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A Review Of Artificial Intelligence Based Non-Invasive Blood Glucose Level Detection

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Abstract: Diabetes is a persistent illness in which a person's body malfunctions to metabolize the glucose in blood effectively. The absence of insulin in the human body is source of diabetes. The most crucial component of health care is the ongoing checking of blood sugar. The majority of effective glucose level monitoring devices rely on blood pricking technique. For frequent measurement, however, this kind of approach might not be the best choice. The comprehensive review of glucose testing methods is presented in this study. The study discusses several non-invasive glucose testing techniques as well as smart medical technology for glucose management. The configuration of an accurate measurement instrument is required to meet the necessity for non-intrusive and painless blood sugar level checking system. The issue of repeatedly puncturing blood samples for blood samples is solved by non-invasive glucose-level checking devices for clinical tests. To provide continuous health monitoring, a Smart Healthcare framework based on the IoMT (Internet-Medical-Things) integrated H-CPS (Healthcare Cyber-Physical System) is needed for glucose measurement. In addition, a few consumer products and a few cutting-edge glucose measurement techniques are covered in the study. The study also included a list of unresolved issues and challenges related to measuring glucose.
Keywords: Diabetes, Glucose monitoring, Non-invasive, Smart Healthcare, Internet of Medical Things, Artificial intelligence

INTRODUCTION

Glucose is a crucial energy source that allows the body to work well. When our blood sugar levels are within the normal range, we typically don't notice them. However, when these levels deviate from the recommended limits, we experience negative effects on our daily functioning. Glucose is a simple sugar, classified as a monosaccharide, which means it consists of a single sugar molecule. Other monosaccharides include fructose, glycogen, and D-ribose. In addition to fats, glucose is one of the body's preferred energy sources. We obtain glucose from foods containing gluten, fruits, vegetables and dairy products. While we eat, our body signals the pancreas to release necessary amount of insulin in response to the rise in glucose levels. Some individuals cannot produce sufficient insulin naturally, so they require insulin injections to manage their glucose levels.Approximately, there are now 463 million adults with diabetes worldwide and by 2045, that figure is projected to increase up to 700 million. The prevalence of diabetes is growing rapidly in many of the countries. Seventy-nine percent of grown-up person having diabetes reside in low-to-middle-income countries. Among people under 65, diabetes affects one in five, and one in two people with diabetes are undiagnosed. Diabetes claimed 4.2 million lives in 2019 and led to in healthcare costs of minimum 760 billion dollars, accounting for 10% of total disbursing on grown-up people. One in six live births has diabetes during pregnancy, and more than 1.1 million children and young people have type 1 diabetes. Additionally, 374 million persons are having an elevated risk of growing type 2 diabetes. Diabetes is primarily categorized into three types (see Fig. 1). In Type 1 diabetes, the pancreas fails to produce insulin, leading to a compromised immune system and an inability to generate insulin naturally.

When enough insulin is not produced by the pancreas to maintain a proper glycemic profile, the type 2 diabetes occurs. Gestational diabetes typically develops in women during the later pregnancy phases.

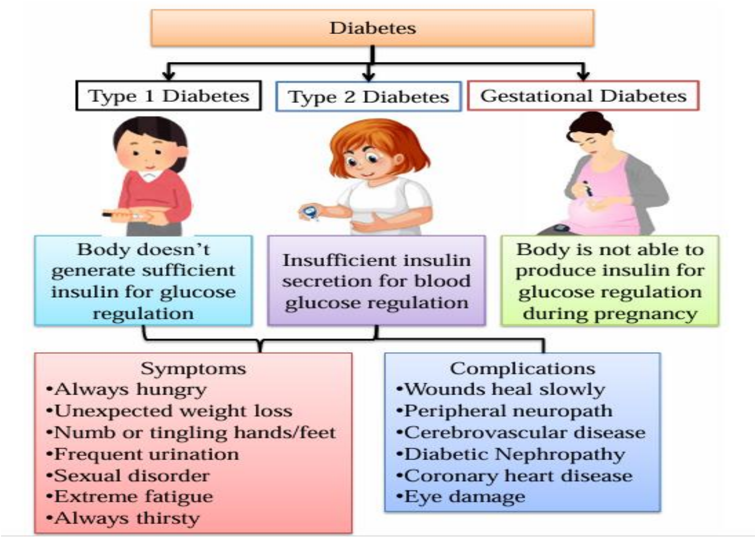

Fig 1: Different kinds of diabetes and their symptoms.

People with diabetes are at risk for chronic issues affecting essential organs and the neurological system. It's recommended that diabetic patients see an eye specialist regularly for comprehensive check-ups. Diabetes significantly enhances the risk of cataracts, which cloud the eye's lens and glaucoma, which raises the risk of diabetic retinopathy, impacting the back of the eye. Patients should have their urine tested for protein annually, as protein in urine stipulates kidney disease. High blood pressure can also lead to kidney problems, so it's important to monitor blood pressure during healthcare visits. Individuals with diabetes have a higher risk of heart disease and strokes which are the leading causes of death in diabetic patients. Managing other risk factors, such as hypertension and high cholesterol, along with blood sugar levels, is crucial. High blood sugar can lead to poor circulation and nerve damage, causing slow wound healing, severe pain, and loss of sensation in the feet. In severe cases, this may necessitate the amputation of toes or even the leg. Elevated blood sugar levels can affect the entire nervous system, leading to various types of neuropathy.

Neuropathy in diabetics includes:

Peripheral neuropathy: Damages peripheral nerves, impacting extremities.

Gastroparesis: Disrupts the normal movement of food through the stomach.

Postural hypotension: Causes a drop in blood pressure due to changes in body position.

Uncontrolled diarrhea.

The best approach for managing these complications is to control blood glucose levels and maintain good overall health. Diabetes occurs because the body is unable to use insulin efficiently or produces insufficient amounts of it. Insulin is the primary hormone that regulates blood glucose levels. It enables cells to absorb glucose for energy or storage. However, prolonged high blood glucose levels can lead to hyperglycemia, while prolonged low levels can cause hypoglycemia. Hyperglycemia can result in severe health issues such as heart disease, stroke, tissue damage, blindness, kidney failure and even death if untreated. Hypoglycemia occurs due to inadequate insulin secretion, leading to a rapid drop in blood glucose levels. Conversely, ineffective insulin use results in hyperglycemia, marked by high blood glucose levels. Both conditions require lifelong monitoring and treatment, as there is no permanent cure.Current glucose measurement methods for diabetic patients are mostly painful, invasive, time-consuming and expensive. The conventional approach makes use of an electrochemical process which requires a blood sample from a finger prick. A self-monitoring blood glucose device provides information about glucose levels and sample collection time without requiring any expert support. Continuous glucose monitoring (CGM) devices offer ongoing glucose level tracking, suitable for patients with high glucose levels.

However, both methods involve discomfort and pain, with continuous monitoring posing risks of tissue damage and infection.Since the early 2000s, endeavors have been made to evolve new non-invasive and minimally invasive devices to reduce the discomfort and pain associated with traditional approaches. The creation of a non-invasive device would permit millions of patients to check their blood sugar levels using a non-invasive technology without creating any pain or permanent tissue damage, generating significant demand. The World Health Organization (WHO) claims that there are currently 450 million diabetic patients worldwide, projected to reach 700 million by the mid-2040s.Recent advancements have explored the properties of glucose particles across different electromagnetic spectrum frequencies, including DC, visible, ultrasound and near-infrared (NIR) regions. Promising results have been observed in the visible and NIR regions, leading to the design and development of commercial devices. However, many of these products are no longer in use as a result of subpar accuracy, sensitivity and selectivity. Those available on the market have not yet matched the accuracy of conventional methods. This presents opportunities for non-invasive glucose monitoring, such as combining multiple techniques to develop a more dependable and economical glucose measurement device.Section 2 outlines the presently recognized techniques. Section 3 details the gadgets and authorized technologies available for non-invasive and minimally invasive monitoring. Section 4 explores the latest techniques and ongoing research in this field. Section 5 identifies the research gaps associated with these new methods. Finally, Section 6 ties together the preceding sections, providing a comprehensive vision for future developments. Since 2010, the prevalence of diabetes has increased worldwide [14]. 9.3% of the world's population (463 million) had diabetes in 2019. By 2030, that number is expected to rise to 10.2% (578 million), and by 2045, it will reach 10.9% (700 million) [15]. Chronic diabetes is brought on by either insufficient insulin production by the pancreas or inefficient insulin utilization by the body [16]. Insulin hormone facilitates the absorption of glucose by body cells. In diabetes, blood glucose levels rise. Type 1, type 2, and gestational diabetes are the three primary forms of the disease [17]. Untreated diabetes can lead to severe health complications, including strokes, nerve damage, heart disease, kidney disease, and blindness. Managing diabetes involves regular physical activity, a proper diet, and appropriate insulin dosages. Oral medications can also help control diabetes in its early stages. Among adults, 5% of diagnosed cases are type 1 diabetes, while 90-95% are type 2 diabetes. This highlights the need for devices that measure blood glucose level for quick and continuous diagnosis [18]. Continuous monitoring of glucose levels is essential in diabetes management. Repeated finger pricking using existing invasive methods can lead to blood-related infections and trauma [19]. Therefore, developing real-time non-invasive devices is crucial. Currently, there are few such devices on the market, and they are often very expensive [20, 21]. As the population grows and resources become scarcer, the implementation of smart cities, which include smart healthcare, is increasingly necessary [22]. Technologies such as the AI, big data, cloud computing and IoT use smart healthcare to enhance effectiveness and user-friendliness [23]. Smart healthcare solutions are needed for non-invasive diabetes detection, particularly in rural and remote areas where immediate medical facilities are scarce [24]. Figure 2 illustrates smart healthcare for diabetes.

