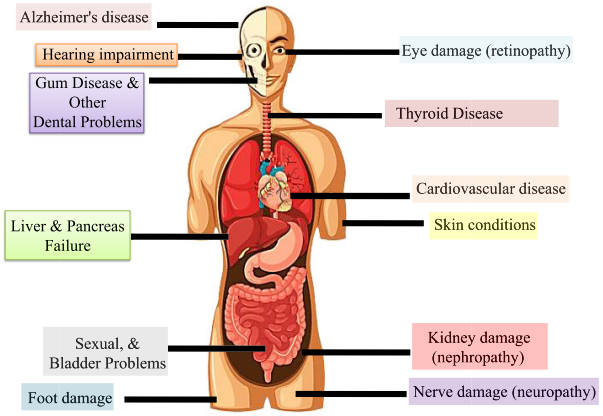

FIGURE 3. Diseases caused by diabetes in humans.

The signs of diabetes include frequent hunger, thirst, fatigue, changes in eyesight, persistent hunger, sudden weight loss, and the quick outflow of urine [12]. Diabetes can result in blindness, heart attacks, renal illness, lower limb amputations, and blindness if left untreated for an extended time. Diabetes would increase the risk of death and add to the cost of care at the moment of delivery and treatment. Additionally, diabetic people may become less productive at work, resulting in the inability to perform certain tasks. Diabetes can also lead to several health concerns, including eating disorders, mood disorders, anxiety disorders, and digestive troubles. It would raise the risk of mortality by about 50%. Diabetes also counts toward the cost of care for treatment. With oral medications, diabetes can be controlled in its early stages. Reducing the risk of amputation, cardiovascular disease, and high blood pressure also controls diabetes. This paper is structured with specific records, which demonstrate the measurement techniques, corresponding lim-

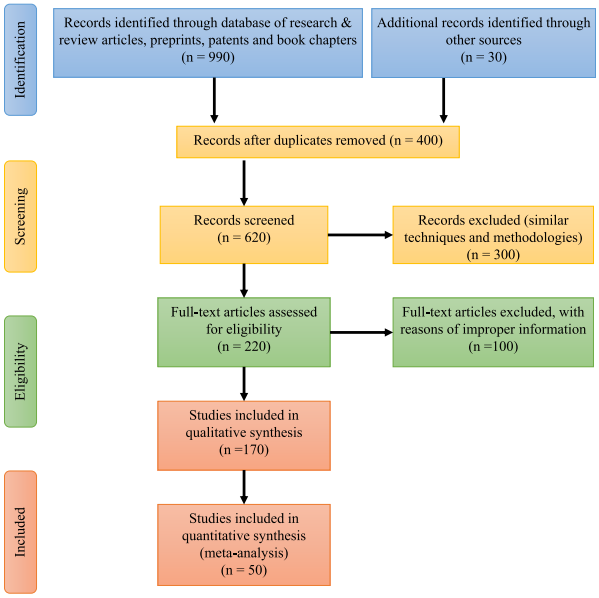

FIGURE 4. Statistical report of review records.

itations, future challenges, and vision. The statistical report of review records is presented in Fig. 4. The paper is framed with segregation of records, which are based on commercially available systems, measurement frameworks and proper descriptions of methodologies. These are represented in Fig. 5. The remainder of the article is structured as follows: Section II briefly discusses various types of diabetes along with the history of glucose-measuring technologies.

Section III explores a summary of different blood glucose-level prediction methods. Section IV explains various available procedures for non-invasive blood glucose-level prediction. Section V explores miscellaneous data processing and training of the models for non-invasive body glucose-level monitoring. Section VI briefly explains different commercial devices for non-invasive blood glucose prediction. Section VII explores the controlling procedures for body glucose-level and various available related commercial devices. Section VIII describes how glucose level estimations and control in smart health are made feasible by the Internet of Medical Things (IoMT). The limitation and open issues of glucose-level measurements are described in Section IX. The conclusion of the work is outlined in Section X. The future work is summarized in Section XI.

II. PUBLIC HEALTH ISSUES OF DIABETES AND THE REQUIREMENT FOR GLUCOSE MONITORING

This section explains the issues of diabetes and the health problems caused by diabetes. It also describes the necessity of blood glucose level prediction.

A. LEVEL OF DIABETES

Diabetes develops due to inadequate insulin about glucose produced within the body [13]. The beta cells in the pancreas produce the body's insulin, which is either inadequate or nonexistent. Diabetes impairs the ability of the liver, muscles, and fat cells to balance glucose and insulin adequately. Three categories are used to classify diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes (Refer Fig. 6) [14]. For a person with type-1 diabetes, their immune system is weakened because the pancreas does not generate insulin within the body As a result, they cannot produce insulin naturally [2], [15]. When a person has type 2 diabetes, their pancreas produces insufficient insulin to stabilize their body's glycemic profile. Pregnant women typically develop gestational diabetes later in the birth process. Globally, 2 billion individuals will be overweight in 2020, with 300 million of those adults being obese. Additionally, there are at least 155 million overweight or obese children worldwide. By 2025, it is anticipated that 8% of people will have hyperglycemia, which will rise to 10% [8]. The significant rise in Type 2 Diabetes incidence at younger ages, has raised concerns for diabetic individuals, particularly in developing nations. In contrast, in nations with maximum industries, most people begin to have high blood sugar around 60 years of age. In the highly developed nations, middle-aged people between the ages of 35 and 64 are most commonly affected [7]. In India, Type-2 diabetes affected 69.2 million people in 2019. Adults with Type-1 diabetes number 2.35 million on average. In general, only around 5% of individuals are considered to be Type-1 diabetics, whereas the remaining 90% to 95% are Type-2 diabetics. Insulin is required for type-1 diabetic patients to maintain blood glucose control. Patients with type-2 diabetes can manage their blood glucose levels by adhering to an optimized diet, taking their medications, and engaging in regular physical activity.

B. THE DIABETES-RELATED HEALTH CRISIS

Diabetes is mostly brought on by an uneven level of BG-insulin in the body, where insulin cannot be produced from natural processes [15], [16]. In contrast to non-diabetes cases, the likelihood of mortality would also rise by up to 50%. Because of continuous monitoring, diabetes can be controlled with correct precautions. The main requirement is a smart healthcare system that enables real-time and precise, accurate self-measurement of blood glucose. Many health organizations worldwide have identified hyperglycemia as the primary problem [17], [18]. There are a lot of techniques for BG measurement [19]. Substantial methods have familiarised professionals and patients with the device [20]. Diabetes often develops between the ages of 18 and 80 [21], [22]. Glucose levels should be between 70 and 150 mg/dl in the normal range and 40 to 550 mg/dl in the pathological range [23]. Developing a device for measuring glucose levels without pricking is one of the challenging issues for healthcare [24]. For the past 20 years, glucose monitoring equipment has been available with features advancement [25].

C. NEED OF GLUCOSE MEASUREMENT FOR DIABETES MANAGEMENT

The glucometer is a device to measure the blood glucose level of the body. Diabetic patients can use such type of devices for

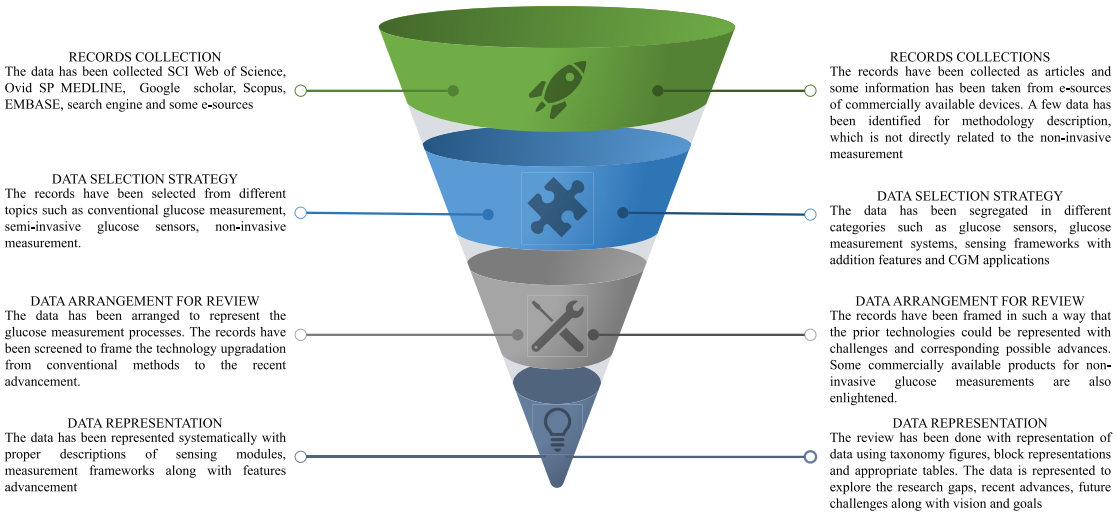

FIGURE 5. Data segregation reports from review records.

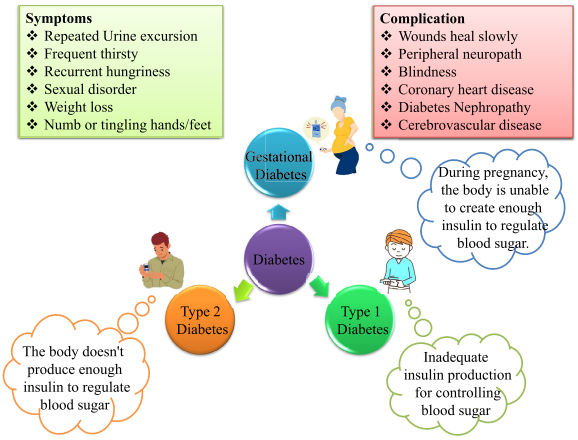

FIGURE 6. Different category of diabetes with symptoms.

frequent glucose measurement. Accordingly, they can modify their food habits and medication to keep their blood sugar levels within the desired range. There is a correlation between tight glycemic control and a lower risk of complications from diabetes. This makes it possible to customize diabetes treatment programs to improve blood sugar regulation and general health. Diabetic people are the main end users of glucometers Diabetic patients are conscious about their blood sugar levels and the variables that affect them through routine monitoring. The device would also be able to provide feedback for control mechanisms adopted by people for diabetic management.

D. A HISTORICAL OVERVIEW OF GLUCOSE MONITORING

A portable medical tool for determining blood sugar levels in the body is the glucose measurement device (also known as a glucometer) [13], [26]. Additionally, the glucose profile (different glucose measurement test) might be demonstrated using a strip-based test dipped in any substance. It is an excellent tool for measuring blood glucose in those with diabetes or hypoglycemia. Lyons and Clark from Cincinnati first proposed the biosensor in 1962 to improve glucose monitoring devices. A lot of people use glucose sensors for measurement. This glucose biosensor comprised an exterior dialysis membrane, an electrode of oxygen, a thin layered GOx, and an inner semipermeable oxygen membrane. To create an enzyme electrode, enzymes might be drawn towards a detector [27]. Nevertheless, the fundamental drawback of first-generation glucose biosensors was the need for high hydrogen peroxide amperometric measurement operating potential for good selectivity. Second-generation glucose sensors (mediated glucose biosensors) have replaced the first-generation glucose biosensors. The suggested biosensors up to this point reflect breakthroughs in terms of device mobility and measurement precision. Nevertheless, these sensing devices weren't utilized for real-time diagnosis because of several proportions and environmental restrictions. Fig. 7 depicts the timeline of glucose measurement [28].

E. DISCUSSED PRIOR TECHNIQUES FOR GLUCOSE MEASUREMENT

Currently, laboratory-based or self-monitoring is used for glucose monitoring. Both of these methods involve pricking of the blood, which is uncomfortable and only provides the facility to monitor blood glucose at that specific moment. Additionally, multiple-time pricking during the day is also uncomfortable for the user. Hence, numerous people are doubtful about choosing this kind of solution. Because of this process of measurement, people don't measure glucose timely. This might result in incorrect insulin doses and unplanned dietary ingredients. However, they are a reliable solution because of their excellent accuracy and strong sensitivity for measuring glucose [29], [30].

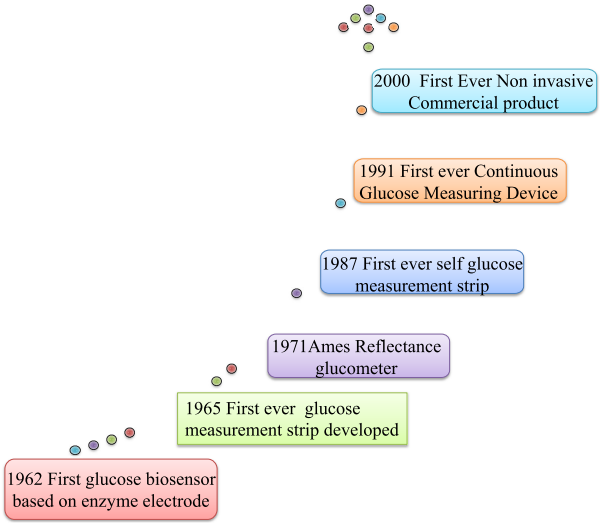

FIGURE 7. The historical evolution of glucometer with technology development.

