Measurement of Blood Glucose using Non-Invasive Methods – A Review

S Mohanram and A Shirly Edward
Department of Electronics and Communication Engineering, SRM Institute of Science and Technology, Vadapalani Campus, No. 1, Jawaharlal Nehru Road, Vadapalani, Chennai, Tamil Nadu, India
Email: 1ms6113@srmist.edu.in, 2edwards@srmist.edu.in

Abstract. Diabetes mellitus has developed into a significant problem during the past decades. Identifying and controlling diabetes can be done by proper treatment and routine like a healthy diet, a weight reduction program, insulin shots treatments, vocal medicines to reduce blood glucose level. Self-glucose checking or clinical testing helps control future complications like blindness, heart disease, kidney damage, or amputations of the limbs due to the disease. Therefore, timely checkups can increase the chances of getting treatment before it is too late. Present glucose evaluating systems for raising diabetic patients are mostly intrusive, hurting, laborious, & cost a sum for frequent testers. The non-invasive glucose testing machinery helps in overcoming these boundaries. Due to this advantage, this subject has gained interest among researchers and many product manufacturing Industries. This evaluation targets to offer current information on available and upcoming trends for non-invasive and nominally invasive techniques. This review also focuses on using the different electromagnetic spectrum bands in detecting the blood glucose level.

Keywords: glucose, insulin, non-invasive, self-glucose monitoring, nominally invasive.

1. Introduction
Glucose is a vital source to charge the body to work in its full potential. If our glucose levels are normal, it commonly goes unobserved. In any case, when they stray from suggested limits, one will note the undesirable impact it has on ordinary functioning [2].

Glucose is the least complex of the sugars, making it a monosaccharide, which implies it has one sugar. It is not the only one. Different monosaccharides incorporate levulose, glycogen, and D-Ribose. Along with fat, sugar is one of the body-favored fuels. Individuals get glucose from gluten items, organic foods, vegetables, and milk products. When we consume food, our body alters the pancreas about the increase in glucose level, so the pancreas releases the required insulin amount [11]. A few patients cannot rely on the pancreas secreting inadequate insulin, so insulin through injections is given to patients [11].
Roughly 4630 lakh adults were alive with diabetes. By 2045, this will raise to 7000 lakhs. The extent of individuals with diabetes is increasing exponentially in most countries. 79% of adults with diabetes are residing in low-to-medium paid countries. One in five under the age of 65 years of age has diabetes. One in two individuals is living with diabetes [12] without any testing. Diabetes caused 42 lakh deaths. Diabetes cost, in any event, 76000 crores in well-being use in 2019 – 10% of complete spending on adults. More than 11 lakh kids and youngsters are living with type 1 diabetes. One out of six live births is subjected to diabetes throughout pregnancy. 37.4 crore people are at an expanded danger of being subjected to type 2 diabetes.

![Figure 1: Diabetic patients count from major countries.](image)

People with diabetes are in peril for long stretch issues impacting the vital human organs and nerve system. It is proposed that patients subjected to diabetes should see an eye specialist reliably for an extended consultation. Figure 1 discusses about diabetic patients count from major countries. The patients with sugar are highly subjected to cataracts, an obscuring in the convergence of the eyes. An increase in glaucoma will increase the eye retinopathy load, which affects the back of the eye. One ought to have one's pee analyzed for protein at any rate once every year. Protein in the pee means kidney ailment. Hypertension may moreover provoke kidney disease. One's heartbeat should be checked when one sees one's social protection provider. All people with diabetes have an extended opportunity for coronary ailments and strokes. Coronary disease is the critical explanation behind death in people with diabetes. It is basic to control various threats, for instance, hypertension and high fats (cholesterol), similarly to glucose. High blood sugars can provoke a powerless circulatory system and nerves hurt, which can provoke moderate repair of wounds. One can experience genuine misery, like losing senses in the feet. In advanced situations, this may provoke surgical amputation of toes or even leg.

The presence of high sugar levels in the blood can impact the sum of the body's sensitive spots. Neuropathy is a framework that can highly impact people with diabetes. Neuropathy is of different kinds,
like peripheral neuropathy, which damages the periphery area and damages the nerves present in organs. Gastroparesis: pathway of food through the stomach moves in the opposite direction. Postural hypotension: Drop in beat because of progress in body position uncontrolled loose bowels. The best way to deal with these issues is to control one's glucose and take extraordinary care of one.