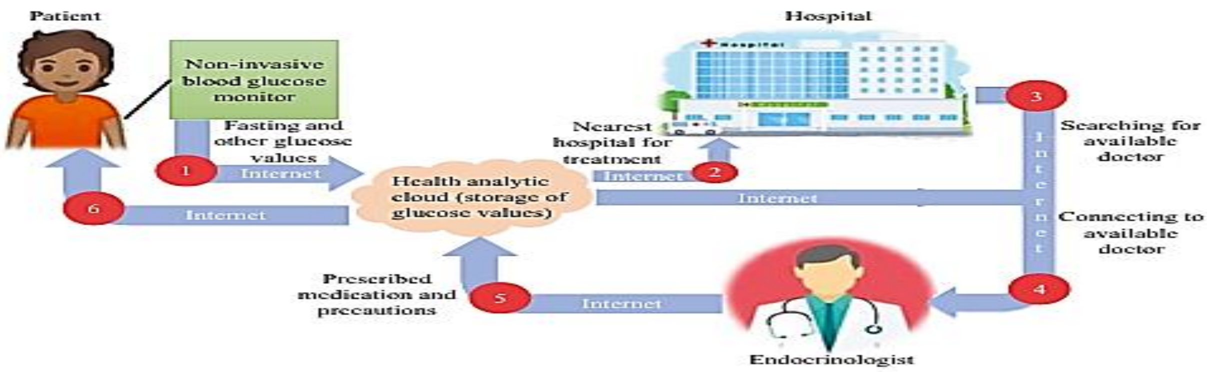

Fig 2: Intelligent treatment for diabetes

The primary challenges in advancing truly non-invasive glucose monitoring technologies include achieving ease of use, accuracy and suitability for home use across diverse populations. A device that successfully addresses these issues could significantly enhance the life quality for millions of diabetic people worldwide [25]. This is particularly important as it reduces the need for frequent bedside visits, especially for critically ill patients receiving intravenous insulin, which poses risks during pandemics like COVID-19. For non-critically ill patients, a user-friendly non-invasive device can facilitate self-monitoring of blood glucose levels for diabetes management [26]. The mHealth application can also transmit glucose readings to doctors in remote locations. Therefore, creating a continuous glucose monitoring tool that is practical, economical, secure, and offers real-time readings is the aim. This can be accomplished by utilizing a non-invasive device paired with advanced post-processing algorithms, and integrating it with a microcontroller that is programmed with an optimal ML algorithm to ensure quick results and high accuracy.Previous research on glucose measurement encompasses invasive, non-invasive and minimally invasive methods. Significant efforts have been made to develop continuous glucose monitoring systems utilizing non-invasive techniques, both optical and non-optical. Optical methods include Raman Spectroscopy, NIR Spectroscopy, and the PPG method. Figure 3 illustrates various blood glucose measurement systems. Following data acquisition from sensors, researchers have focused on refining computational models for accurate glucose level prediction. For example, Sejdinović et al. developed an artificial neural network to classify prediabetic and type 2 diabetic patients [27], testing the model with a specific sample ratio. Alić et al. created an expert system using a feed-forward artificial neural network (ANN) to classify metabolic syndrome (MetS) [28]. Another ANN was applied to predict lactose intolerance [29], and a physiological behavior model was developed to simulate the glucose-insulin regulatory mechanism [30]. Various neural networks have also been introduced for other medical purposes, such as differentiating between cancer and non-cancer patients [31].The PPG method, a non-invasive technique, employs sensors similar to those in pulse oximeters to record PPG signals. Paul et al. developed a PPG-based blood glucose monitoring system using a pulse oximeter, where light intensity variations at the receiver were used to predict glucose levels based on voltage changes with glucose concentration [22]. Similarly, Monte-Moreno designed a PPG-based sensor for estimating blood glucose using machine learning models [32]. Efforts in continuous glucose monitoring have also explored wearable microsystems with minimally invasive approaches, including the first wearable device for extracting glucose from the skin [33]. Optical Coherence Tomography (OCT), another non-invasive method, estimates glucose based on the OCT slope [34]. Raman Spectroscopy, which relies on chemical and molecular interactions, has been investigated for glucose estimation [35]. Attempts have also been made to use saliva for non-invasive glucose detection [36, 37]. Ramashyamam et al. proposed NIR spectroscopy-based glucose estimation using PPG with specific wavelengths (935 nm, 950 nm, and 1070 nm) and FPGA with an Artificial Neural Network [38]. A microcontroller-based, painless blood glucose measurement system was explored [39]. Insulin pump-integrated diabetes management systems were developed for improved glycemic control, and pulsed laser diodes were presented to collect photoacoustic signals for glucose estimation [40]. The intelligent Glucometer iGLU, utilizing optical methods and machine learning models, was built with the Internet of Medical Things (IoMT) framework for remote monitoring [24]. This NIR spectroscopy-based gadget uses regression models to interpret three-channel data in order to monitor glucose.Despite these advancements, many solutions face accuracy challenges. The PPG method, which measures light intensity variations with blood volume, may not yield precise glucose values. Wearable microstrip solutions are often too bulky for continuous glucose measurement. OCT techniques can be time-consuming for glucose concentration estimation and may lack specificity and sensitivity. Raman Spectroscopy solutions require significant space, affecting portability. Saliva-based glucose detection is unreliable due to sample variability. Laser-based solutions are not ideal for frequent glucose monitoring. Thus, short-wavelength NIR spectroscopy is taken the most effective method for continuous glucose measurement, addressing many of these limitations.

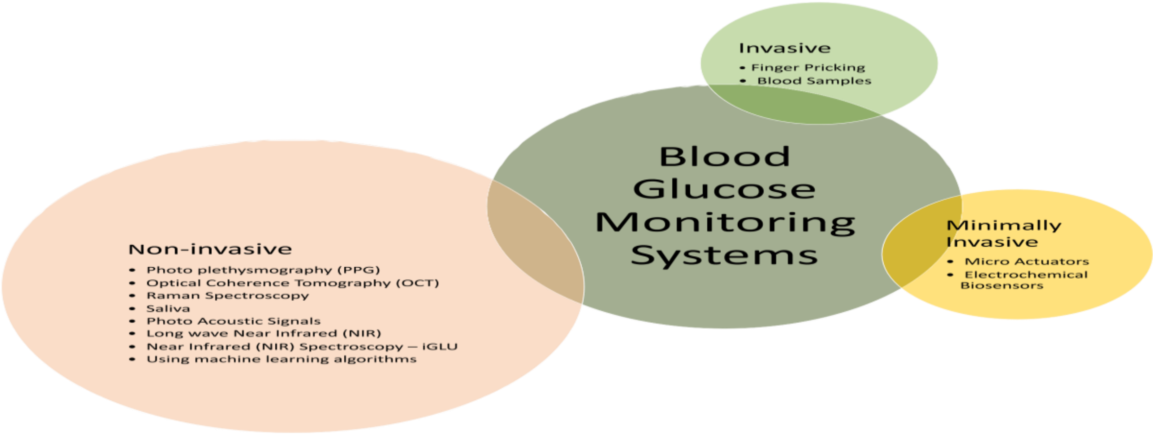

Fig 3: An outline of methods for measuring blood glucose

An overview of blood glucose measuring system measurement methods is provided in Fig. 3.