Since a few years ago, scientists have been investigating several approaches to predict body glucose based on physical detection rather than conventional pricking approaches. The interstitial fluid (ISF) is used in this non-invasive approach instead of blood to detect glucose molecules. The difference in approaches of invasive and non-invasive measurement is represented in Fig. 8. There have been several attempts

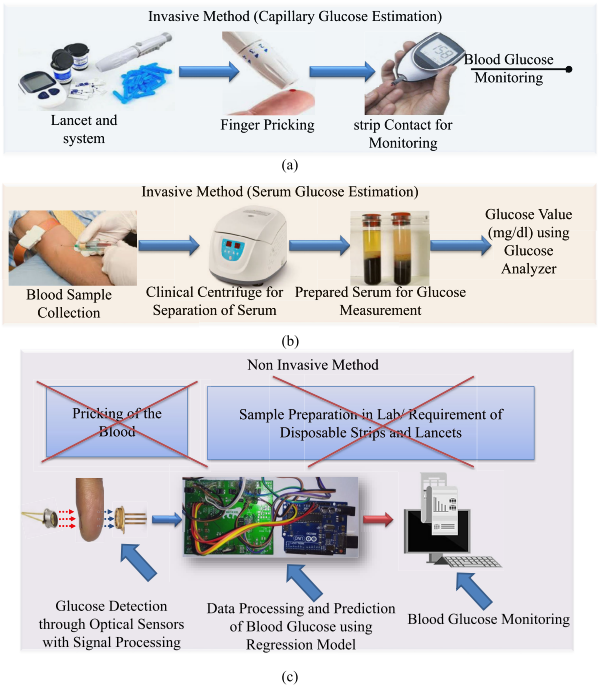

FIGURE 8. Invasive versus noninvasive glucose measurement.

to assess glucose through sweat, tears, saliva, and body skin [31]. The key difficulty is having accurate measurements with excellent sensitivity and dependability. Such a method could work well for self- and Continuous Glucose Monitoring (CGM) applications. These CGM methods provide measurements on fixed time slots during the day, which would be helpful for better controlling glucose levels and also for vital early detection. Appropriate treatment would be possible for patients with hypoglycemia and hyperglycemia. These techniques would help the dietitian and medical representative to prescribe a proper diet plan for the individual.

F. BASIC REQUIREMENT OF CONTINUOUS GLUCOSE MONITORING

There are non-invasive, semi-invasive (or minimally invasive), and invasive methods for measuring glucose. An invasive method may result in trauma, which confirms the impossible situation of continuous monitoring. Without drawing blood, non-invasive procedures may be helpful for Continuous body Glucose monitoring. However, the most effective method for comfortably measuring blood glucose is non-invasive glucose measurement [32].

The CGM helps to analyze blood glucose levels at each mealtime properly. Fluctuation in glucose-insulin values can be seen after insulin secretion, physical activity, and prescribed medicine with diet. Regular glucose level fluctuation analysis is also helpful for the diabetologist to prescribe the required treatment. Patients with type 1 diabetes who monitor glucose values for insulin doses would benefit from CGM. Continuous monitoring makes it easier to control diets. The CGM flow diagram is presented in Fig. 9 [29], [30]. Patients can use the CGM to assess their BG level at any time. Estimating the prior three months' BG level for identifying HbA1c value would be useful.

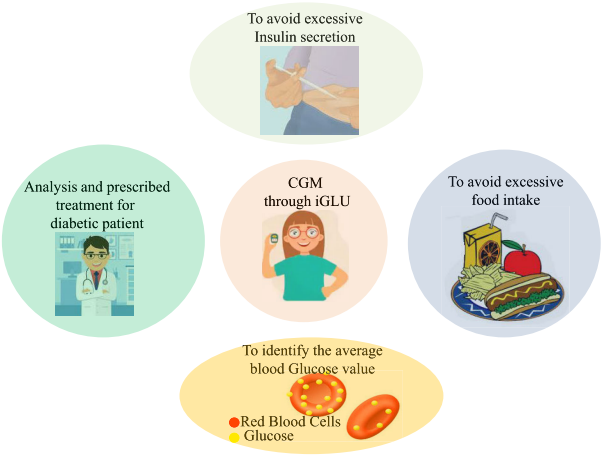

FIGURE 9. Purposes of continuously monitoring blood sugar.

III. A GENERAL OVERVIEW OF GLUCOSE-LEVEL MEASUREMENT METHODS

An overview of the various glucose-level measuring techniques is included in this section. Much work has been done to measure BG levels using invasive, semi-invasive, and non-invasive methods. A lot of researchers have explored

using non-invasive BG measurement techniques. Technically, Optical and non-optical processes stand for precise measurement. Some optical approaches used the PPG method, NIR spectroscopy, and Raman spectroscopy. In Fig. 10, a taxonomy of the various techniques is shown [26], [29], [30], [33].

A. INVASIVE METHODS

Commercially available electrochemical sensors are widely used in continuous blood glucose measuring systems [34]. When blood glucose molecules are detected, the value is monitored instantly using strip-based measurement [35]. The initial stage of blood glucose monitoring for various commercially available devices uses the lancets (for pricking the blood) [36]. Due to measurement, the process involves taking a blood sample from the fingertip more than three to four times a day, there is a factor of anxiety [37]. The minimally invasive biosensor for glucose monitoring was created using glucose oxidase and only needs a 1mm skin puncture to take measurements [38]. A small drop of blood drawn represents the photometric method for BG level estimation [39].

B. SEMI-INVASIVE PROCEDURES

A semi-invasive technique employing an embedded sensor has been proposed to monitor glucose tissue levels regularly. The sensor is wearable and placed on a membrane containing immobilized glucose oxidase. The development of implanted devices for glucose monitoring is presented in the paper [40]. The diabetes patient-specific semi- or minimally invasive technique employing biosensors [41]. The wearable micro system investigated for routine glucose measurement is presented as [42]. One similar method is explored for BG level estimation using a transponder chip and a micro-fabricated biosensor [43]. The Dexcom sensor's semi-invasive technique was represented for BG-level prediction using the transponder chip signal. The artificial pancreas system with glucose sensor for diabetes management is discussed in work [44]. The primary drawbacks of minimally invasive techniques are the survival of sensors for a long time and limited corresponding environmental constraints.

The portable small system checks BG levels continuously. It is a semi-invasive technique for measuring glucose. The main concept of the approach is that it employs a wearable micro-actuator that is made of shape memory alloy (SMA) to take blood samples. The implementation of PCB makes use of an enhanced version of SMA. It may be regarded as the earliest portable glucose monitoring device due to its efficacy and viability, but its size makes it uncomfortable.

C. NON-INVASIVE METHODS

All of the above-mentioned issues would be eliminated by non-invasive measurement [45], [46]. The glucose-measuring is possible without pricking through intelligent healthcare technologies [32]. Many strategies are explored for glucose estimation [47]. Compared to invasive and semi-invasive methods, non-invasive measurements are more practical for continuous glucose monitoring [45], [46]. The literature has found that glucose measurement using the optical approach is more accurate and dependable [48]. Non-invasive measurements using Raman spectroscopy, near-infrared spectroscopy, photo spectroscopy, polarimetric, and scattering spectroscopy are among the common optical techniques [49], [50] etc. According to the researcher, the development of non-invasive measuring equipment would be considerably more practical from the user's point of view [51], [52]. Recently developed non-invasive systems are trained using serum glucose values, which provide an impressive level of precision (refer to Fig. 11). Fluctuation of the body glucose to interstitial body glucose dynamics is thought of for a continuous body glucose monitoring system's accuracy [53], [54]. For portable setup, several calibration techniques have been explored and implemented [55]. A number of deliberate attempts have been made to develop the self-monitoring system [56].

D. THE TRADE-OFFS BETWEEN INVASIVE AND NON-INVASIVE GLUCOSE MEASUREMENTS

Current glucose monitoring techniques for the growing global population of sugar patients are invasive, time-consuming, uncomfortable, and need a lot of disposable goods, which continually add to family expenses. Such restrictions are overcome by the non-invasive glucose measuring technology, an area of study that has grown substantially in recent years. However, there is a compromise between these two approaches, as seen in Fig. 12.

E. NON-INVASIVE PREDICTION FOR SERUM VS CAPILLARY GLUCOSE

When compared to the capillary glucose level, the serum glucose value is more accurate. Most traditional methods test capillary glucose rapidly using a one-touch device, but it is challenging to identify serum glucose measurements instantly. It has been seen that capillary blood glucose levels are consistently greater than serum glucose levels. An accurate blood glucose reading would aid in taking the proper management measures. Because serum glucose is more reliable for diagnostic purposes compared to capillary glucose, it is crucial to monitor it. Capillary blood glucose prediction is preferred more frequently than serum glucose estimation. Blood glucose cannot be measured continuously or frequently enough to treat diabetes. Blood sugar can be managed considerably more effectively if serum glucose can be measured regularly. Only serum blood is used for the laboratory examination of HbA1c, which offers a three-month body glucose prediction. Serum and capillary glucose levels are being monitored using optical methods for non-invasive measurements. The basis for measuring blood glucose is IR light that has been obtained after being absorbed and scattered by glucose molecules flowing through blood

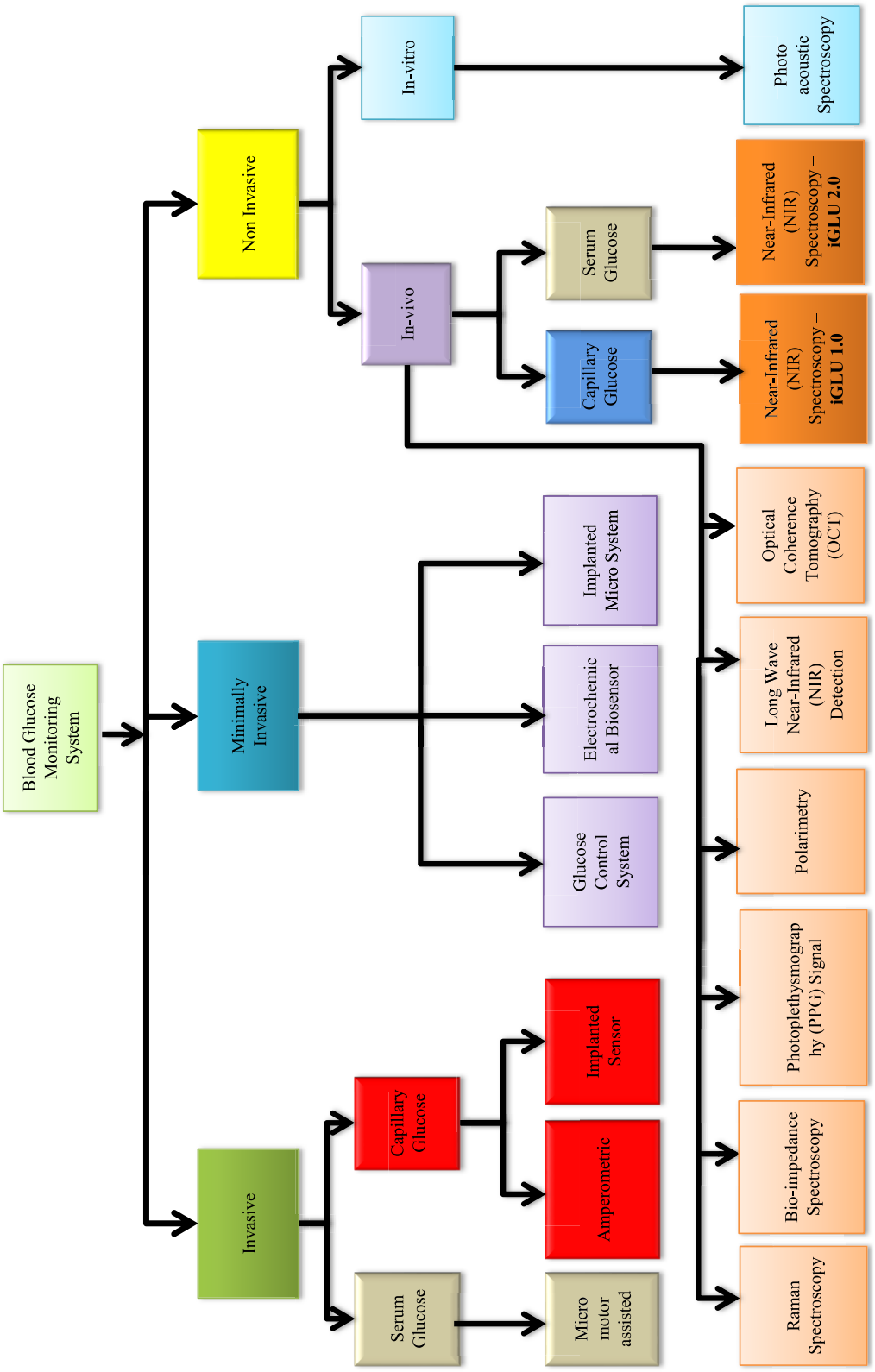

FIGURE 10. An overview of the Options for Glucose Measurement [26], [29], [30], [33].

capillaries. Except for the post-processing computing models needed for blood glucose estimates, the methodologies for the two glucose measurement methods are relatively comparable.

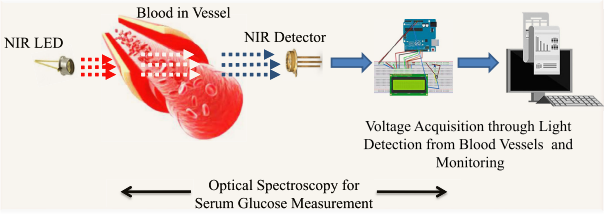

FIGURE 11. Measurement of Serum Glucose using NIR Spectroscopy.