Diabetes occurs due to an unusual amount of insulin present in one's body due to insufficient insulin production or inadequate insulin utilization by the cells in the body. Insulin is the major hormone that controls the amount of glucose present in the bloodstream. Glucose in the blood is absorbed by the cells to get strength or stock it for later use. Nevertheless, suppose there is a high level of glucose in the blood for a long duration. In that case, it could lead to hypoglycemia contrast. Suppose there is low glucose in the blood for a long duration. In that case, it is termed hyperglycemia, which leads to severe health problems, namely stroke, heart disease, kidney failure, tissue damage, blindness, and as a result, death may occur if left unattended.

Deficient secretion of insulin in the human body leads to hypoglycemia, pronounced as a rapid fall in blood glucose levels. In contrast, futile use of insulin leads to hyperglycemia, which is termed as the presence of high glucose in the blood. Both cases do not have a permanent solution; regular monitoring of the blood glucose level and treatment must be carried out throughout the patient's life. Present glucose measuring approaches for the rising diabetic patients are mostly intrusive, painful, laborious, and cost a sum for frequent testers. The traditional method uses an electrochemical technique, which requires a blood sample taken from the patient through finger-pricking.

A self-monitoring device for blood glucose provides information about the glucose level and the sample collection time. It does not need any qualified people to help. Simultaneously, a continuous glucose-monitoring device (CGM) means continuous monitoring of the blood glucose level, adapted for a patient with a higher glucose level. However, there is discomfort and pain involved in both the techniques, whereas continuous monitoring poses a threat of tissue damage and infection. As a result, by the early 2000s, there has been constant work for developing novel non-invasive devices and nominally invasive, aimed at reducing the uneasiness and agony caused by the intrusive methods. The invention of a non-intrusive device would allow millions of patients to monitor their glucose levels without any discomfort or pain and long-term damage to tissues and create a vast demand. Based on the World Health Organization (WHO) report, currently, we have 45 crores of diabetes patients worldwide, and the figure could reach 70 crores by mid-2040.

Recent growth has attempted to study glucose particles' features at various frequencies in the electromagnetic spectrum, ultrasound, DC, visible regions, and near-infrared (NIR). Nevertheless, good results were detected in visible and NIR regions in spectra, leading to marketable devices' design and development. Most of the products are no longer in use due to their poor selectivity, sensitivity, and accuracy. Those already available in the market have not reached the traditional technique level's accuracy level. This situation opens non-invasive glucose monitoring to numerous opportunities like combining numerous procedures, giving way to a more dependable and economical device for glucose measurement.

The current review is restricted to the methods shown in Figure 1. Section 2 describes the currently accepted methods. Section 3 lists currently available devices and approved technologies used in NI and Nominally invasive. Section 4 elaborates on the newly adopted techniques and research. Section 5 describes the research gap that is identified with the newly adopted methods. Finally, the conclusions offered in Section 6 interconnect all the earlier segments and deliver a clear vision of what has to be established shortly.
2. Traditional Methods

In the treatment of keeping up the sugar level in a consistent territory, the “screening glucose” is a basic method to estimate sugar level in the bloodstream and control it in a modestly standard range. Figure 2 displays Noninvasive & Minimally Invasive methods in details.

2.1 Ames Reflectance Meter

Tom Clemens invented the Ames Reflectance Meter in 1969. This meter made self-testing of blood glucose level a job; no experienced medical staff was required. Exposing the needle to blue light...
illuminated the presence of Dextrostix in the paper strip. Depending on the presence of Dextrostix, the illumination varies.

2.2 Reformat
Scientist Boehringer Mannheim launched the primary advantageous glucose measuring meter, which was suggested for the human administration specialist office in 1974. It does not require much blood.

MediSense in 1987 launched the first biosensor structure named “ExacTech.” An impetus terminal strip was applied and created by Oxford and Cranford University.

Four periods of glucose meter: It was made during the 1990s. It made sizes extending from 30 to 0.3μ, and afterward, the testing time would be moved from 5 sec to 2 min, while that of current meters normally less than 15 sec.