Technique for Glucose Measurement:

Currently, glucose monitoring is done either through laboratory-based techniques or home-based monitoring, both of which are invasive and involve blood pricking. This process is inconvenient and uncomfortable for users, often requiring multiple blood samples throughout the day, leading many patients to avoid it. As a result, notable modifications in glycemic profiles may go overlooked due to unexpected side effects and low patient conformity, potentially causing improper insulin dosages and unrecognized food ingredient impacts. Despite their drawbacks, these methods are reliable because of their high sensitivity and accuracy in glucose measurement.In recent years, novel approaches for glucose measurement have been explored, focusing on physical detection principles rather than traditional chemical methods. Non-invasive techniques, which do not require blood samples, utilize interstitial fluid (ISF) to detect glucose molecules. Various attempts have been made to measure glucose through saliva, sweat, tears, and the skin surface. However, achieving precise measurement, good sensitivity, and reliability remains a significant challenge. Non-invasive methods could be ideal for Continuous Glucose Monitoring (CGM) and self-monitoring purposes, allowing frequent daily measurements for better glucose control and essential preventive measures for people with hypoglycemia and hyperglycemia. These methods also aid dietitians and healthcare providers in preparing appropriate diet plans based on glucose fluctuations.Following sensor data collection, numerous researchers have focused on developing optimal computer models to accurately predict glucose levels.A multitude of novel research projects have surfaced, necessitating a continuous updating of the existing data. As seen in Figure 4, one of these novel techniques makes use of photoplethysmography (PPG).

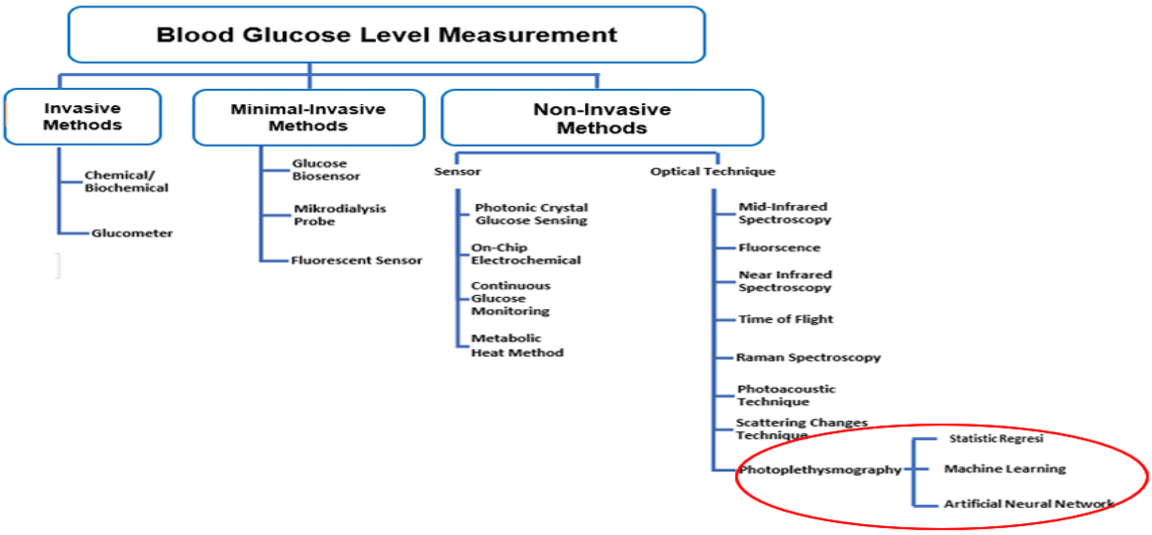

Fig 4: Methods for Measuring Blood Glucose.

Methods for Measuring Glucose Levels: A General Outline

An overview of the several invasive, non-invasive, and minimally invasive glucose-level measuring techniques is given in this section. Significant work has been done in these areas, particularly with non-invasive techniques, which rely on both non-optical and optical techniques. Raman spectroscopy, NIR spectroscopy, and the PPG method are a few of the optical approaches.

Invasive Techniques:

Economical electrochemical sensors are used in a large number of commercial continuous blood glucose measuring devices to respond quickly for glucose detection in blood [42]. Lancets are used to prick the blood for primary blood glucose monitoring in various commercial devices [44]. This process can be distressing due to the need to prick the fingertip multiple times a day for regular observation [45]. Minimal-invasive biosensors for the purpose of monitoring glucose have been created using glucose oxidase, requiring about 1mm penetration into the skin for measurement [46]. Photometric techniques have also been used to identify glucose in little amounts of blood [47].

Low-Invasive Techniques:

Low-invasive methods include the development of prototype sensors for frequent glucose tissue monitoring [48]. These sensors are wearable and implanted on a membrane containing immobilized glucose oxidase. Implantable devices for glucose monitoring have also been developed [49], as well as biosensors designed for semi or minimal invasive glucose monitoring [50]. Wearable microsystems have been explored for frequent glucose measurement [51]. Continuous glucose monitoring has been attempted with microfabricated biosensors using a transponder chip [52] and semi-invasive Dexcom sensors use the transponder chip's signal for calibration [53]. Glucose sensors have been integrated with artificial pancreas systems for better diabetes control [54]. However, minimally invasive approaches often face limitations in accuracy and may have shorter monitoring lifespans. One such wearable microsystem for ongoing blood glucose monitoring, a minimally invasive technique is employed with a micro-actuator containing shape memory alloy (SMA) to extract blood samples from the skin [55]. Despite its feasibility and performance, the device is large and inconvenient.

Non-Invasive Methods:

Non-invasive measurement methods aim to provide painless and accurate solutions, avoiding the issues associated with invasive and minimally invasive methods [56], [57]. For smart healthcare, portable non-invasive glucose measuring devices have been created. These methods are more convenient for continuous glucose measurement compared to invasive and semi-invasive methods [56], [57]. Optical methods for non-intrusive glucose estimation like Raman spectroscopy, near-infrared spectroscopy, polarimetric, scattering spectroscopy [60], and photoacoustic spectroscopy [61], are considered reliable and precise. Researchers believe that a non-invasive estimation device would be much more user-friendly [62], [63]. For continuous glucose monitoring devices to be accurate, blood glucose must be calibrated to interstitial glucose dynamics [64], [65]. Numerous calibration algorithms have been created and applied for portable devices [66]. Significant efforts have been made to develop self-monitoring systems for glucose measurement [67]. The Invasive and Non-invasive approaches for glucose measurement is shown in Fig 5 below.

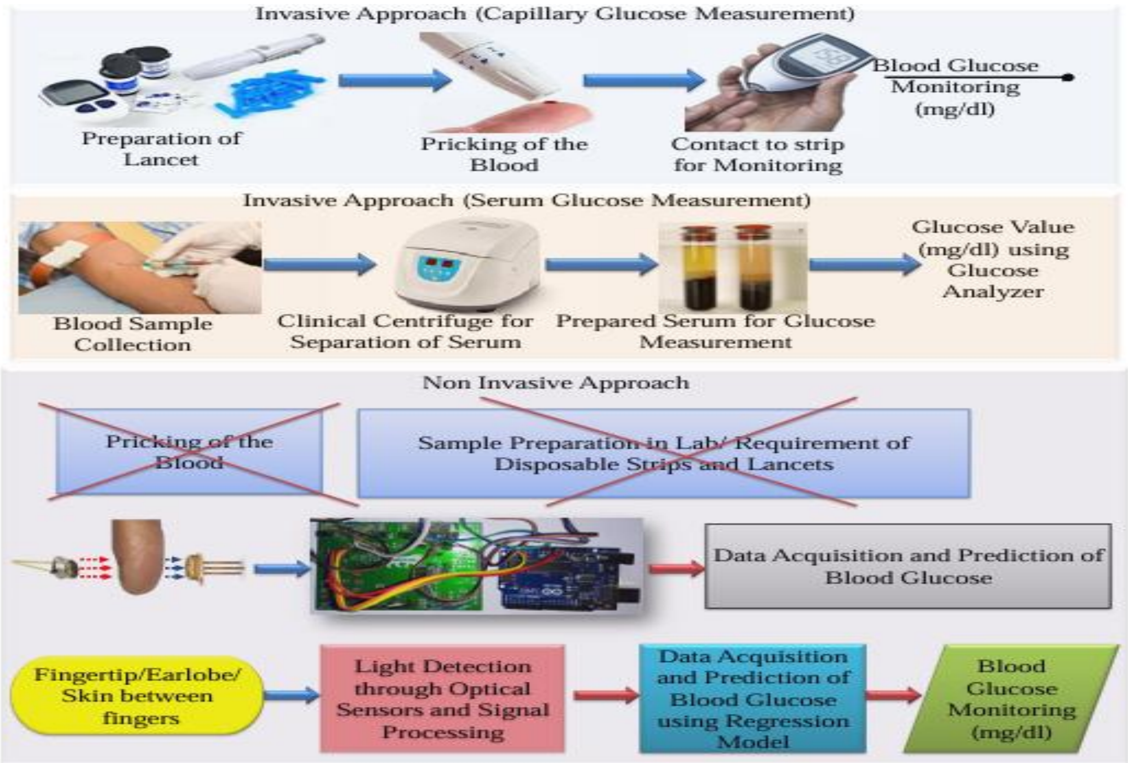

Fig 5: Invasive versus Noninvasive Glucose Measurement.