F. A NON-INVASIVE METHOD FOR SALIVARY GLUCOSE LEVEL ESTIMATION

Salivary glucose measurement has been performed on adults and children [57]. There are distinct elements in saliva are categorized: (1) Saliva from certain glands, and (2) total saliva. Individual glands collect the gland-specific saliva, including the parotid, sub-mandibular, sublingual, and minor salivary glands. The knowledge of salivary composition helps to diagnose diabetic patients.

Based on the patient's risk factors, family history, age, and sex, diabetes level can be confirmed after justifying the symptoms. Other glucose measurement techniques include photo-metric measurements, which only require extremely tiny sample volumes [39]. The fundamental method provides the predicted BG value using a chemical test strip. The test area's reflections are measured, and the estimated glucose level is obtained.

IV. TECHNIQUES HIGHLIGHTED FOR NON-INVASIVE BLOOD GLUCOSE-LEVEL PREDICTION

This section provides an in-depth analysis of the different body glucose monitoring methods without pricking. The methods are currently being considered for future aspects of non-invasive measurement. There have been several attempts to monitor glucose non-invasively utilizing optical methods [28], [30], [58], [59]. These methods primarily rely on a variety of spectroscopy-based approaches. The researcher believes that designing a non-invasive measuring system would be considerably more practical from the user's standpoint. Fig. 13 shows an overview of different kinds of body glucose measuring techniques without pricking. Their pictorial representation is shown in Fig. 14. A comparative and qualitative analysis of different methods without pricking is summarized in Table 1.

A. NEAR-INFRARED (NIR) SPECTROSCOPY

When infrared radiation is incident on an object, the mechanism refers to vibration spectroscopy and infrared spectroscopy (IR spectroscopy) [60], [61]. The many IR spectroscopy types are displayed in Fig. 15. Reflection, scattering, and absorption spectroscopy are the most common types of IR spectroscopy [62]. The IR absorption wave induces molecular vibrations that result in a spectrum band with a wavelength of cm^{-1} [63]. The basic data acquisition module using IR spectroscopy is represented (refer to Fig. 16).

In this instance, the item (which may be a finger or an ear lobe) is exposed to light with a near-infrared wavelength range of 700 nm to 2500 nm [65]. According to [66], [67], it is possible for the light to interact with blood constituents and be dispersed, absorbed, and reflected. According to the Beer-Lambert law, the received light's intensity varies with blood glucose levels [68], [69]. The receiver would aid in measuring the amount of glucose present in the blood artery, according to Nikawa et al. [70]. A vernier effect-based ultra-sensitive optical sensor for measuring glucose levels is disclosed. Using the lateral offset single side-hole optical fiber (SSHF) construction. Two integrated parallel Mach-Zehnder interferometers (MZIs) have differing free spectral ranges (FSRs). The problem is then resolved by a unique FSR regulating technique that is developed using the optical path difference (OPD) theory [71].

1) LONG AND SHORT-WAVE NIRS

An effective method for measuring glucose precisely is optical detection. An optical approach based on FIR (far infrared) aids in obtaining the resonance process between O-H and C-H for the initial overtone. Long-range NIR, however, performs well in in-vitro tests. Similarly, for vitro-based glucose monitoring, a fiber-optic sensor is utilized in conjunction with laser-based mid-infrared spectroscopy. Continuous glucose measurement has been made possible using a multivariate calibration model for error analysis [72]. Compared to short-wave NIR, the FIR method has a restriction of shallow penetration. The short NIR would aid in more precise detection of the glucose molecule [73]. Fig. 17 illustrates the idea of NIR spectroscopy for glucose detection. NIR spectroscopy's unique wavelength has previously been used for accurate non-invasive glucose measurement in the past [74]. For the detection of glucose, a particular wavelength, such as 940 nm, has been investigated [75]. With NIR spectroscopy, the vibration of the C-H molecule has been seen at 920 nm [74]. In several additional studies, the validity of glucose absorption in the 1300 to 1350 nm range and the identification of glucose stretching in the NIR range [76], [77]. The existence of glucose element has been estimated at 1300 nm in related work [78].

2) PRIOR APPROACHES OF NIR SPECTROSCOPY

In the literature, a technique to calculate non-invasive blood glucose utilizing NIR spectroscopy and PPG has been proposed [79]. This technique uses a photodetector, NIR LED, and an optode pair. An analog front-end system produces a PPG signal at NIR wavelengths (935, 950, and 1070 nm). The glucose levels have been assessed using an FPGA-based Artificial Neural Network (ANN). For painless and autonomous blood extraction, a microcontroller is utilized [80]. The best solution uses Blood Glucose Measurement (BGM), which transmits and displays blood

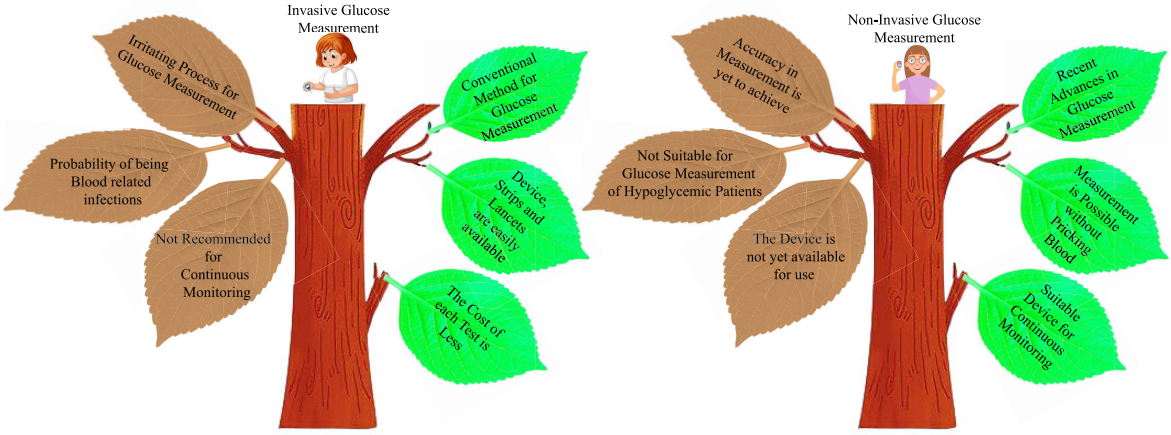

FIGURE 12. Glucose measurement trade-offs between invasive and non-invasive methods.

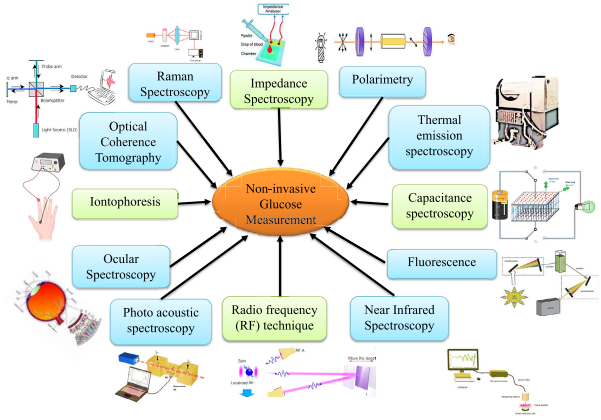

FIGURE 13. Different spectroscopy techniques for non-invasive glucose prediction.

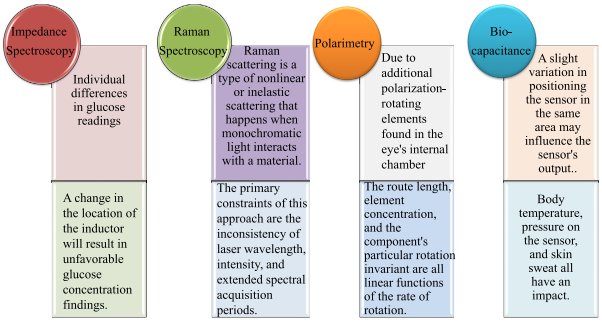

FIGURE 14. Proximate outlook of different prevalent spectroscopy approaches for glucose measure without pricking.

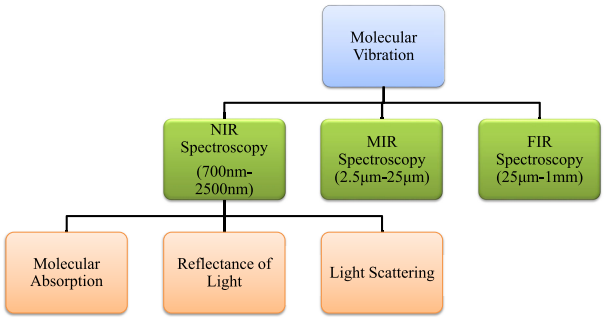

FIGURE 15. Classification of vibrational spectroscopy [64].

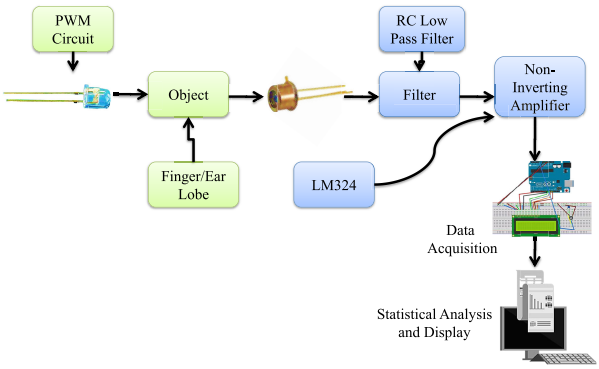

FIGURE 16. Block diagram representation of IR spectroscopy.

glucose data using a microcontroller. A remote device monitors the insulin pump, which is necessary for managing diabetes. Because it produces sound waves, this form of measuring technique takes advantage of changes in the intimidation of the susceptible body part [81]. The acoustic waves will respond more strongly when the glucose concentration is higher. The signal is then boosted to increase SNR and lower noise before being sent to the computer for additional processing. Photo-acoustic amplitude estimates feature extraction and glucose estimation. The acoustic signals are composed using double laser diodes and a PZT. The arrangement is expensive and cumbersome because the LASER is being used. A portable and precise glucose concentration measuring device is developed using the well-known photoacoustic near-infrared spectroscopy. The investigated in-vitro instrumentation techniques have a compact form factor, making them a good option for a non-invasive, in-vivo wearable blood glucose monitoring system. But, due

TABLE 1. Comparing the quality of several glucose monitoring techniques without pricking.

Approach	Benefits	Drawbacks
Near Infra − Red (NIR)	• signal strength is inversely correlated with the glucose molecule. • Other interacting materials, such as plastic or glass, might be used with the glucose sensing approach.	• Complicated machine-learning model required due to low strength signal. • High scattering
Mid Infra Red (MIR)	• Stronger glucose molecule absorption • Low scattering	• The light only partially penetrates tissue. • Noise in the signal because of blood composition.
Far Infra Red (FIR)/ Thermal emission spectroscopy	• It is not necessary to calibrate frequently. • Least susceptible to dispersion	• The material's temperature and thickness affect the radiation's intensity. • Precision issue in glucose measurement due to strong water absorption
Raman Spectroscopy	• Less susceptibility to water and temperature • High specificity	• laser radiation not suitable for CGM • Low SNR and susceptible to noise interference
Photo acoustic	• Easy-to-use sensor design • No tissue harm due to optical radiation	• Susceptible to acoustic noise, temperature, mobility, etc. • Conveys some noise from some blood components that don't contain glucose.
Polarimetry	• The laser intensity fluctuation won't significantly alter the predicted glucose levels.	• External laser source is necessary, and good eye alignment is necessary. • Sensitive to changes in temperature and PH
Reverse Iontophoresis	• Based on a straightforward electrode setup for enzymes • Accurate glucose measurement from interstitial fluid	• Calibration requirement • Not user-friendly solution due to the current going through the skin
Fluorescence	• Due to immunity to light scattering, very sensitive to the detection of glucose molecules • Due to recognizable optical characteristics, good sensitivity	• Very sensitive to pH and oxygen levels • short life spam
Bio impedance spectroscopy(IMPS)	• Low-cost solution • Easier for frequent measurement	• Sweating, movement, and temperature constraints • Extended calibration duration is necessary
Millimetre and Microwave sensing	• Deep penetration depth to detect glucose precisely • No risk for ionization	• Poor selectivity • Very sensitive to physiological factors including breathing, heart rate, and perspiration
Optical Coherence Tomography	• High resolution and good SNR • Not susceptible to the change in blood pressure or heart rate	• Glucose levels may fluctuate depending on skin and movements • Suffers from tissue inhomogeneity
Surface Plasma Resonance	• High sensitivity to detect small glucose molecules	• Lengthy calibrating procedure and large size • Sensitive towards change in temperature, perspiration, and movement
Time of flight and THz Time domain Spectroscopy	• High glucose molecule absorption • High dispersion	• A longer measuring time • Worse depth resolution
Metabolic Heat Conformation	• Uses the idea of well-known physiological characteristics to predict glucose levels.	• Sensitive to changes in temperature and perspiration
Electromagnetic sensing	• Inexpensive and readily miniaturized • No risk of ionization	• Dielectric constant-related lack of selectivity is mostly affected by other blood components. • More sensitive to even small temperature changes
Ultrasound Technology	• Dependable technique that doesn't significantly injure tissue cells • Extending below the skin or tissue for a long time	• limited precision hence multi-model approach utilized • Expensive measuring technique
Sonophoresis	• Favourable technique since there are no skin adverse effects. • Based on a well-used enzymatic technique	• Constraints of Environmental factors

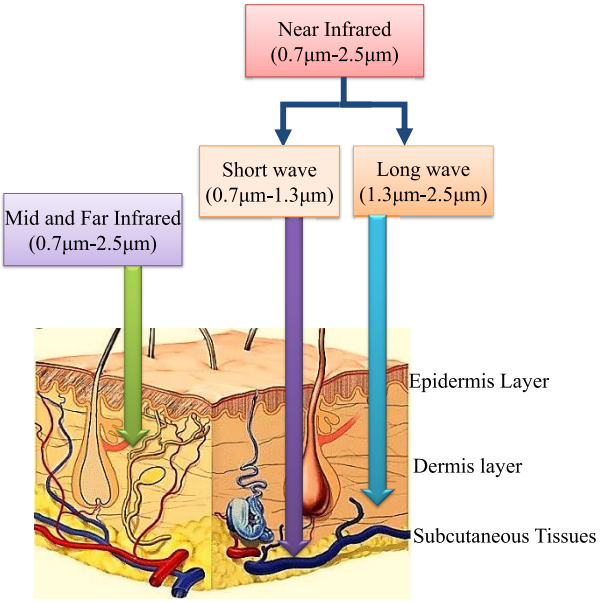

FIGURE 17. Penetration depth of various infrared signals in human skin [26], [33].

to some drawbacks, it could not be possible to consider commercialization [82].

3) BG MONITORING DEVICE WITHOUT PRICKING (IGLU)

The prototype intelligent glucometer device (iGLU) is employed to collect data. After processing the sensor data, a sophisticated computing model is explored. Three channels have been used to implement this prototype. It stores data on the cloud and employs remote data monitoring [83]. The explored prototype uses dual short wavelengths and a NIR Spectroscopy [84]. It collects the sensor data in three different ways. For optical detection, each channel includes a separate emitter and detector. An ADC with a suitable sampling rate has been used to handle the data for estimating BG values. Regression analysis examines the optimized model and calibrates and validates the data. Patients and physicians may utilize and keep an eye on the data that is kept in the cloud. Based on the values of the saved data, treatment may be offered. This is a low-cost solution with greater than 90% accuracy.

4) WHY ARE NIR METHODS PREFERRED OVER OTHER NONINVASIVE METHODS?

Numerous non-invasive techniques have been used to monitor glucose, including IMPS, NIR light, and PPG signal processing. However, other methods, except optical detection, haven't been able to deliver accurate measurements. One better option is PPG. Although the PPG signal changes depending on blood concentration [85], [86]. Accurate blood glucose predictions might not be helpful in exceptional cases. It means that the device should measure the precise BG of all people. Each person has distinctive characteristics for their sweat and saliva. As a result, it could not be an accurate method for measuring glucose. Other spectroscopy has also been used to measure glucose levels. Nevertheless, they cannot offer reliable, affordable, or portable predictions of body glucose. The optical detection of glucose utilizing long NIR waves has shallow penetration, making it unable to detect glucose molecules under the skin [73]. Small NIR waves have been considered a viable remedy for real-time glucose measurement [75], [87].

B. MID INFRA-RED (MIR) SPECTROSCOPY

Mid-infrared (MIR) spectroscopy provides high resonance of glucose molecules comparatively [88]. Due to the skin's propensity for greater water absorption, skin penetration depth is quite low. This method aids in the determination of ISF glucose in vivo. There have been various attempts to detect glucose accurately using samples from the palm and saliva.

C. PRIOR PPG APPROACH FOR BLOOD GLUCOSE MEASUREMENT

Through the PPG signal, the change in blood volume caused by the tissue's absorption of light has been discovered [86]. With the use of a light detector and pressure pulse, the change in blood volume has been detected [85]. It is possible that the glucose molecule is not the cause of the change in blood volume since it would be equivalent to a change in light intensity. This might lead to incorrect glucose readings. The difference between NIR and PPG is seen in Fig. 18. The NIR spectroscopy principle is the primary method of glucose measurement. The intelligent glucose measuring device iGLU is explored for accurate BG value prediction. There have been several studies for PPG signal-based glucose detection [89]. The patient's body data has been stored to assess the existence of glucose molecules using PPG. Different machine-learning algorithms have since been applied to estimate the value of body glucose [90]. Using ARMA models, the various parameters from a total of 70 healthy and diabetic participants have been considered for the prediction [91]. There have also been several other methods for estimating glucose utilizing PPG signals [92], [93], [94].

Photo-plethysmography (PPG), an optically based technology, is employed in cutting-edge medical treatment. It is a method of measuring glucose without pricking. The PPG signal is recorded using a sensor comparable to a pulse oximeter [86]. The detector, which will work in the NIR area, is constructed using a photo transmitter and receiver. A PPG signal may be measured at wavelength 920 nm by monitoring variations in light absorption. With each heartbeat, the veins in the finger expand and contract. Blood flow has been observed based on this mechanism, and glucose level estimation is explored. There is a way to measure blood sugar using an oximeter device and transmit the PPG signal for glucose monitoring system [89]. The signal is first acquired as a photo-current, which is then

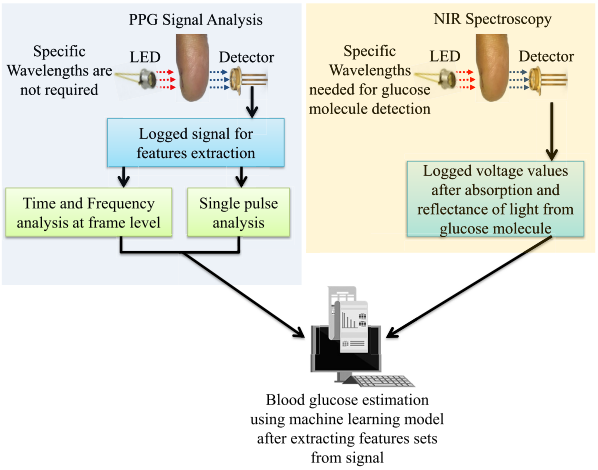

FIGURE 18. Comparison of PPG and NIR for glucose prediction without pricking [26], [33].

converted into quantifiable voltage values for filtering. Lab View calculates the body glucose status after processing the filtered signal. A prototype of a system that uses machine learning methods and a PPG system to assess body glucose statuses has been created without pricking [85]. In this prototype, a sensor, a training detector, and a signal conditioning part are utilized to formulate the PPG data. The functional relationship between the PPG waveform's shape and the BP and glucose levels may be established. PPG will adjust the light intensity depending on variations in blood volume. The analysis of PPG signals does not demonstrate glucose molecule detection. Consequently, the system's precision is restricted [26], [33]. Fig. 18 demonstrates the distinctions.

D. IMPS APPROACH

Dielectric spectroscopy is known as impedance spectroscopy (IMPS) [95]. Fig. 19 depicts the stages involved in impedance spectroscopy (IMPS). This method determines the skin's dielectric characteristics [96]. The skin is exposed to the current [97]. The impedance range is acquired as a result of the directed tiny current at various wavelengths [98]. The frequency range is 100 Hz to 100 MHz [99], [100]. Changes in sodium ions and potassium ions concentration will be reflected in changes in glucose concentration [89]. Thus, there will be a shift in the cell membrane potential differential [101]. As a result, the dielectric value will alter and forecast the human body's glucose level [102].

The detection of salivary glucose using a sensor of detecting enzymes in a cell has been investigated [103]. To detect glucose in human saliva, polypyrrole (PPy) supported with copper (Cu) nanoparticles on an alkali anodized steel (AS) electrode is available in [104]. Because each person's sweat and saliva have different qualities, a high accuracy level cannot be achieved using these procedures. This method cannot be used to monitor glucose in smart healthcare.

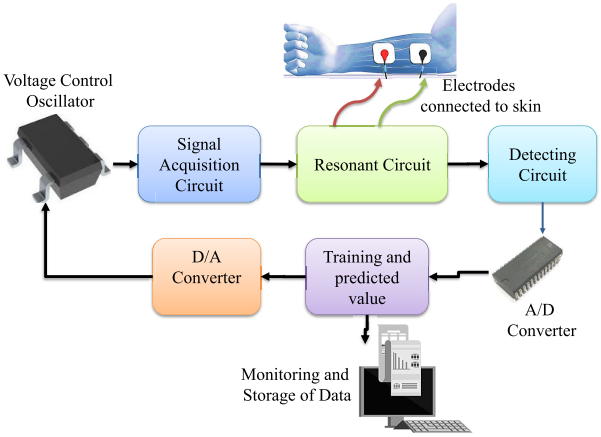

FIGURE 19. Representation of Steps of IMPS.

E. RAMAN SPECTROSCOPY

A glucose molecule's polarization will alter due to light's interaction with it [105]. Through the use of LASER light, this method makes it feasible for the solution's molecules to rotate and oscillate [106]. The molecule's vibration influences the scattered light emission [107]. This idea allows for predicting blood glucose levels as [108]. When compared to infrared spectroscopy, this method offers more precision [109]. Numerous studies using Raman spectroscopy have been conducted to detect glucose precisely. "In-vivo" measurement has also been used for the validation. Fig. 20 outlines the fundamentals of Raman spectroscopy, while Fig. 21 explains how to use it to measure glucose without using a needle.

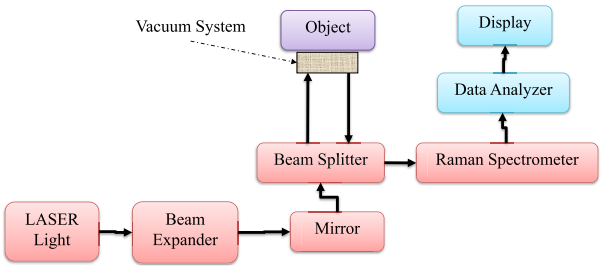

FIGURE 20. Building blocks of raman spectroscopy.

F. TIME OF FLIGHT AND THz DOMAIN

Time of Flight (TOF) measurements are used to estimate blood glucose levels during in vitro measurement [110]. A brief laser pulse is introduced into the sample to measure photon migration. While leaving the sample, this photon will encounter scattering and absorption phenomena. The optical analysis of the photons would be beneficial for accurate glucose measurement.

G. PHOTO ACOUSTIC SPECTROSCOPY

The photo-acoustic technique is the acoustic effect for assembling the acoustic strain wave from an object (direct

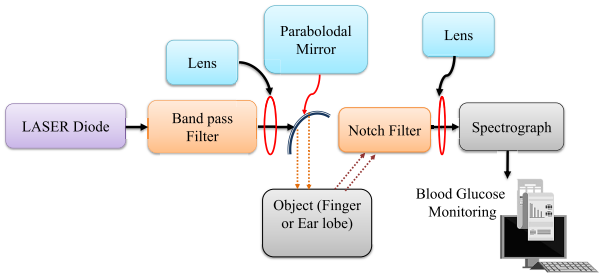

FIGURE 21. Noninvasive glucose measurement using raman spectroscopy.

Fig. 22) [111]. The estimate of blood glucose detection in this spectroscopic method is provided by the absorption of modulated light input [112]. According to its optical circumstances, an item absorbs high-intensity optical light [81]. This procedure enabled excitations of certain molecules based on their resonance frequencies [113]. The absorbed light is seen as heat, causing a rise in the sample's local temperature and thermal expansion [114]. The increase in volume creates acoustic pressure [115]. Through particular keen wavelengths that are vibrant for the vibration of glucose molecules, the resulting photoacoustic wave may be utilized to estimate the glucose concentration [116]. The glucose molecule modifies its properties at a certain resonance frequency. The acoustic waveform has changed [117]. Previously, optical light with a wavelength of 905 nm was utilized for excitation [118], [119].

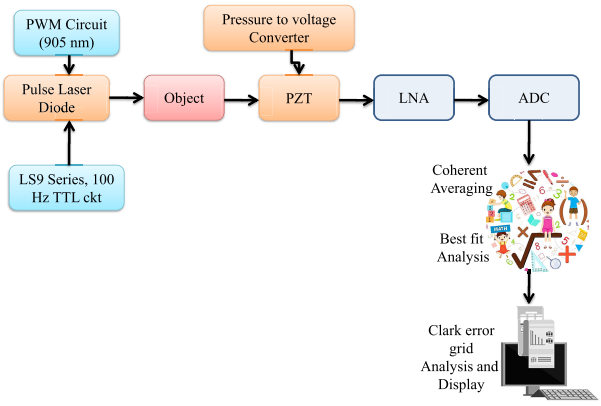

FIGURE 22. Photo acoustic spectroscopy.

H. CAPACITANCE SPECTROSCOPY

The inductor stray capacitance in the capacitance spectroscopy technique changes with body capacitance (Fig. 23) [120]. To gauge body glucose levels, one uses the body capacitance [121]. A flexible inductor-based sensor uses the coupling capacitance concept to detect body glucose. The inductive sensor and skin of the body do not come into contact in this method due to the current [122]. Depending on body glucose, the inductive sensor's stray capacitance will change. With this method, the impact of fat and muscle on blood glucose will be minimal [123].