Invasive Versus Non-Invasive Glucose Measurements: The Trade-Offs

Current glucose estimation methods, widely used by the rising number of people with diabetes globally are invasive, time-consuming, and unpleasant. They also require numerous disposable items, adding to household expenses. Non-invasive glucose measurement techniques address these limitations and have therefore become a major focus of research. However, there are trade-offs between these two methods, as illustrated in Figure 6.

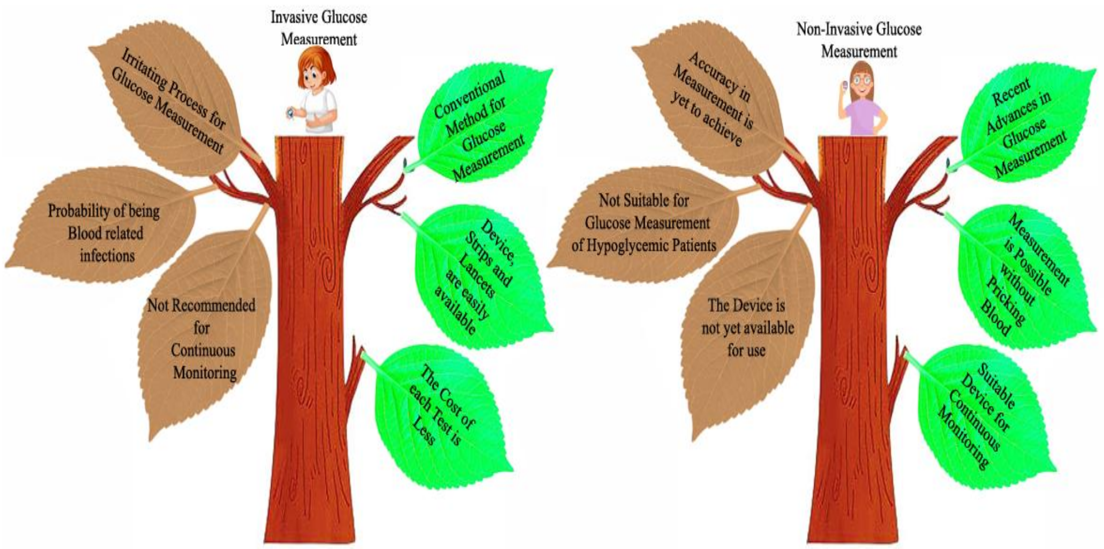

Fig 6: Invasive and non-invasive glucose measurement: trade-offs.

Serum Glucose versus Capillary Glucose for Non-invasive Measurement

Serum glucose levels provide more precise readings that closely match actual blood glucose levels compared to capillary glucose levels. Traditional methods can quickly measure capillary glucose, but determining serum glucose is more challenging. Typically, capillary glucose levels are higher than serum glucose levels. Accurate blood glucose measurement is crucial for effective treatment decisions, making serum glucose a more trustworthy indicator for prescription drugs. Despite this, measurement of capillary blood glucose is more commonly used for diabetic patients. However, serum glucose measurement offers better blood glucose control if done regularly, though it is not feasible for continuous monitoring. Serum blood is also necessary for the laboratory examination of glycosylated hemoglobin (HbA1c), which represents blood glucose levels over a period of 6–8 weeks. In non-invasive methods, Optical spectroscopy is used to measure both serum and capillary glucose. This technique relies on detecting IR light absorption and scattering by blood vessel glucose molecules. The fundamental process is comparable for both kinds, but post-processing computational models differ to estimate blood glucose levels.

Non-invasive Technique for Estimating Salivary Glucose Levels:

Saliva-based glucose measurement [68] is highly convenient for both children and adults. There are two types of saliva: total saliva and gland-specific saliva, collected from glands like the parotid, submandibular, minor salivary glands and sublingual. This method is informed by patient history, including risk factors, age, family history, diabetes duration, sex and associated illnesses. Other glucose measurement techniques use photometric glucometers, requiring minimal sample volumes [69]. These rely on chemical test strips reacting with the sample, capturing reflections from the test area to estimate glucose levels. This method requires validation across a large patient population.

Methods for Non-invasive Assessment of Glucose Levels:

This segment delves into various noninvasive glucose-level monitoring methods, primarily using optical techniques based on different spectroscopy methods. A comparative summary of noninvasive methods is provided in Table I.

Near-Infrared (NIR) Spectroscopy: This is called "infrared spectroscopy" or “vibration spectroscopy”. This method involves exposing matter to infrared radiation [70], [71]. It includes reflection, scattering, and absorption spectroscopy [72]. Infrared absorption causes molecular vibrations, creating a spectrum band with wavelengths measured in cm^{-1} [73]. NIR light (700-2500 nm) is applied to the skin (e.g., finger or earlobe) [74], interacting with blood components, leading to scattering, absorption, and reflection [75], [76]. The Beer-Lambert law [77], [78] states that the intensity of light received changes with the content of glucose. The recipient measures glucose molecules in blood vessels [79].Comparing Short-Wave and Long-Wave NIR Spectroscopy: Optical detection offers precise glucose measurement. FIR (Far Infrared) techniques resonate with OH and CH bonds for the first overtone, performing well in vitro. Additionally, fiber-optic sensors that use laser-based mid-IR spectroscopy facilitate the measurement of glucose in vitro, using multivariate calibration for error analysis [80]. FIR has limited penetration depth compared to short-wave NIR [81], which accurately detects glucose molecules. Specific wavelengths (e.g., 940 nm) have been effective for precise glucose measurement [82].

NIR Spectroscopy-Based Methods: Literature proposes non-invasive glucose measurement with PPG and NIR spectroscopy [87]. This involves NIR LEDs, photodetectors and an optode pair. At NIR wavelengths (935 nm, 950 nm, 1070 nm), PPG signals are obtained via system with an analog front-end. An ANN is used to estimate glucose levels on an FPGA. A microcontroller facilitates painless, autonomous blood extraction [88]. The Blood Glucose Measurement system uses a microcontroller for glucose display and insulin pump tracking for diabetes management. This method involves detecting pressure changes in sensitive areas, generating sound waves [89]. Higher glucose concentrations produce stronger photoacoustic signals, which are amplified for processing. Glucose estimation uses photoacoustic amplitude from signals gathered by pulsed laser diodes and piezoelectric transducers, though this setup is expensive and large. In previous studies, the stretching of glucose in the near-infrared region [84], [85] has been identified, and the glucose absorption has been confirmed for the range of 1300 to 1350 nm. In the investigation, the existence of the glucose component was detected at 1300 nm [86].

The iGLU or non-invasive blood glucose measurement device: The "Intelligent Glucose Meter (iGLU)" [90] combines NIR spectroscopy [91] and machine learning for data acquisition. This device uses three channels for data gathering, with 128 samples per second processed by a 16-bit ADC. Data is calibrated, validated and stored on the cloud for remote monitoring by patients and doctors using regression algorithms. This low-cost device offers over 90% accuracy, but no real-time results are provided.

The Reasons NIR Is Suggested Over Other Noninvasive Methods: Numerous non-invasive methods, including PPG signal analysis, NIR light spectroscopy, and impedance spectroscopy, have been explored. However, non-optical methods lack precise measurement capabilities. PPG, a promising alternative, varies with blood concentration [92], [93], limiting its accuracy. Saliva and sweat properties differ among individuals, making these methods unreliable. Other spectroscopic techniques fail to offer portable, cost-effective, and accurate glucose prediction. Long-wave NIR lacks sufficient penetration [81] to detect glucose beneath the skin, whereas short-wave NIR is more effective for real-time detection [83], [94].

Mid-Infrared (MIR) Spectroscopy: MIR spectroscopy [95] effectively detects glucose molecule bending and stretching. However, it has shallow skin penetration due to high water absorption, mainly measuring ISF glucose in vivo. Some attempts have been made to measure glucose precisely through palm samples and saliva.

Blood Glucose Level Measurement using PPG: PPG signals detect changes in blood volume through light absorption [92] [93]. These changes result from blood volume fluctuations, not glucose molecules, potentially causing inaccurate measurements. The differences between NIR and PPG are illustrated in Fig. 7. The iGLU device uses NIR spectroscopy for precise glucose measurement. There are several blood glucose detection techniques using PPG signals [96]. Various ML models have been used to forecast blood sugar levels [98] based on PPG signals [97]. For glucose estimation, smart solutions using PPG signals and intelligent algorithms have also been developed [99], [100], [101].