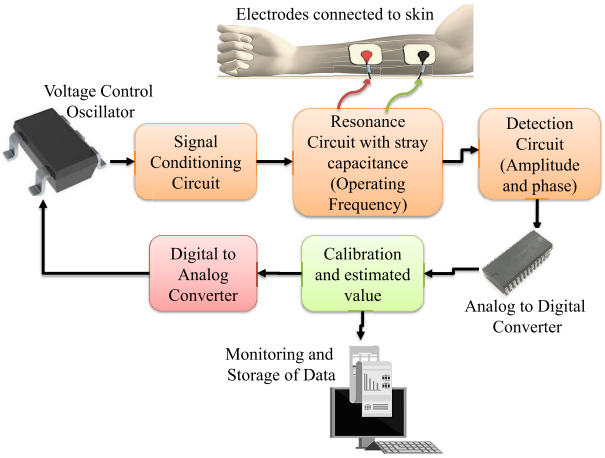

FIGURE 23. The typical steps of capacitance spectroscopy.

I. SURFACE PLASMON RESONANCE (SPR)

The Surface Plasmon Resonance (SPR) uses an electron oscillation technique at the metal and dielectric contact to detect glucose [124]. It primarily picks up changes in refractive index before and after analyte contact. Due to its mobility, the optical fibre-based SPR is employed for glucose PoC monitoring.

J. RF & MICROWAVE SENSING APPROACH

The fluctuation in the s-parameters response in the RF method directs the difference in body glucose [125], [126]. Fig. 24 illustrates specific stages of this approach. The output is determined via the antenna or resonator [127], [128]. They observe the transitions in dielectric constant value via the dispatch [129]. Through the antenna or resonator, the change in resonance frequency spectrum may be used to detect changes in the dielectric constant [130], [131]. Blood dielectric constant changes according to the distinct blood glucose levels. The human finger is a suitable measuring object, but the measurement accuracy is affected because of method limitations and constraints. These include the consistency of the skin, fingerprints, pressure exerted by the object during measuring, and object placement on the sensor [132].

Reduced flexible antenna size prevents installation issues and skin-crumbling effects on the signal acquisition region. Furthermore, an effective antenna sensor design is necessary for continuous diabetes monitoring. An adjustable antenna detector positioned within the thumb spica splint glove has created a continuous glucose monitoring device [133].

K. OCULAR SPECTROSCOPY

Through the tears, glucose concentration is assessed using the Ocular Spectroscopy method. To forecast the body's glucose content, a certain lens is used [134]. The lens has a hydrogel wafer put on it. This wafer's 7 μm thickness was achieved using boronic acid preparation. After the wafer has been placed on the lens, optical rays are introduced to the lens. The

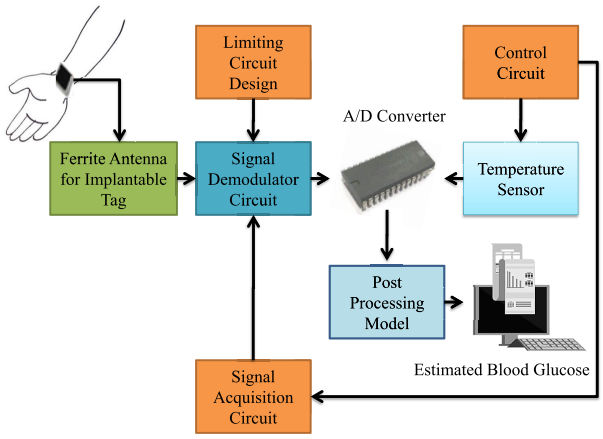

FIGURE 24. Glucose measurement using RF sensing technique.

wavelength of the reflected light will then alter. A difference in light range will be interpreted as a difference in the amount of glucose present in tears.

L. IONTOPHORESIS

A tiny electric current diffusely flows through the skin during the iontophoresis or ionization procedure. For the same procedure, three electrodes are employed [135]. The various behavioral electrodes get a tiny voltage through the electrodes. Glucose is transported to the cathode during this process. The working electrode may perform the biosensing function by producing current during involved voltage via electrodes. This biosensor measures the body's glucose passively. The wrist is commonly used for measuring [136].

M. OPTICAL COHERENCE TOMOGRAPHY

The reflectance spectroscopy principle is the foundation for the optical coherence tomography method. In this method, the sample (which is positioned in an interferometer) is stimulated using low coherent light. A moving mirror is set up in the reference arc of an interferometer. Conversely, a photodetector is positioned to pick up the interferometric signal. The light in this signal has been reflected and backscattered. We were able to obtain excellent 2-D photos thanks to this approach. In interstitial fluids, the glucose concentration rises as the refractive index rises. The scattering coefficient changes as the refractive index changes [107]. So, indirectly, the scattering coefficient and glucose levels are related.

N. POLARIMETRY

With greater precision, the polarimetry technique is frequently utilized in clinical laboratories. For glucose monitoring, the optical linear polarization-based method is employed [137]. This method is often based on the trajectory of a vector caused by the consistency, temperature, and BG content. Polarized light is passed through the path, retaining glucose molecules due to glucose prediction. Increased dispersal via the skin makes it feasible for the beam to depolarize. A polarimetric trial is performed using the eye to overcome this limitation. Due to the blood's temperature and pH level rotation, this procedure is completely affected [138]. The measurement process is represented in Fig. 25.

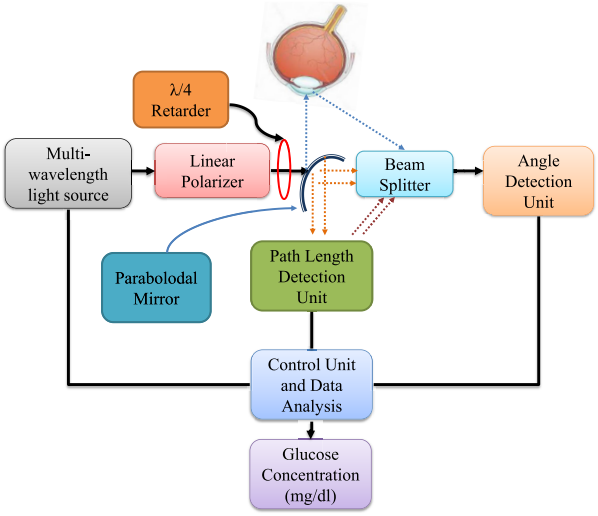

FIGURE 25. Non-invasive glucose measurement using polarimetry.

O. THERMAL EMISSION SPECTROSCOPY

The thermal emission technique is based on the body's infrared wave, which is created naturally. The body's glucose level will influence the IR waves that are released. The tympanic membrane of the human body's typical mid-IR emission is modified by tissue emitting. This method's selectivity is identical to that of absorption spectroscopy. This method allows for determining glucose through the boneless part of the body. A similar approach is used for measuring glucose in the paper [139]. Measuring heat emission from the tympanic membrane might offer an accurate and acceptable practical solution in the clinical setting.

P. ULTRASOUND

Like the reverse iontophoresis method, the ultrasound approach relies on lower-frequency segments to remove molecules from skin [140]. Additionally, it has greater skin permeability than reverse iontophoresis and is similar to sonophoresis. For glucose to be taken externally via the skin, an ultrasonic exposure lasting a few minutes to several minutes is required. Few attempts have been made to utilize this kind of technology, and no commercial devices have been developed.

Q. METABOLIC HEAT CONFORMATION (MHC)

MHC procedure aids in measuring the value of glucose combined with metabolic heat and oxygen levels, as well as numerous physiological parameters consideration [141]. The computing prototype for metabolic energy preservation is altered by considering various physiological characteristics, including blood flow volume, heat metabolic rate, oxygen

saturation in the hemoglobin, and pulse rate. In tests on people, this technique demonstrated high repeatability and passable accuracy.

R. FLUORESCENCE

The Fluorescence approach relies on UV radiation's ability to excite blood vessels at certain frequency ranges [142]. The next step is the detection of fluorescence at the designated wavelength. Using fluorescence through tears, glucose may be detected. Visible light diffraction was used for this purpose. A UV LASER excites the glucose solution medium at 380 nm. Estimates of fluorescence, which is directly related to glucose content, were made. The signal is unaffected by changes in light intensity across the surroundings while using this approach.

S. KROMOSCOPY

The Kromoscopy method uses four distinct wavelengths and diverse spectroscopic responses to NIR light [143]. It uses a multi-channel method with overlapping band-pass series filters to identify the glucose molecule. In this procedure, the sample is exposed to IR radiation, which is then distributed among four detectors equipped with band-pass filters. Each detector will pick up the light from the tissue's identical structural features. The glucose concentration was then determined using a complicated vector analysis.

T. ELECTROMAGNETIC SENSING

Changes in blood glucose content allow the Electromagnetic Sensing technique to detect differences in blood sample conductivity [144]. Every time the blood glucose concentration changes, an electromagnetic sensor will monitor the alternation of the electric field. This approach makes use of the blood samples' dielectric parameters. The electromagnetic sensing frequency band lies between 2.4 and 2.9 MHz. The glucose molecule is most sensitive at a certain frequency that is ideal for the medium's temperature. An enduring, positively discreet, and semi-invasive implant-type electromagnetic sensor is investigated for continued body glucose monitoring that can follow differences in the glucose level [145].

U. BIOIMPEDANCE SPECTROSCOPY AND DIELECTRIC SPECTROSCOPY

The conductivity and permittivity of the membrane of red blood cells can be used to monitor blood glucose fluctuation [146]. Bio-impedance spectrum measurements are made in the 0.1 to 100 MHz frequency range. It aids in determining the resistance to electric current flowing through human biological tissue. The alteration of plasma glucose would enable the alteration of potassium and sodium to have the alteration of conductivity of the red blood cell membrane. The multi-sensor technique is typically used with this spectroscopy for accurate glucose measurement to monitor sweat, moisture, movement, and temperature. A bio-impedance transducer is proposed for noninvasive monitoring of insulin bio-availability following subcutaneous injection. The local impedance shift caused by the medication evaporating from the injection volume is used to measure insulin bio-availability indirectly. Employing a second-order polynomial function, an accuracy of $9\mu l$ was accomplished in a healthcare application environment. The anticipation was $4.2\mu l$, which is much less than the usual amount of one insulin unit ($10\mu l$) [147].

V. REVERSE IONOSPHERESIS METHOD

A tiny DC current is carried from the anode to the cathode on the skin's surface to create interstitial fluid (ISF). Iontophoresis is used for ionized molecule penetration at the skin's surface by such a low current [148]. Electroosmotic flow over the skin carries the electric potential from the anode and cathode. This would make it possible to extract the molecules via the skin as the glucose molecules are transported toward the cathode. Through the oxidation process, the enzyme technique aids in detecting the concentration of glucose molecules. The technique is well-liked and has a decent chance of measuring glucose levels accurately.

W. SONOPHORESIS

The Sonophoresis method is established on the cutaneous permittivity of the interstitial fluid (ISF) [149]. Additionally, the enzyme technique is used to test glucose. Glucose molecules have been placed on the skin's surface using a low-frequency ultrasonic pulse. The ISF's cutaneous permittivity is raised to enable glucose at the skin. The stratum corneum experiences contraction and expansion, which opens the ISF channel. This approach has been used in certain attempts to detect glucose, although it has been noted that it may be more useful for medication administration than for glucose monitoring.

X. OCCLUSION SPECTROSCOPY

The approaches based on occlusion spectroscopy rely on the idea that light scattering is inversely proportional to glucose content [150]. By exerting pressure with a pneumatic cuff, the flow is stopped for a brief period of time. The pulse brought on by the pressure excursion would cause the blood volume to alter. The light is passed through the sample, and the intensity fluctuation in the received light determines the glucose concentration. The brief delay in blood flow increases the received signal's SNR value. As a result, there would be an improvement in sensitivity for glucose detection and strong resilience for precise glucose measurement.

Y. SKIN SUCTION BLUSTER (SSB) TECHNIQUE

The Skin Suction Bluster method takes advantage of the idea of blister formation using vacuum suction over a small region of skin [151]. On fluid that has been taken from the blister, glucose is measured. Although it contains fewer glucose molecules than plasma, it is still enough for measuring

glucose. This procedure is painless, well-tolerated, and has a low risk of infection. The HbA1c value, which indicates the three-month average glucose value, is always helpful to diabetic patients.

Z. MULTIMODAL APPROACH BASED MEASUREMENT

For increased-level reproducibility of blood glucose measurement without pricking, 2 concurrent spectroscopy merging IMPS and mNIR spectroscopy is investigated [152]. To overcome each technique's limitations, these two approaches are blended [153]. To estimate the glucose level, an IMPS-based design predicts the skin dielectric constant using a resonant circuit [154]. The mNIR spectroscopy technology is employed to increase NIR spectroscopy accuracy. Three wavelengths—850, 950, and 1300 nm are employed in this approach [155]. IMPS and mNIR are merged by an ANN using a processor to provide precise and accurate measurements [78]. As a result, multimodel techniques have been researched in the literature for accurate glucose measurement (Fig. 26) [82], [156].

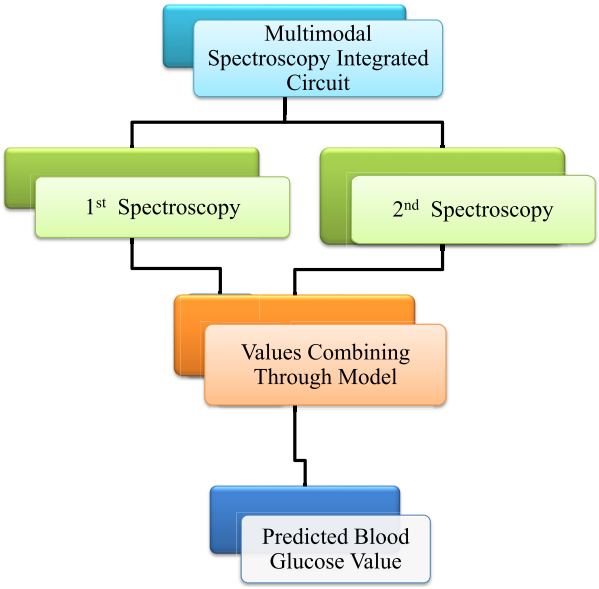

FIGURE 26. Multimodal design established non-invasive body glucose estimation.

V. CALIBRATING AND POST-PROCESSING METHODS FOR NON-INVASIVE BODY GLUCOSE LEVEL MONITORING

The post-processing and calibration methods are presented in this Section. The methods are used in various frameworks or systems for non-invasive BG level measurement.

A. AFTER SENSING TRAINING METHODS

An increased degree of precision and noise deduction from the acquired signal has been achieved by applying several calibration techniques. The model for errorless continuous monitoring is designed using these post-processing approaches [167], [168].

1) PERFORMANCE OPTIMIZATION USING SIGNAL ACQUISITION

The variance of random noise has been reduced using an adaptation of the coherent averaging approach [169]. By averaging N different individual samples from continuous frames, the influence of noise is reduced [170]. To boost SNR, frames with the highest count have been selected for averaging [171]. This suggested coherent averaging has been employed extensively through MATLAB and the coherent averaged signal collected. It has been suggested to calibrate measured data using the Golay code. Golay code implementation has resulted in the filtering or elimination of odd-measured data [169], [172], [173].

2) COMPUTATION MODELS FOR GLUCOSE MEASUREMENT

Several researchers have suggested the regularized least square regression model for measurement [174]. Photoacoustic signals are used to determine the estimated value. The calibration for estimating glucose concentration is done using these photoacoustic signals [175]. A multivariable linear regression model can be used to achieve this [176]. It is suggested to use a post-processing SVM approach to achieve high levels of accuracy [177]. A glucose monitoring system's SVM is a superior alternative for accurate measurement [178]. The use of ANN for data merging has also been suggested [179]. The suggested neural network model combines the measured data from several approaches [180]. The DSP processor has been involved in implementing artificial neural networks [78], [154]. To aggregate and calibrate data for the final estimated glucose concentration, the proposed computing model has been employed [181]. The implanted device, which contains low-price and power-optimized system networking and cutting-edge computing for BG monitoring, has to be implemented as a portable commercial device. An explored optimized neural network is used to illustrate a novel deep learning model [182]. An optimized non-invasive system design, a NIRS technology with specified wavelengths, and physiological characteristics are used to forecast the precise glucose value. Using the DNN model, the proposed system demonstrated an accurate model with MARD and AvgE of 12.50% and 12.10%, respectively. R2 coefficient of determination was found to be 0.97 [183].

B. MODEL VALIDATION METRICS

The calibration procedure is employed for measurements to provide accurate blood glucose values [184]. The measured glucose concentrations are compared to the obtained glucose concentration values [185]. The CEG analysis has been regarded as the most accurate measuring method for evaluating the performance of any equipment [186]. The process flow is explored in Fig. 27.

TABLE 2. Techniques comparison with prior works [26], [33].

Prior Work	Sensing Technology	Response	Distinctive wavelength	Estimating range	Linearity (%)
Kundu, et al. [157]	Opto-chemical	-	-	70-400 mg/dl	80
Sun, et al. [158]	NIR	-	NIR	60-450 mg/dl	95
Wei, et al. [159]	PPG	-	-	-	86
Singh, et al. [160]	Optical	-	-	32-516 mg/dl	80
Mayuko, et al. [161]	NIR Images	-	700-1650nm	-	-
Lee, et al. [162]	PPG	NIR	550nm-1550nm	-	75
Song, et al. [79]	Impedance and Reflectance	NIR	850-1300 nm	80-180 mg/dl	-
Pai, et al. [163]	Photoacoustic	NIR	905 nm	upto 500 mg/dl	-
Dai, et al. [164]	Bioimpedance	-	-	-	-
Beach, et al. [165]	Biosensing	-	-	-	-
Ali, et al. [88]	Transmittance and Refraction	NIR	650 nm	upto 450 mg/dl	-
Haxha, et al. [76]	Transmission	NIR	940 nm	70-120 mg/dl	96
Jain, et al. [166]	Absorption and Reflectance	NIR	940 nm	80-350 mg/dl	90
Jain, et al. (iGLU 1.0) [29], [33]	Absorption and Reflectance	NIR	940 and 1300 nm	80-420 mg/dl	95
Jain et al. (iGLU 2.0) [26], [30]	Absorption and Reflectance	NIR	940 and 1300 nm	80-420 mg/dl	97

TABLE 3. Comparison of prior works analytically with parameters [26], [33].

Works	R value	MARD (%)	AvgE (%)	MAD (mg/dl)	RMSE (mg/dl)	Samples (100%)	Used model	Measurement sample	Device cost
Lee, et al. [162]	-	-	-	-	9.46	A&B	Human	Blood	Moderate
Kundu, et al. [157]	0.78	-	-	-	-	-	Animal	Blood	Costly
Mayuko, et al. [161]	-	-	-	-	15.24	-	Human	Image	-
Sun, et al. [158]	-	7.31	-	-	21.06	A&B	Human	Blood	-
Wei, et al. [159]	0.87	11.33	9.8	-	-	A&B	Human	Blood	-
Singh, et al. [160]	0.80	-	-	-	-	A&B	Human	Saliva	Cheaper
Song, et al. [79]	-	8.3	19	-	-	A&B	Human	Blood	Cheaper
Pai, et al. [163]	-	7.01	-	5.23	7.64	A&B	in-vitro	Blood	Costly
Dai, et al. [164]	-	5.99	5.58	-	-	-	in-vivo	Blood	Cheaper
Beach, et al. [165]	-	-	7.33	-	-	-	in-vitro	Solution	-
Ali, et al. [88]	-	8.0	-	-	-	A&B	Human	Blood	Cheaper
Haxha, et al. [76]	0.96	-	-	-	33.49	A&B	Human	Blood	Cheaper
Jain, et al. [166]	0.90	5.20	5.14	5.82	7.5	A&B	Human	Blood	Cheaper
Jain, et al. (iGLU 1.0) [33]	0.95	6.65	7.30	12.67	21.95	A&B	Human	Blood	Cheaper
Joshi et al. (iGLU 2.0) [30]	0.97	4.86	4.88	9.42	13.57	Zone A	Human	Serum	Cheaper
Joshi et al. (iGLU 3.0) [156]	0.98	5.34	5.64	8.3	12.7	Zone A	Human	Capillary & Serum	Cheaper

C. ANALYSES OF REAL-TIME PRECISION USING THE CEG METHOD

The clinical accuracy for biomedical applications has been examined using the Clarke Error Grid as a benchmark tool. It corrects for the physiological time delays involved in measuring body glucose and offers a point and rate accuracy prediction. The design and improvement of precise biomedical equipment will be made substantially simpler by utilizing Clarke error grid modeling. C.G. Clark created this approach in 1970 to assess the reliability of clinical trials and aid in comparing predicted blood glucose levels to blood glucose values obtained using more traditional methods. Diabetes treatment began to take notice of the Error Grid Analysis in 1987. Zones A, B, C, D, and E divide the grid's five separate zones. If the data fall into either zone A or B then the device represents clinical accuracy at the desired level. It means that the particular device, which is on trial, that can be considered for clinical use. The Beckman analyzer has accurately or adequately forecasted the glucose findings. Zone C values could cause unnecessary adjustments, resulting in a bad result. If the readings are in zone D, it denotes a dangerous failure to measure glucose through the technology. Zone E displays the ''incorrect treatment'' [187]. The different zones are represented using CEG analysis in Fig. 28. CEG analysis is visualized for the representation of accuracy. This represents the correlation between the actual glucose value and the predicted glucose value for every instance.

VI. COMMERCIAL DEVICES RELATED TO GLUCOSE MONITORING

Numerous non-invasive glucometers needed for correct treatment are available on the market (e.g., the Freestyle Libre sensor and SugarBEAT from Nemaura Medical). Similar to

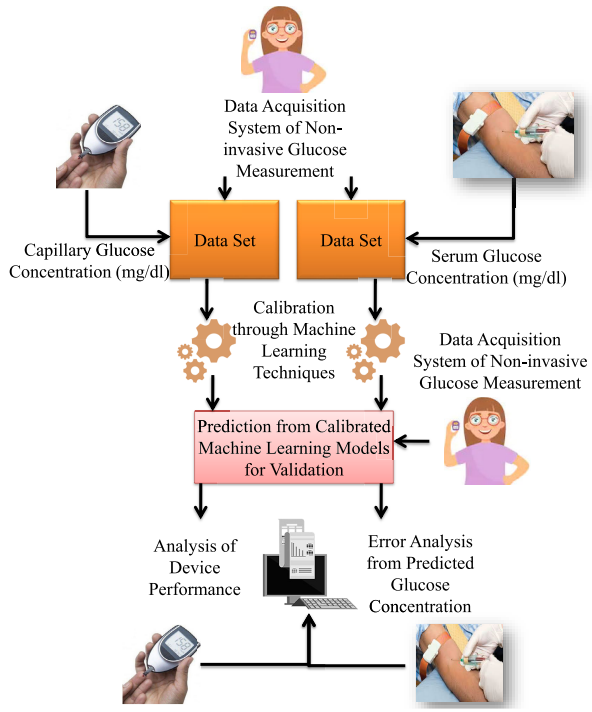

FIGURE 27. Metrics model for system precision measurement.

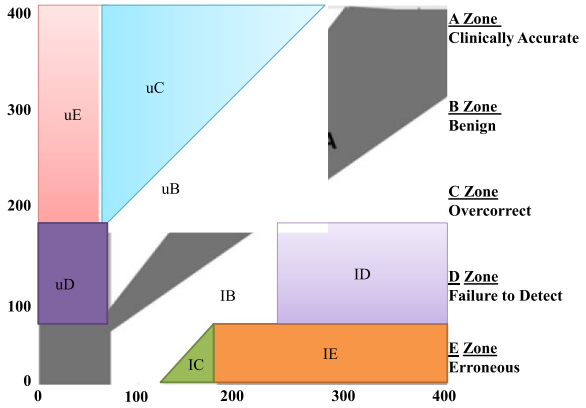

FIGURE 28. Clarke error grid analysis.

skin patches, they would include a daily disposal function and adhesive to enable continuous body glucose monitoring. Since most commercial goods cannot monitor glucose accurately, they are often used to treat diabetes. Products like DiaMon Tech, Glucowise, Glucotrack, Glutarac, and CNOGA medical equipment are available. Although Glutrac is a clever medical equipment, it accurately measures blood sugar. While the accuracy is still unacceptable, the cost is greater. The CGM has been implemented using the non-invasive Omelon B-2 stripless device. Glucosense, a fluorescence technique-based product, has been developed to monitor glucose levels continuously. Texas University created a flexible textile-based biosensor for measuring glucose levels. Every accessible technology has poor accuracy and is expensive.

A. COMPARING WEARABLE AND NON-WEARABLE GLUCOSE MONITORS

In the literature, both non-wearable and wearable systems have been tried for glucose monitoring. Most non-wearable methods rely on various spectroscopies, including photoacoustic, Raman, etc. The semi-invasive implanted devices are mostly biosensors in nature. Wearable devices include sweat patches, glucowatches, and smart contact lenses. LifePlus has created a wearable, non-invasive CGM device that is being considered for public purposes. Many non-invasive types of equipment are portable and useful for routine monitoring [13]. Continuous glucose monitoring is more adequate if blood glucose levels can be measured daily. Therefore, wearable technology has more cutting-edge solutions than non-wearable technology.

B. CONSUMER PRODUCTS FOR NON-INVASIVE GLUCOSE MEASUREMENT

There are several goods available such as GlucoTrack®, glucometer from Labiotech [188], and similar methods are likewise expensive and have accuracy problems. The glucowise is yet another non-invasive device for continuous glucose measurement from Medical Training Initiative (MTI)™. Additionally, 2M Engineering has created the non-invasive solution based on Raman scattering spectroscopy [189]. These devices are uncommon because of their high price and high accuracy. In addition, the high degree of glucose-measuring accuracy, Glucotrack™ has been devised by integrity applications Ltd. [190]. Three non-invasive glucose monitoring techniques were employed in succession: electromagnetic, thermal emission, and ultrasonic spectroscopy. Combining three methods provided precision and accuracy comparatively [191]. The results of comparing many consumer goods for noninvasive glucose measurement are summarized in Table 4. Different glucose monitoring-based commercial devices were not only explored to represent the corresponding methodologies and approaches but the devices are represented with their observations and limitations as well. The technical details of the methodologies used have already been explained, which were used to develop the commercial devices of glucose monitoring.

VII. METHODS FOR GLUCOSE LEVEL CONTROL AND CONSUMER GOODS

Different models for diet regulation have been created utilizing different glucose-insulin balance factors. To predict the amount of glucose consumed by diabetes patients, the metrics primarily comprise NHGB, RTG, peripheral glucose utilization, and glucose absorption rate. These are helpful variables for calculating blood glucose levels using the right insulin dosage and a predetermined eating schedule. The blood glucose-insulin control model was created to balance the body's glucose and insulin levels in diabetes patients using the right medications [192].

TABLE 4. A comparative perspective of a specified commercial product for noninvasive glucose monitoring.