One advanced optical technique is Photo-Plethysmography (PPG), a non-invasive method for glucose measurement in healthcare. PPG sensors, similar to pulse oximeters, operate in the near-infrared region at 920 nm, measuring light absorption changes to obtain PPG signals. Glucose concentration inversely affects light absorbance, and the resulting photocurrent is filtered and converted into measurable voltage values. Lab view software processes these indicators for calculating blood glucose levels. Machine learning techniques and PPG systems have been developed for the non-invasive assessment of glucose. This model uses an activity detector, a PPG sensor and a signal processing module to analyze PPG waveform features, correlating them with blood glucose levels.

In PPG, light intensity varies with blood volume changes, which are not specific to glucose molecules, limiting the system's accuracy [7], [89]. Fig. 7 highlights these differences.

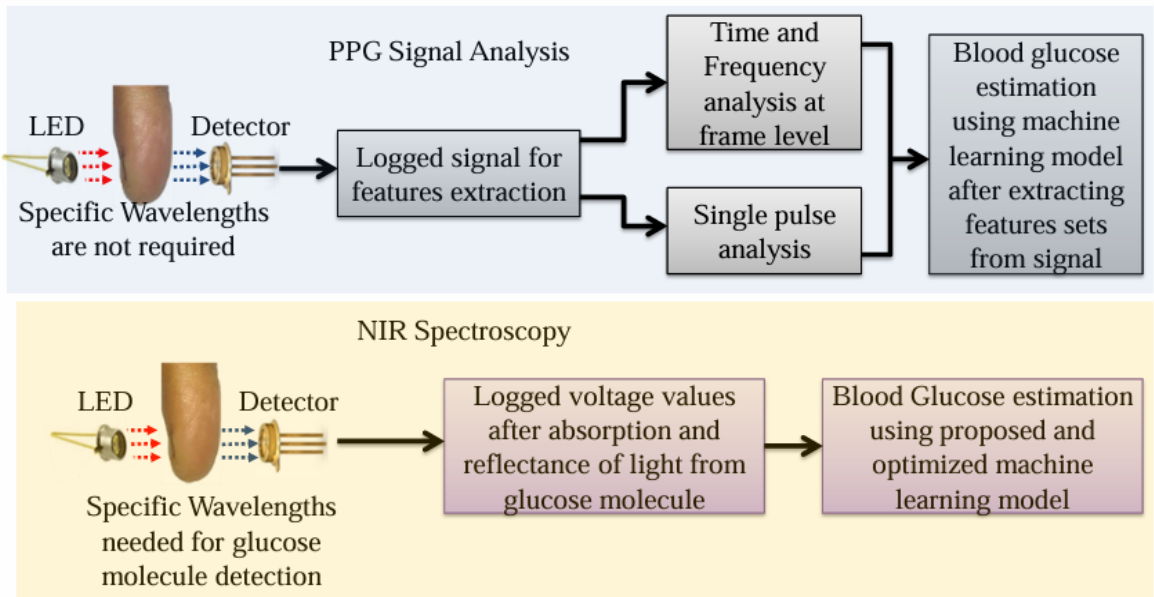

Fig 7: Non-invasive Glucose Measurement: PPG vs. NIR [7], [89].

Table 1: a qualitative analysis of various non-invasive methods for measuring blood sugar levels.

Sl. No.	Techniques	Advantages	Disadvantages
1.	Raman Spectroscopy	High specificity, low sensitivity to water and temperature	Cells may be at risk when a laser radiation source is used for continuous glucose monitoring (CGM). Furthermore, the technique's low signal-to-noise ratio (SNR) is caused by noise interference.
2.	Photoacoustic spectroscopy	Compact and simple sensor design with non-harmful optical radiation for tissues.	The signal is susceptible to interference from acoustic noise, temperature changes, and motion. Additionally, it may carry noise from non-glucose blood components.
3.	Optical Coherence Tomography (OCT)	It offers high resolution and excellent signal-to-noise ratio (SNR), remaining unaffected by blood pressure and cardiac activity.	Glucose readings can fluctuate due to skin conditions and movement, and the method is affected by tissue inhomogeneity.
4.	Near-Infrared (NIR) Spectroscopy	Transparent water in the near-infrared spectrum Materials required are rather inexpensive. The analyte concentration is directly correlated with the signal strength. The bare minimum of sample preparation is needed. The method also functions when there are substances present that interfere, such as glass or plastic containers	False readings may result from heterogeneous glucose distributions. The concentrations of glucose are too low for precise detection. elevated level of scattering issues with glucose determination's selectivity.
5.	Polarimetry	The prediction of glucose levels remains relatively unaffected by variations in laser intensity.	It necessitates an external laser source and demands precise alignment with the eye, being sensitive to alterations in pH and temperature.

Raman Spectroscopy:

Raman spectroscopy detects changes in the polarization of glucose molecules [101] when they interact with light. The technique involves the oscillation and rotation of molecules induced by incident LASER light [102]. Blood glucose levels can be predicted [104] due to these molecular vibrations that affect scattered light [103] emission. Compared to infrared spectroscopy [105], Raman spectroscopy offers higher accuracy. Extensive research has validated its precise glucose measurement capabilities, including in vivo testing. Figures 13 illustrate the basic framework and the use of Raman spectroscopy in noninvasive glucose measurement.

Spectroscopy via Photoacoustics or Photoacoustic Spectroscopy:

Photoacoustic spectroscopy leverages the photoacoustic effect to generate acoustic pressure waves from an object [106]. This method allows for the measurement of blood glucose [107] by having the item absorb modulated light input. The high-intensity absorbed optical light based on the object's optical properties [108], excites specific molecules at their resonant frequencies [109]. The absorbed light converts to heat, causing localized temperature increases and thermal expansion [110], which generates acoustic pressure [111]. These photoacoustic waves [113] are utilized to forecast the amount of glucose present at particular resonant frequencies, that correspond to glucose molecule vibrations [112]. Prior research utilized 905 nm wavelength [114], [115] optical light for excitation.

OCT or optical coherence tomography:

OCT relies on the principles of Spectroscopy of reflectance. This method involves passing low-coherent light across a sample, within an interferometer. The interferometric signal including both backscattered and reflected light is captured by a photodetector and a moving mirror in the reference arm. The method produces high-quality 2D images. Glucose concentration is linked to variations in interstitial fluids' refractive index. The scattering coefficient [101] is changed by variations in the refractive index which indirectly indicates glucose levels.

Polarimetry

Polarimetry is a highly accurate technique frequently used in clinical laboratories for glucose monitoring [116]. This method measures the rotation of a light vector influenced by the thickness, temperature, and concentration of blood glucose. When polarized light travels through a glucose-containing medium, it can become depolarized due to high scattering through the skin. To mitigate this, polarimetric tests are conducted through eye, allowing light to go through the cornea. The approach remains unchanged by variations in temperature and blood pH levels [117].

IV. Related Work and Literature survey:

Tjahjadi, H. et al [1] presented a number of state-of-the-art non-invasive methods that use photoplethysmography (PPG) signals to gauge BGL (blood glucose levels). Artificial intelligence algorithms can be used to carry out these procedures accurately and efficiently. Blood glucose is the most crucial indicator for determining whether a person has health problems. The PPG signal is a reflection of blood circulation. PPG-based BGL measurement using AI is a non-invasive measurement technique because BGL measurement is still invasive nowadays. They studied the information gathered from 2009 to 2022 to investigate how this technology has been developed. It appeared that non-invasive BGL using PPG signals and AI technologies has a bright future. The results of the methodological mapping in this evaluation could serve as a guide for future research when selecting which BGL measurement methodology to employ.

Figure 8 illustrates how the PPG data was collected by employing a finger sensor that is non-invasive. Every PPG signal is categorized as "normal" or "diabetic" according to the glucose meter measurement findings. The machine learning algorithm processed the PPG signal to generate a classification for the patient. After categorization was finished and compared to this categorization produced with a glucometer, the results were placed into the confusion matrix [9]. PPG functions just as well when using DL or ML techniques [12].

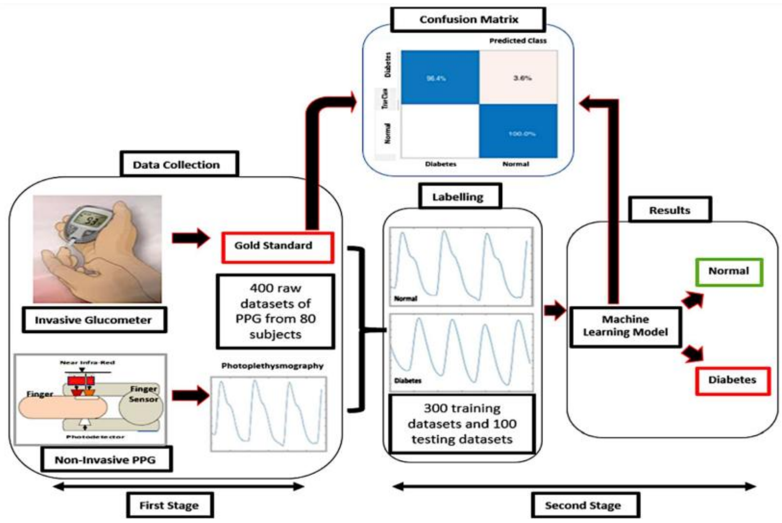

Fig. 8. An illustration of a non-invasive BGL classification system that detects diabetes early through the use of ML technique as per PPG data. phases in the processing include data gathering, segmenting it, labelling it and classifying the outcomes [9].

Srinivasan, V. B. et al [2] provided a CNN-based Deep Learning classifier as a non-invasive approach. To diagnose diabetes, they employ the scalograms produced from transmissive PPG signals gathered from the MIMIC-III database. A little altered VGGNet model was trained with 584 patient data from various sets of inputs. Every patient receives a probabilistic diabetes score from them, which is then utilized to divide the patient population into those with and without diabetes. Using a combination of PPG signals, classification of hypertension, age, and gender as inputs, the finest model was able to provide an accuracy of 76.34% and an AUC of 0.830 on 224 test subjects. They have successfully used as one of the earliest CNN-based techniques in the literature to use the MIMIC-III waveforms dataset to detect diabetes.

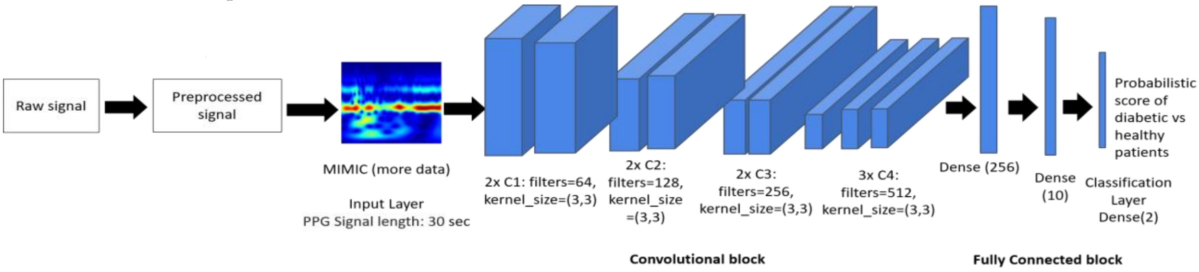

Fig 9: The A CNN-based classifier for predicting diabetes is made up of four parts: a fully connected block, a convolutional block, a scalogram generator, and preprocessing.

To enable patients and the general public to receive comfortable healthcare services Liu, J.et al [3] created a glucose monitoring device that is non-invasive employing Edge-AI for connected healthcare. In this study, a number of predictive algorithm models are used to translate the physical signal value to the actual blood glucose measurement. They did this by using a self-built infrared research device having a peak wavelength of 2900 nm and a wavenumber of 3448 cm^{-1}. Separate measurements and analyses are performed on the transmittance and reflectance signals. According to the results, the transmittance and reflectance signals (R2=0.990, R2=0.984) both meet performance expectations. EGA (Clarke Error Grid Analysis) is also used to assess and display the outcomes. According to the EGA data, regions A and B contain nearly all of the projected values, making them clinically correct and uncritical choices. They demonstrated how the technology for non-invasive blood glucose monitoring can offer strong technical support to linked healthcare services by combining smart device and Edge-AI convergence.

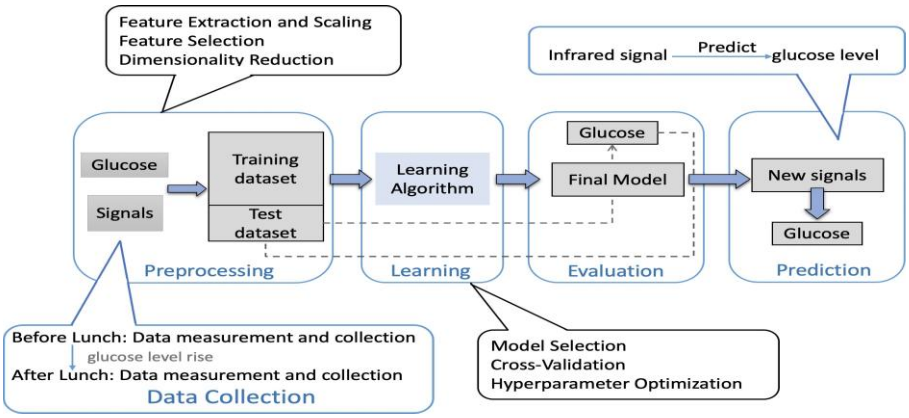

Fig 10: Measurement system with data collection and predictive model

Mary, L. J. [4] et al offered a process for creating a hybrid AI model that uses patient data to identify diabetes. The device provides correct and constant details on the wearer's health state by combining body vitals calculated with a smartwatch that has a bioactive sensor. The hybrid model achieves a high degree of accuracy in diabetes diagnosis by combining classical AI computations with DL. The framework gathers information on a wide range of physiological measures, such as pulse, skin conductance, and circulatory strain—all of which are well-established to be highly correlated with diabetes. Before the collected data is used to build the hybrid model, it is pre-processed. The regular AI calculation is used to categorize the data into diabetes or non-diabetic groups, while the profound learning calculation is used to exclude

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important level highlights from the raw data. The hybrid method increases the accuracy of diabetes localization by fusing the benefits of standard AI with DL.

The advent of photoplethysmography as a non-invasive approach for measuring blood sugar levels in diabetes care provides a substitute to invasive technologies' drawbacks. It has been demonstrated that applying AI technology to PPG signals for non-invasive blood glucose level (BGL) measurement using ML or DL methodologies improve the resulting performance. Susana, E. et al [5] presented a quick overview of the latest and planned technological advancements in photoplethysmography-based monitoring blood glucose levels without invasive procedures. The research's main focus is on the prospects and limitations for furthering this line of inquiry.

Gade, A. et al [6] introduced a novel model based on exhaled breath and NICBGM. Here the pre-processing work was done using median filtering (MF). Next, the following are extracted: " Continuous Wavelet Transform (CWT), Improved Discrete Wavelet Transform (DWT), QT intervals, R-peak detection, Entropy-based feature, PR intervals and short-time Fourier transformation (I-STFT)". Moreover, the best features are selected and run via a hybrid technique that combines "Long Short-Term Memory (LSTM) and Deep Max out (DMO)". DMO and LSTM then take the mean to get the desired outcome. To optimize the LSTM weights in this case, the WBU-HGSO or Wild Beest Updated HGSO model is employed. An analysis demonstrating the WBU-HGSO-based model's superiority is the last phase.

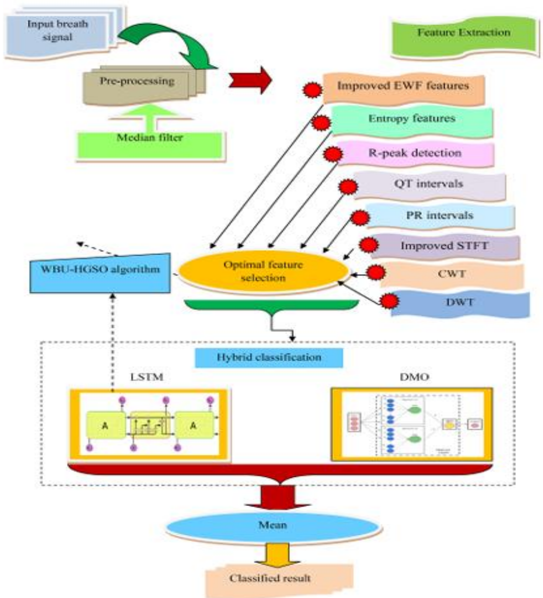

Fig 11: Diagrammatic model of the selected plan.

Joshi, A. M. et al [7] presented a brand-new non-intrusive wearable consumer gadget known as iGLU 2.0 utilized by customers to accurately track their blood sugar levels over time. We have created a new brief spectroscopy in the near infrared (NIR) range that is used in this gadget. It incorporates IoMT (Internet of Medical Things) for intelligent healthcare, in which users and caregivers can access and store healthcare data on the cloud. The regression model that was optimized and analysed is healthy, prediabetic and diabetic individuals to verify and adjust the system.. The mechanism for accurate measurement in iGLU 2.0 is then implemented for serum glucose level using the robust regression models. AvgE (Average Error) and mARD (Mean Absolute Relative Difference) which are computed as 6.09% and 6.07% respectively for capillary blood glucose prediction and estimated as 4.88% and 4.86% respectively for serum glucose, are used to validate the performance of iGLU 2.0.