Organization	device	Technique	Sample	Overview	Image
Cygnus Inc. (USA)	GlucoWatch G2 Biographer	Reverse iontophoresis	Wrist skin	It would be worn as a watch with a disposable component, an auto sensor that would be connected to the back of the wearer's shirt and make skin-to-skin contact to check their blood sugar continuously. This was approved by the FDA on August 26, 2002.	
CNOGA (Israel)	Combo glucometer	Tissue photography analysis	Finger	This device can quickly analyze a variety of bio factors via tissue photography analysis from fingertip capillaries. This is CE approved but still pending for FDA approval.	
Pendragon Medical (Switzerland)	Pendra	Impedance Spectroscopy	Wrist Skin	The erythrocyte membrane's ability to transport sodium aids in measuring glucose; changes in transmembrane sodium fluxes are caused by impedance fields, which are recognized by the device to provide the final glucose result. This is not clinically validated.	
OrSense Ltd. (Israel)	OrSense NBM-200G	Occlusion Spectroscopy	Fingertip skin	It is based on the optical principle of a finger coupled to a sensor probe with a ring shape. The probe comprises a light source and detector for the red/near-infrared (RNIR) spectral band. It has pneumatic cuffs that provide systolic pressure and an optical signal for measuring blood sugar. This is not clinically validated.	
C8 Medisensors (USA)	C8 Medisensor Glucose detector	Raman Spectroscopy	Fingertip skin	This method is based on the detection of dispersed light after a monochromatic light source passes through the skin. The colours produced by Raman spectra aid in pinpointing the chemical composition of the glucose molecule. FDA approved it in 1999.	
Integrity Applications (Israel)	Glucotrack	Combining of Electromagnetic, ultrasonic and Thermal	Ear lobe tissue	Three distinct methods are combined in this device to boost precision and accuracy. It is approved by CE and KFDA. It is in the early stage of FDA approval.	
Tech4Life Enterprises (USA)	Non invasive glucometer	Infrared Spectroscopy	Finger	Patients with hyperglycemia or those who are pre-diabetic are benefited from routine monitoring of accurate blood glucose measurements every 30 seconds. This is not clinically validated.	
MediWise Ltd. (United Kingdom)	Glucowise	Radio Wave Spectroscopy	Forefinger skin/Earlobe	This wireless non-invasive device measures glucose levels immediately. For the purpose of detecting blood glucose, it is based on electromagnetic waves with certain frequencies. It makes use of a thin-film metamaterial layer to improve penetration for accurate glucose measurement. FDA approval is still awaited	
Nemaura Medical (UnitedKingdom)	SugarBeat	Reverse iontophoresis	Arm, Leg and abdomen	This painless, continuously accurate blood glucose monitor has been demonstrated to be effective. SugarBEAT® offers needle-free, real-time glucose measurement. Typically, calibration requires a single finger-prick test. When a new patch is needed, a single finger prick is performed. CE-mark approved. FDA approval is still pending.	
Abott Ltd. (USA)	Free Style Libre	Glucose oxidase method	Fore-arm skin	To measure glucose levels through interstitial fluid, enzyme glucose-sensing technology is employed. Through the use of a sensor, the glucose oxidase technique allows for the measurement of both glucose and an electrical current proportional to the concentration of glucose. It is recently FDA approved.	
VivaLyf (India)	EzLyf	Near Infra Red	Finger	A beam of light would interact to glucose molecules of the finger for absorption measurement then glucose is measured through the spectrum between the molecules and the wave. FDA approval is still pending	

A. DIABETES CONTROLS TECHNOLOGIES

The decision models for deliverable insulin administration are provided to demonstrate the blood regulation factors. A model of insulin secretion and glycemic profile has been proposed for type 2 diabetic patients [193], [194]. With the aid of individuals who do not have diabetes, the differential equation with the delay model is used to create the non-linear model [195]. A popular ''Uva/Padova Simulator'' that had received FDA approval for the required clinical studies was also investigated. The parameters are derived for virtual type 1 diabetic patients [196]. Non-diabetic participants have experienced the OGTT [197]. To describe the approach using time monitoring, data from people with type 1 diabetes were gathered. For type 1 diabetic patients, the model is mathematically provided for BG value estimation in the PP mode [198], [199]. Using data from two days of clinical observations, the decision model for BG-insulin equilibrium over a more extended time is investigated [200]. For the goal of routine glucose monitoring, a meal identification algorithm was created for T1DM patients. The technique incorporates a mathematical model for bolus meals that delivers insulin and glucose [201]. To obtain the values for the inconsistent condition extent algorithm, diabetic and healthy patients were considered. An intelligent PID controller (iPID) was created for a person with type 1 diabetes after the food intake schedule was analyzed in the absence of food profiles to keep the balance of blood sugar level profiles [202], [203].

B. GLUCOSE CONTROLS CONSUMER PRODUCTS

When insulin secretion is not synchronized through the pancreas for proper glucose consumption. Then, glucose levels would be imbalanced. Anyone with type 1 diabetes must be prepared for insulin treatment. Patients who are going to be treated using insulin injections daily may also use an insulin pump. Insulin can also be administered via self-injection. Throughout the day, an insulin pump continuously administers short-acting insulin. The insulin pump has eliminated the need for long-acting insulin. A pump also helps to lower blood sugar levels and replaces the need for many daily injections and continuous insulin infusion. Numerous varieties of insulin doses are already in demand as commercial goods, namely insulin pumps from Animas, Medtronic, Roche, Tandem, and Omnipod. With regard to their enhanced features, these insulin pumps are more sophisticated than one another. To have greater control over the glycemic profile, a state-of-the-art technique for measuring glucose is compared in Table 5.

VIII. MEASUREMENT AND CONTROLS OF GLUCOSE LEVELS: IOMT PERSPECTIVES

The requirement of an intelligent and automated healthcare system for diabetes patients in smart cities and smart villages to improve the quality of life [209], [210]. Continuous monitoring for emergency care, ambient intellect, & QoS for an appropriate PoC means are characteristics of smart healthcare systems [211], [212]. For diabetics, accurate and non-invasive glucose measurement is necessary, as well as the ability to save data utilizing IoMT for effective therapy [27]. Traditional glucose measurement techniques have limited capabilities and cannot support patients at remote locations. The diabetic individual would like the ability to store their data on a cloud server and regularly check their glycemic profile during the day. The point-of-care therapy for those with diabetes would be possible with regular monitoring, thanks to the smart healthcare system.

The virtual paradigm has enabled smart healthcare to connect persons to physicians at remote locations for quick remedy & treatment [209]. Using modern healthcare, consistent monitoring of critical problems provides appropriate treatment. Smart healthcare can improve service quality while lowering costs with the active assistance of remote healthcare solutions. The intelligent sensors would continually collect patient data and assist in storing it in a cloud data center. Additionally, it is helpful for data analysis and the simple information interchange between patients and doctors via mobile applications. The healthcare real-time system is successfully employed to apply intelligent algorithms to meet the many difficulties of the healthcare industry.

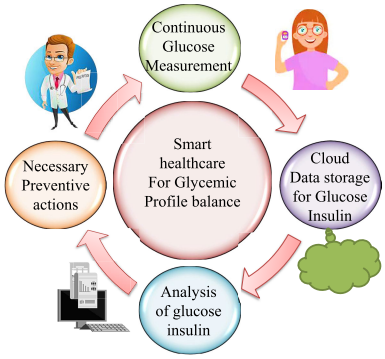

FIGURE 29. Diagnosis and management of blood sugar in a smart healthcare system.

The diabetic patient's diets may be planned with glucose management prescribed from a dietitian along with continuous glucose monitoring. To facilitate the CGM, the proposed device should be precise, affordable, and easy to use [29], [33]. The serum glucose measurement is always considered more accurate than capillary analysis. Therefore, the continuous monitoring solution for quick serum glucose measurement is preferred for smart healthcare. The novel serum glucose monitoring-based device is a portable solution incorporating IoMT to continually record glucose data in the cloud. Patients located at remote locations might benefit by analyzing the data from medical professionals. The continuous glucose monitoring in smart healthcare is demonstrated in Fig. 29. Remote health monitoring is the need of diabetic patients and helps patients to long-term complications such as renal disease, CVD, sexual problems,

TABLE 5. A comparison of a few state-of-the-art methods for measuring blood sugar.

Technique	Sample	Summary	Findings
photoplethy--smography (PPG) [86]	Finger	By using machine learning algorithms to extract PPG signal properties, it is possible to predict blood pressure, blood sugar, and systolic and diastolic values.	ML models applied where random forest technique has best prediction results as R^2_{SBP} = 0.91, R^2_{DBP} = 0.89 and R^2_{BGL} = 0.90. CEG showed 80% values are in A zone
photoplethy--smography (PPG) [162]	Finger	Multi-channel PPG along with Pulse Arrival Velocity (PAV) have been implemented for measurement	The dual-channel PPG with PAV's amplitude ratio produced the most accurate estimates of blood sugar level.
ATR spectroscopy [204]	oral mucosa inner lips	greater measurement repeatability and spectra about 1155 cm^{-1} for various blood glucose levels during fasting and before fasting were obtained using a multi-reflection prism and greater sensitivity.	the R^2 is above 0.7. The Sensitivity is very low, and all the measured values are in A region
Opto-chemical sensing [157]	Direct in the blood	The sensor is built on a basic optical fibre that may be introduced into the bloodstream using a catheter.	The device is evaluated to measure glucose in vivo using a non-human model. The sensor has a detection limit of 50.89 mg/dl and glucose sensitivity of 0.0354 a.u./mg.dl.
Millimeter, NIR wave [158]	Body object	Analysis of data from a multisensor network that combines the results of a random forest machine learning (ML) framework with information from supplementary sensors including mm-wave, near-infrared, and others.	The model predicts glucose with MARD, and RMSE values are high. The CEGA shows the model's predictions fall within the boundaries of Zone A, which is a clinically acceptable range.
Optical Coherence Tomography [205]	Fingertip	It measures the optical rotation angle and depolarization index for aqueous glucose solutions with low and high scattering, respectively. Angle value increases as glucose value increases, although the depolarization index drops.	The correlation factor has a value of R^2 0.9101. The average deviation is around 0.027.
Contact lenses fluorescence [206]	Tears	Making a soft, intelligent contact lens that uses transparent, flexible nanostructures to fully integrate glucose sensors, wireless power transfer circuits, and display pixels to show sensing signals in real-time.	The use of smart and soft lenses would enable real-time wireless glucose monitoring in tears.
IMPS and mNIRS [78]	Left Hand and wrist Hand	IMPS and mNIRS use the indirect dielectric characteristics of the surrounding tissue around blood and the optical scattering characteristics of glucose itself in blood, respectively, the proposed IC can remove various systemic noises to enhance the glucose level estimation accuracy	8.3% - 15.0% mean absolute relative differences (mARD) using IMPS and 15.0–20.0% using mNIRS have been reported for the normal range of blood glucose levels. From CEG analysis, all of the measurement results are clinically acceptable of Zone A and 90% of total samples can be used for clinical treatment
Microwave Detection [207]	earlobe	The absorption spectrum of microwave signal helps to measure using two antennae. The sine wave of 500 MHz is for blood glucose measurement.	It can measure BG up to 500 mg/dl. It has a mean standard deviation (MAD) of 0.5226 while the minimum SD value is 0.04.
PPG [93]	Finger	AI was used with a cell phone camera to anticipate blood sugar levels. First, the incorrect data was isolated, and any type of training wasn't needed for the entire system.	The prototype could measure glucose in the normal range. The results show overall accuracy at the desired level
MEMS [42]	Finger	It is a minimally invasive procedure called e-Mosquito that uses a micro-actuator made of shape-members alloy (SMA) to collect blood samples. It is regarded as the first wearable technology to automatically take blood from a patient and analyze their blood glucose levels.	The method provided good linear correlation in Conventional flow and the e-Mosquito prototype.
Transmission spectroscopy [160]	Saliva	Following completely absorbing the necessary quantity of saliva on the strip, the specimen would be transported to the detection zone via paper microfluidic activity, where a chemical reaction within GOx and salivary glucose begins to produce a pH change, leading to an adjustment in strip color that was tracked through the RGB detection on the small device that helps with recognizing glucose.	With very high sensitivity and a limit of detection (LOD) within a response time, the designed biosensor could detect glucose concentrations between appropriate range
VNIR [208]	Wrist	The biosensor enables the manipulation of pulsing of arterial blood from the wrist tissue. The VNIR spectroscopy was employed for reflected optical signals to estimate blood glucose.	The Rp value after averaging is approximately 0.86, while the standard prediction error is comparatively low.
MIR ATRS [204]	Inner lip mucosa	A novel optical fibre probe was developed utilizing a multi-reflection prism and ATR spectroscopy. Measurement repeatability was greater due to the prism's large, flat, wide contact surface and sensitivity with the number of reflections.	The experiment's findings show the presence of glucose in several spectra while fasting and after a glucose infusion. Peak absorption is defined by the calibration plot at 1155 $cm^{-}1$, with a glucose measurement error of less than 20%.
Short NIR [33]	Fingertip	A novel noninvasive glucometer with short NIR waves and light absorption and reflectance at specific wavelengths (940 and 1,300 nm) has been introduced. A unique, accurate ML-based method for glucose sensor calibration using calibrated and verified healthy, prediabetic, and diabetic samples has been reported.	Pearson's correlation coefficient (R) is 0.953, mARD is 7.32 %, and RMSE value is 11.96 mg/dl. All the values lines in Zone A (94%) and Zone B (6%).

vision issues, and airborne diseases. The other advantage of remote health monitoring is to provide a better diagnosis from available experts within a short duration. Patient monitoring from a remote location is also helpful for early diagnosis of

diabetes and diet management activities. The patients will be aware of upcoming issues from their current lifestyles. The role of remote monitoring has become significant since the COVID-19 pandemic. Hence, patient remote monitoring is an integral component of smart healthcare.