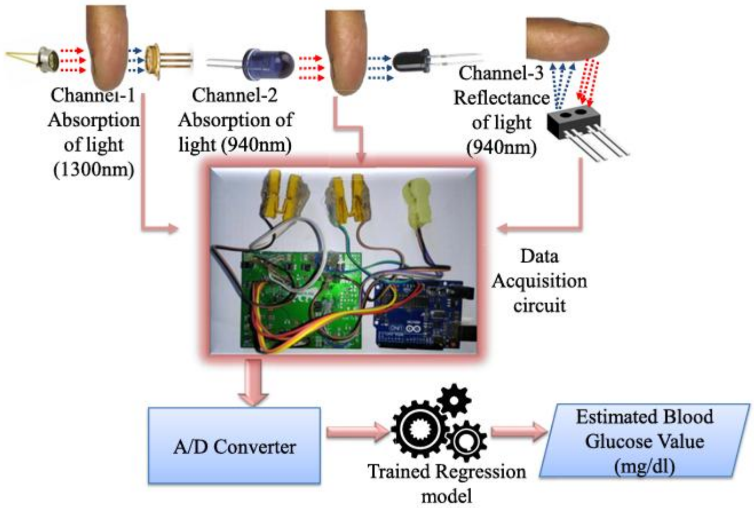

Fig 12: top-level illustration of the iGLU 2.0 gadget.

For the precise measurement of serum glucose levels, a novel dual NIR spectroscopy system combining reflection and absorption spectroscopy at 940nm and 1300 nm has been presented in Figure 12 process flow

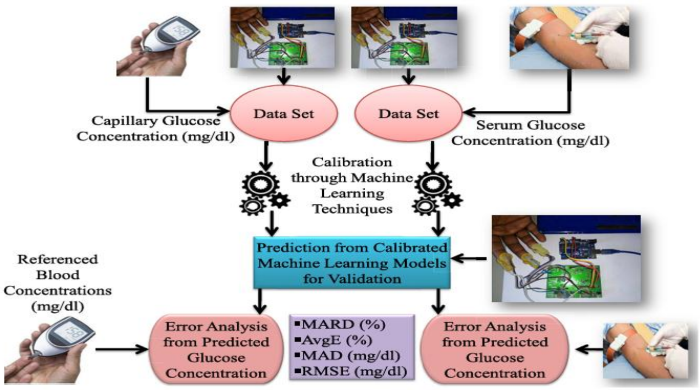

Fig 13: The device's validation and calibration process flow.

Fig. 13 depicts the processes in the calibration and validation procedure. To estimate the performance, RMSE (Root Mean Square Error), the MAD (Mean Absolute Deviation), mARD, and AvgE are computed.

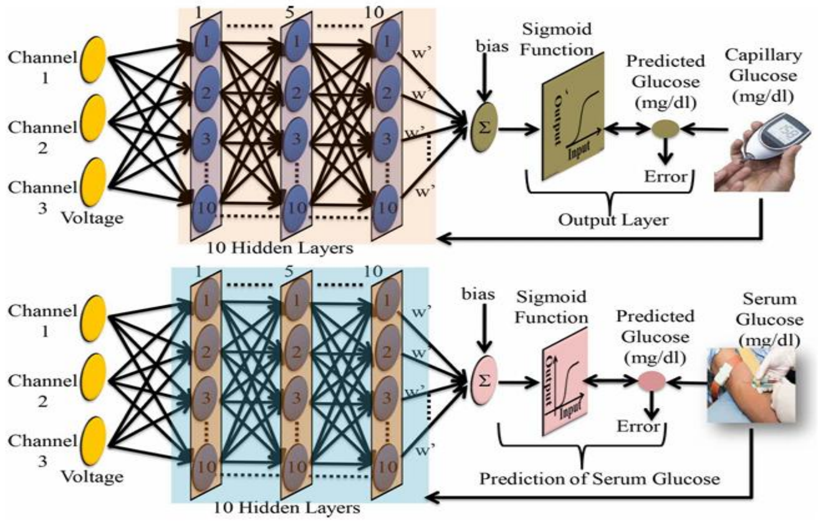

Fig 10: The model utilized for calibration is a Deep Neural Network (DNN).

Applying sigmoid activation functions to the suggested DNN models has been done. The Levenberg-Marquardt backpropagation algorithm is used to instruct the models [36]. Figure 10 displays the DNN model's diagram. The DNN model's overall accuracy was found to be highest when it had ten hidden layers.

Table 2: A Comparative Analysis of Advanced Techniques for Glucose Measurement

Ref. No.	Significant Contribution	Methodology/Model used	Performance	Limitations
[2]	creation of a CNN-based classification algorithm that can dynamically acquire the attributes of the diabetes patients from PPG scalograms by utilizing metadata and PPG signals.	CNN-based classifier, scalogram creation and pre-processing.	With 224 test patients, the optimal model created by combining PPG signals, gender, age and hypertension classification as inputs achieves an accuracy of 76.34%, specificity of 76.11%, AUC of 0.830 and sensitivity of 76.66%	This can be further enhanced by incorporating additional MIMIC-III dataset data to the training dataset, which could increase our model's performance and enable it to pass the FPG test.
[3]	Utilized a homemade IR measurement device having a wavelength of 2900 nm and a peak wavenumber of 3448 cm—1, which determine the value of physical signal. Then, applied several prediction algorithm models to correlate physical signal with actual amount of blood glucose. Separate measurements and analyses done for the transmittance and reflectance signals.	(i)For physical data collection a self-developed equipment with mid-infrared diodes is used. On the transmitting end, Arduino produces PWM waves and on the other side, to collect the signal and decrease the noise arduino is utilised.	The transmittance prediction performance of the signal is determined by XGBoost ($R2=0.990$, $RMSE=3.300$). AdaBoost provides the top performance in predictions for the reflectance signal ($R2=0.984$, $RMSE=4.151$).	The absence of a significant no. of samples of data is the study's limitation because it can be difficult to obtain huge amounts of data quickly.
[4]	recommended solution provides continuous, non-invasive checking method that lowers false positives and increases accuracy by utilizing ML algorithms and wearable technologies. This yield a sizable quantity of data for study, pinpoint risk factors of diabetes, and offer certain therapies to halt the progression of the illness.	Algorithm for Predicting Blood Glucose: i) Gather patient data with various parameter values. ii) Split the collected data into two sets, one for testing and the other for training the model. iii) Using the training data, build a linear regression model with HBCA1 as the target variable and other variables as attributes. iv) Using the training data, build a logistic regression model with	Achieves MAD 6.82(mg/dl), mARD10.64(%) RMSE 9.14 (mg/dl) and AvgE 9.033% and CEG(A&B) 100%	--

		the presence of diabetes as the goal variable and the other factors as input features. v) Use the subsequent procedures to merge the two models: In order to predict the blood glucose level, use the linear regression model and the smart watch's input data. Identify the presence of diabetes by incorporating the anticipated BGL into the logistic regression model as an additional input characteristic. vi) Make use of the test data to assess the performance of hybrid model. vii) Repeat steps 3-6 with different combinations of target variables and input features to find the best model. viii) After the identification of best model, use the model to predict BGL and the presence of diabetes in real time by installing it on the wristwatch.		
[6]	i) suggests using the NICBGM model, which is where attributes like enhanced STFT, DWT, and CWT, as well as I-EWF, R-peak detection, QT intervals, PR intervals, and entropy-based features are developed. ii) the WBU-HGSO algorithm is used to choose features in the best possible way. iii) after that, HC (DMO and LSTM) is used to classify the resulting features. iv) uses the WBU-HGSO technique to optimize the LSTM weights.	suggested an exhaled breath scheme-based NICBGM-based model where the signals were pre-processed using MF. After that, the following were extracted: QT intervals, PR intervals, I-EWF, R-peak detection, entropy-based features, enhanced STFT, DWT, and CWT.	For the maximal scenario, WBU-HGSO + HC achieved an accuracy of 0.92; in contrast, BI-GRU, DBN, RNN, CNN, SVM, HC + HGSO, HC + WBHO, SCMP + HC, and APEHBE + Ensemble classifier obtained lower accuracy. WBU-HGSO + HC produced higher outputs in the mean scenario. The WBU-HGSO +HC	The primary disadvantage is that it monitors interstitial glucose levels rather than blood glucose levels in real time, which results in a gap in the treatment of hyperglycemic patients. Analysis of large datasets have to be taken

		Additionally, the best features were chosen and subsequently run utilizing a hybrid plan that blends LSTM and DMO. The final, superior result was then obtained by averaging the LSTM and DMO values. In this case, WBU-HGSO technique was utilized to optimize the LSTM weights.	has improved to 98% of accuracy at the 60th LP.	into consideration in the future.
[7]	i) a novel dual NIR spectroscopy system combining reflection and absorption spectroscopy at 940 nm and at 1300 nm has been presented for the exact measurement of serum glucose levels. ii) new polynomial regression and DNN models have been constructed depending on dual-NIR spectroscopy and real-life serum data for accurate glucose level prediction. iii) The acquisition module's design makes use of NIR LEDs with spectral wavelengths of 1300 nm and 940 nm to gather BGL measurement sample. iv) A continuous glucose monitoring apparatus is created that can assess blood glucose levels for all types of diabetics, ranging from 80 to 420 mg/dl.	depending on the concept of Near-Infrared (NIR) optical spectroscopy a novel wearable glucometer provides non-intrusive BGL measurement. Regression analysis (Multiple Polynomial Regression (MPR3)) is utilized to further process collected data for estimation of sugar levels. With the use of calibrated ML models (DNN) and dual NIR spectroscopy based on absorbance and reflectance, the suggested wearable glucose monitor delivers an accurate assessment of serum glucose levels.	mARD and AvgE are computed as 6.07% and 6.09% respectively, for capillary blood glucose prediction and calculated as 4.86% and 4.88% and respectively for serum glucose.	It requires the development in ML models for the necessary insulin production for critically diabetic patients' automatic insulin delivery in iGLU 2.0 activated. IoMT framework that Investigating the effects of continuous glucose monitoring using iGLU by other important medical disorders like epileptic seizures will also be emphasized. The confidentiality and safety of individual health information in future, as well as solutions for the IoMT-enabled iGLU device is needed.
[8]	i)A novel method for diagnosing liver illness has been chosen, which combines physiological and iris characteristics. ii) Three hospitals in Islamabad/Rawalpindi, Pakistan, provided 879 patients' primary data. iii) Eleven cutting-edge classifiers from various classification model families were examined for the detection of chronic	The non-invasive diagnostic for chronic liver disease that is being presented uses an ensemble classification model that analyzes physiological and iris characteristics.	i)The model that was presented had the best results, particularly in terms of F-Score, specificity, and accuracy. ii) For the comparative analysis, eleven different classifiers were used. iii) Higher-quality data	i)The model is restricted to the early identification of chronic liver disease. It suggests consultation with a medical professional for the kind of chronic

	liver disease. iv) The ensemble approach, or stack learning, was used to combine numerous classifiers in order to boost accuracy. v) To ensure good data quality, the physiological characteristics' missing values were filled in using KNN technique.	Furthermore, stack learning was used to merge eleven distinct cutting-edge machine learning methods.	was obtained through completing the missed data in physiological data utilizing the KNN algorithm.	liver disease and its thorough diagnosis. ii) The model takes much time to be trained. iii) The intricacy has increased due to the stack learning combination of eleven classifiers. iv) To get 98% accuracy, the model needs a sizable data set. The classification of liver disease will require a large database.
[9]	The diabetes's causes and classification, the framework information on non-intrusive monitoring of blood glucose, the fundamentals of optical technologies, are all introduced. The fiber laser's fundamentals, construction and essential properties of light pulse output are then covered. It is possible to employ fiber lasers to replace other light sources regarding non-invasive blood glucose testing, and five optical methods are covered in detail. Thirdly, it explains the techniques for assessing the device's performance, several crucial algorithms, and the method of processing electrical signals for non-invasive blood glucose testing systems.		This review explains the methods for evaluating the non-invasive blood glucose monitoring device's performance, as well as some key algorithms and electrical signal processing in the device.	--
[10]	The viability of employing commercially available WDs for noninvasive BG level assessment in diabetic patients is further supported by this study. By using AI models, we were able to infer the association linking glycemic measures and attributes that may be obtained via non-invasive Wearable Devices with a high level of precision.	The study utilised an open-source dataset that had information on 13 subjects by age group who were diagnosed with WDs. The dataset included BGL readings, body temperature, sweating, shivering, heart rate, diastolic and systolic blood pressure, and blood oxygen level (SPO2). feature engineering, Data	By using AI models, it enables to assess the association between features that may be extracted from non-invasive WDs and glucose measures with a high degree of accuracy and RMSE range from 0.099 to 0.197.	-

		collection, ML model construction and choosing and metrics calculation and assessment were all part of our experimental design.		
[11]	Developing, creating, and verifying a wearable IoMT PPG gadget for non-invasive BGL assessment. A new input-reinforced CNN named GlucoNet designed and developed to calculate PPG signal blood glucose. • GlucoNet's analogy with current architectures • GlucoNet's deployment and performance assessment as an edge AI mode.	Algorithm: Gluconet Architecture, Device used: PPG sensor, Dataset used: Among the 357 participants, 88 had pre-diabetes and 124 have diabetes; used for more than 21,000 glucose readings; only time series PPG signals were used.	100% of predictions were made in zones A (55%) and B (45%) of the Clarke error grid, with an MAE of 25 mg/dL and a MAPE of 17.8% (±12.8%). An end-to-end glucose monitoring system with edge AI that is demographic-agnostic and doesn't require feature engineering.	-
[13]	The PIDD dataset and information gathered from the iGLU, an intelligent glucose monitor, are used for non-invasive BGL measurement. ML-based regression techniques are applied. Clarke Error Grid examination was conducted on iGLU dataset to validate the proposed method's feasibility. Additionally, the suggested ML model is compared to other similar studies using various performance evaluation metrics, such as Mean Absolute Deviation (MAD), mean Relative Root Mean Square Error (RMSE) and Absolute Deviation (mRAD) and Average Error (AvgE).	ML algorithms including K-Nearest Neighbors (KNN), Random Forest, Linear SVC, Gradient Boosting, Decision Tree, Gaussian Naïve Bayes, and Logistic Regression and NN were employed to identify diabetic samples. Additionally, XGBoost Regression, Multi-Polynomial Regression, Linear Regression, Support Vector Regression, Decision Tree, Random Forest, and NN were employed to forecast blood sugar levels using data collected by the iGLU device.	The AUC value of 0.87 for both logistic regression and random forest suggests the effective diabetes prediction of our model. A decision tree with 70% accuracy and an RMSE of 8.56% can also be employed to predict the glucose level.	more work be done to address the privacy and security concerns with continuous glucose monitoring. Efforts would also be made to incorporate a strong mechanism for type 1 diabetes patients' insulin medication delivery.

V. Obstacles in Non-invasive Blood glucose Assessment:

There are many difficulties in commercializing non-invasive assessment of glucose level devices. Several key issues remain unresolved, which pose significant obstacles to achieving accurate measurement of non-invasive glucose. These difficulties are illustrated. Researchers have recently focused on addressing the precise measurement of glucose in hypoglycemic patients and ensuring long-term continuous glucose monitoring without instantaneous errors. Factors such as body temperature, blood pressure and humidity, which can affect BGL measurement values, have not been adequately considered in the literature. Additionally, cost-effective and portable solutions for continuous glucose monitoring have not been properly addressed.

Achieving accurate glucose measurement within the range of 40 mg/dl to 450 mg/dl continues to be a significant challenge. Additionally, effectively integrating glucometers with the IoMT for continuous cloud-based data logging has not yet been fully addressed. Developing a mathematical model for automatic insulin secretion based on real-time glucose readings within an internet framework still requires improved solutions. Privacy and security concerns related to insulin and blood glucose measurement systems also remain unresolved. Finally, efficient power management mechanisms for continuous glucose measurement with insulin delivery systems need further development.

VI. 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 efficient in various zones to facilitate ongoing health surveillance and viable solutions to reduce the shortcomings of all other techniques. Various methodologies may be utilized in the future for precise glucose monitoring. Consumer devices need to be highly effective across different areas to facilitate continuous health monitoring. They should be regularly used as portable devices for real-time applications. Future devices should be low-cost and user friendly for continuous health monitoring systems.

VII. Future work:

The future plan for a non-invasive BGL 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. Access to the data is restricted to patients and medical professionals 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 [119]. 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. For future advancements, it is essential to have a secured device with comprehensive user control and authentication. A security framework based on Physical Unclonable Function (PUF) is beneficial for IoMT devices [118], [120]. The potential of an appropriate H-CPS that incorporates blockchain-based data and device management should also be evaluated [121], [122]. 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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