A detailed description of a closed-loop system that displays glucose level monitoring and insulin discharge is shown (refer to Fig. 30 [2]). By Controlling diabetes using closed-loop automatic production of insulin, this virtual architecture can offer a superior method for evaluating insulin dosages. Such an integrated cloud framework may analyze diabetic

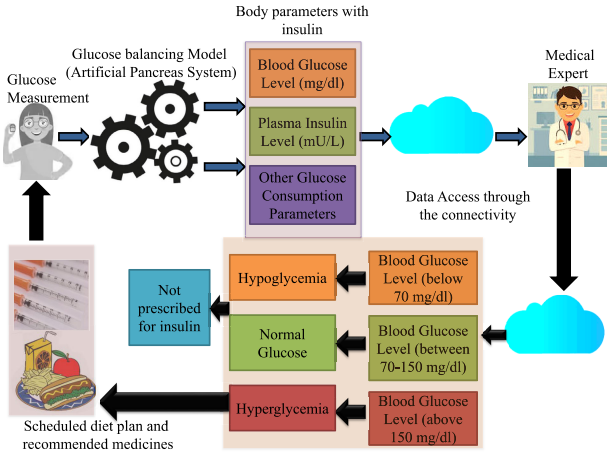

FIGURE 30. An IoMT framework-based closed-loop automated insulin secretion diabetes control system [2].

patients, treat them for blood glucose management in intelligent healthcare, and provide adequate healthcare in smart infrastructure with a few healthcare staff.

Medical device security and privacy concerns are the most important aspects of any IoT network. Because control operations often occur through wireless media, wearable device hardware security is extremely important. The control of the glucose monitoring device's security flaws is demonstrated in Fig. 31.

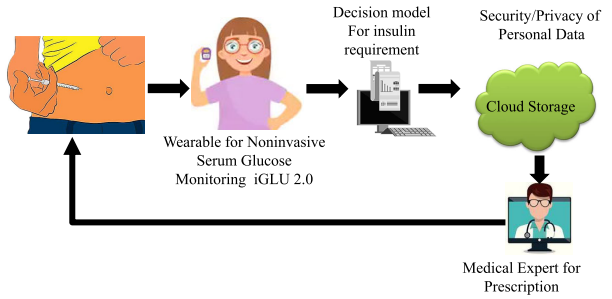

FIGURE 31. Our long time goal of security-assured non-invasive sugar level measurement and controlling in our suggested iGLU.

Due to linked health systems in an unstable and unsafe IoMT framework, device security is crucial [213]. Another essential security component of smart healthcare is the reliability of usable medical data. All patient medical records are kept on a server. Thus, the safety of this information is crucial. To have safe monitoring and appropriate patient care regulated access with correct authentication is necessary.

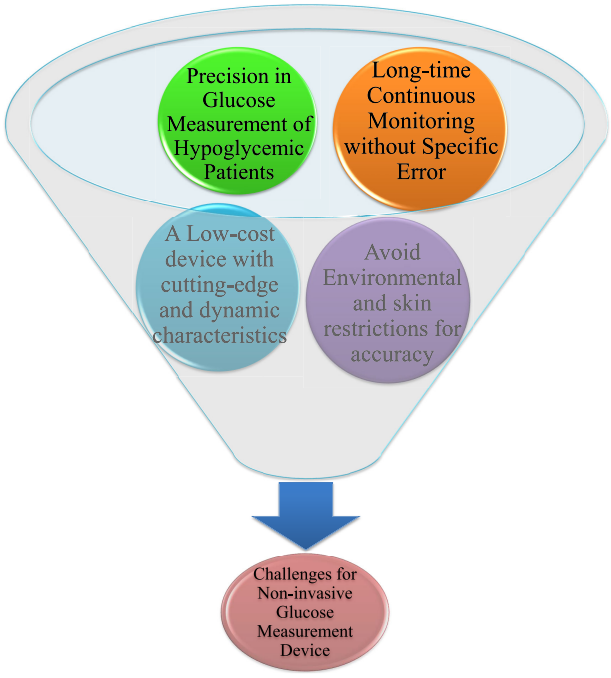

FIGURE 32. Glucose-level measurement: open challenges.

IX. SHORTCOMINGS AND OPEN CHALLENGES OF EXISTING WORK

This section outlines the shortcomings and discusses some unresolved issues with controlling and measuring glucose levels.

A. LIMITATIONS OF CURRENT METHODS AND PRODUCTS

1) To estimate BG level, photoacoustic spectroscopy has been used. Real-time measurement and validation have not been done. In the laboratory, an artificial solution was made to monitor BG level. The prototype module with the laser and corresponding detector is expensive. The prototype needs much more space and does not offer a portable option. It is, therefore, not a better option for continuous glucose monitoring.
2) When monochromatic light interacts with a particular material, a nonlinear scattering process called Raman spectroscopy occurs. Raman spectroscopy can be used as a laboratory test, but it also takes up a lot more space. Therefore, the system built using this methodology won't work for regular glucose monitoring.
3) Data is also gathered using the eye retina for body glucose monitoring, which is one of the alternative non-invasive glucose detection approaches. Such a method is not always helpful for the measurement of glucose.
4) In the case of the bio-capacitance technique, a small change in the detector's position may impact the

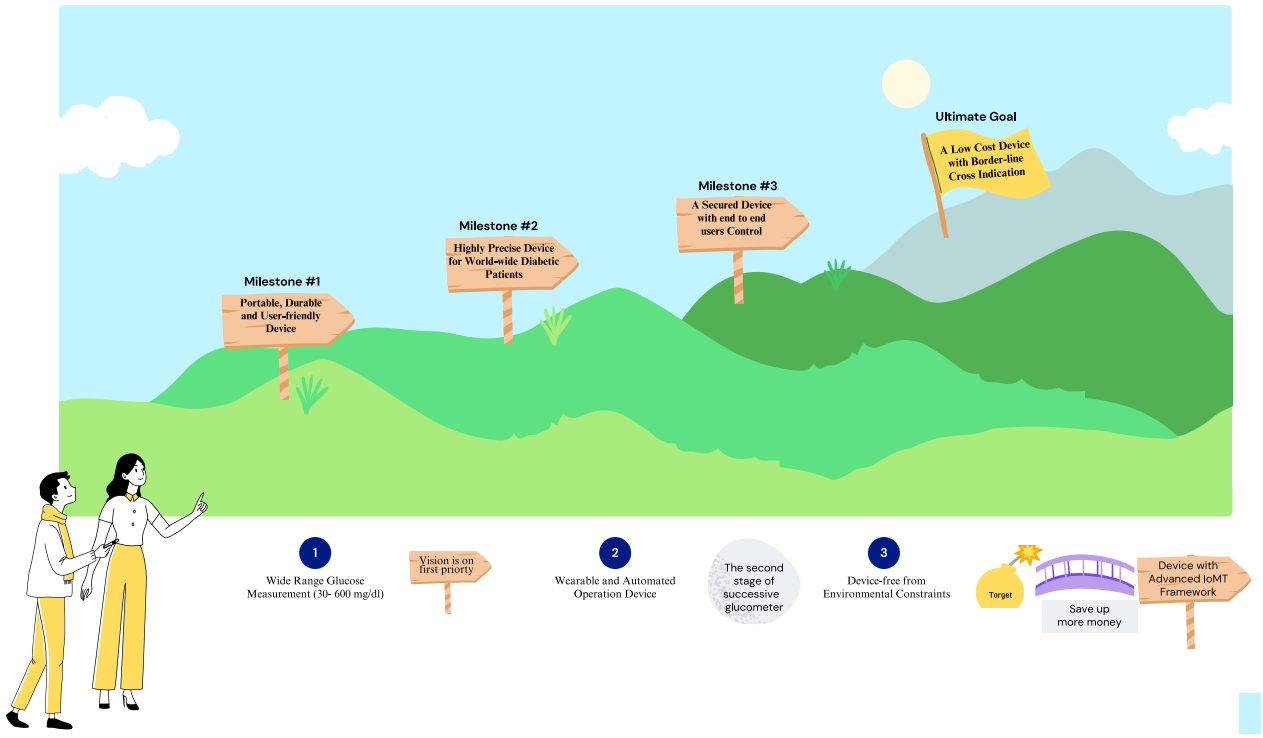

FIGURE 33. Our long-term goals for non-invasive glucose-level monitoring.

sensor's outcome, which reflects the change in BG level. The detector output may also be impacted by skin sweat, body temperature, and pressure on the sensor.

5) Impedance spectroscopy (IMPS) is used to detect glucose by connecting electrodes, influenced by skin. Since each person's saliva and sweat may differ, the accuracy of the glucose measurement won't be consistent. As a result, this method is not accurate for measuring glucose in smart healthcare.
6) A PPG signal is employed to remove characteristics for predicting body glucose levels. However, the PPG can be an accurate body glucose-measuring method whose output value varies solely with blood volume. As a result, the presented method has not been able to detect the glucose molecule in the blood sample correctly.

B. OPEN CHALLENGES IN NON-INVASIVE BODY GLUCOSE MEASURING

The expansion of a non-invasive body glucose measurement device is analyzed with limitations. However, numerous unresolved issues that pose serious obstacles to accurate non-invasive glucose measurement have been explored. These difficulties have been identified in Fig. 32. Hypoglycemic patient monitoring is not possible without pricking for a long time as the non-invasive devices are required to be developed for precise measurement below 80 mg/dl [214].

- In the literature, factors that impact glucose measurement results include BP, temperature, and humidity level. However, these factors are not evaluated.
- Additionally, the affordable and portable continuous glucose technology has not been fully addressed.
- The accurate glucose measurement is still not possible at higher blood glucose range without the blood pricking method
- The development of a smart healthcare framework using the integration of a glucometer with the Internet of Medical Things for continuous data logging to the cloud has not been visible in commercial devices [215].
- With the use of a cloud server, the decision model for automatically secreting insulin to monitor glucose values has to be explored.
- The privacy and security problems with the insulin and body glucose monitoring system have not been explored commercially.
- Continuously monitoring glucose with an insulin supply system requires an efficient power management system.
- The continuous glucose monitoring device would be portable and battery-operated so power management of the device needs to be addressed.

The non-invasive glucose measurement would be also an ideal choice for infants. Newborn babies tend to enter into hypoglycemia conditions during febrile seizure episodes. It is required to adopt the continuous glucose monitoring approach to check the glucose value during the high fever condition. request pricking of blood samples from newborn babies is irritating and panic. It is generally not recommended to prick multiple times as the body's blood level is comparatively lower. Continuous monitoring of other

blood parameters for newborn babies would help to provide rapid diagnosis and treatment to avoid recurrent febrile seizure episodes. The non-invasive glucose measurement would be helpful for Type 1 diabetes patients for adjustment of their insulin dosage as per their current body glucose.

X. CONCLUSION

The study provides an overview of BG measurement, controlling mechanisms, and continuous monitoring strategies. Numerous methods have been described in the state of the art as proofs-of-concept, demonstrating a strong connection between device response and the reference value for blood glucose. Some techniques are not implemented for commercial purposes. Some approaches are neither accurate nor cost-effective solutions. The prior technologies are discussed with design strategies, observed issues, and measurement limitations. Due to the limitations and issues, advancements have also been discussed in terms of solutions. The main focus of the paper is to demonstrate various techniques with corresponding issues and solutions, along with advancements. Optical detection uses short NIR, which has been considered a future appliance or prototype device that should be more effective in various zones to support continuous health monitoring and viable solutions to reduce the shortcomings of all other techniques. Various methodologies may be utilized in the future for precise glucose monitoring. The consumer devices should be more effective in various zones to support continuous health monitoring. It must be used regularly as a portable device for real-time applications. Future devices should be low-cost and user-friendly for continuous health monitoring systems.

XI. FUTURE WORK

The future plan for a non-invasive glucose measurement device is highlighted in Fig. 33, which represents the future milestone with significant features. There is a requirement to develop a portable, durable, and user-friendly device so that it can be used on a large scale all over the world. The upcoming non-invasive devices should be able to check blood glucose for all age pepole precisely. The patient's data should be safe and confidential. The data can be accessed by patients and medical experts only. The upcoming device should be low-power and send a warning signal to patients after reaching at alarm level. These expected features are future milestones. An advanced IoMT framework integration for the device is necessary. This cutting-edge IoMT framework will connect the future measuring device with all nearby diabetes care centers for optimum care. Combining food intake and glucose measurement of particular can significantly provide the root cause and corresponding treatment for smart healthcare [216]. The future of technology expects reliable, portable, and user-friendly devices. The feature of borderline cross indication on the device should be explored in future measuring devices. Everyone will be aware to check their own BG level to analyze the body's proper function. A secured device with end-to-end user control and authentication is also necessary for future advancement. Physical unclonable function (PUF) based security framework is advantageous for IoMT devices [213], [217]. The effectiveness of a suitable healthcare cyber-physical system (H-CPS) with blockchain-based data and device management has to be considered [218], [219]. Glucose metres could be combined with wearables and food diaries to track individual reactions to various meals and activities. This would enable people to customize their diet and exercise routines for better performance and health.

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