2.3 Clinical Significance
Enzymatic-amperometric and hexokinase customary strategies are exceptionally exact, touchy, and precise. The clinical reactions are illustrated well with the equation in figure 2 when glucose and oxygen combine to form gluconic acid. Additionally, realized its conservative size would probably be utilized for speedy testing and investigations of sick patients, particularly in crisis and emergency unit.

\[
\text{Glucose + O}_2 \rightarrow \text{H}_2\text{O}_2 + \text{Gluconic Acid}
\]

\[
\text{H}_2\text{O}_2 + 2\text{I}^- + 2\text{H}^+ \rightarrow \text{I}_2 + 2\text{H}_2\text{O}
\]

The Hexokinase system, in any case, called the photometric method, includes a movement of invention reactions, as showed up in Figure 3. In the fundamental stage, the glucose reacts with the concoction hexokinase, inside seeing adenosine triphosphate and magnesium particles, to make glucose-6-phosphate and adenosine diphosphate. In the ensuing stage, nicotinamide adenine dinucleotide experience oxidation with glucose-6-phosphate dehydrogenase until being lessened to 6-phosphogluconate and nicotinamide-adenine-dinucleotide-diminished, respectively. The proportion of NADH is comparative with the proportion of glucose in the model, and it has the property of charming light at 340 nm. The proportion of ingestion is comparative with the proportion of NADH, meaning that glucose can be assessed using standard spectrophotometric techniques. Figure 3 explains about Measurement of glucose using Hexokinase strategy.

![Hexokinase Diagram](image)

**Figure 3:** Measurement of glucose using Hexokinase strategy

The main difficulties related to clinical methods are their intrusiveness. Any traditional method needs blood samples from their patients, time, costs for a frequent or regular checkup, and the need for a laboratory environment and trained professional. Also, not all test center apparatus is extremely precise.
2.4 In-House Monitoring Schemes
There are two kinds of devices available in the market for individual use and assessment: self-checking and continuous glucose checking. Self-checking can be done at a stipulated time in a day subjected to diabetes type, food taken, medicine prescription, etc. On the contrary, continuous assessment devices monitor glucose every few minutes a day spontaneously, making it easy to observe changes rapidly. On the other hand, both schemes' consistency and precision are suitable during times of need.

2.5 Self-Observation Devices
Self-monitoring devices are also known as glucometers, which require blood samples, drawn from patients through an invasive method. Glucose is the measurement in the same old-fashioned way. However, the difference is, all reaction and evaluation process takes place in the test strip present in the meter. When a drop of blood is placed in the strip, the glucose present in the blood oxidizes due to the glucose oxidase (GOx) enzyme reaction. It produces a definite quantity of current compared to the glucose level. The current is observed by the meter and passes through an I to V converter to give the voltage equal to glucose present. Some of the other enzymes are glucose dehydrogenase present alone with a coenzyme. Figure 4 elaborates measurement of glucose using Finger Pricking Approach.

2.6 Accuracy Valuation Tools and Standards
(Wilbert Villena Gonzales et al., 2019) There are many apparatus rules to assess the devices' precision and effectiveness. The mean-estimation and the error-index are metric estimations to evaluate precision. The standard ISO 15197 gives rules, necessities, and specifics that assessment contraptions should be in line for human use. Taking everything into account, all countries, through their national association, has to follow ISO's principles to overview whether each contraption is proper for commercialization in their district or not.

2.7 Mean Absolute Relative Difference
(Reiterer et al., 2017) MARD is directly the most, by and large, recognized metric estimation to survey the display and precision of glucose disclosure devices, contraptions since it is easy. The standard strategy to
figure the MARD is by using two courses of action of data, taken simultaneously, during clinical primers. One parcel of data is the blood glucose obsession evaluated by the contraption under test, while a standard examination place system gives the resulting educational list (e.g., YSI-2700). At that point, the two estimations are analyzed. Unfortunately, contrasting the MARD of various gadgets may prompt misinterpretations. Thus, MARD ought not to be taken aimlessly as a flat-out pointer of exactness.

2.8 The Clarke Error Grid

It was presented in 1987(Klonoff et al., 2014) by five University of Virginia specialists and depended on clinical practice. All specialists decided a similar situation: An objective range for the patient's BG estimations was 70-180 mg/dl. Inside this range, the patients are very much controlled; underneath or over this range, they need to mediate with restorative activities.

Zone A Graph 2 is the zone on the two sides of the corner to corner. The zone's state results from the judgment that a distinction between BG meter esteems and reference BG estimations of under 20% or BG values just as reference esteems are in the hypoglycemic range (< 70mg/dl) lead to clinically address choices by the clients. On the opposite side, graph 3 of the scale is risky if the qualities estimated with the BG meter will trigger something contrary to the right choice important to treat the genuine BG esteem estimated by the reference strategy. Zone DGraph 4 is the zone with BG meter esteems in the objective scope of 70 to 180mg/dl; however, with reference esteems underneath 70mg/dl or above 180mg/dl. The inverse is valid for zone C Graph 5, where the genuine worth is more than 100 mg/dl underneath the BG meter, an incentive for BG meter esteems above 180mg/dl (upper C). In the rest of zone BGraph 6, the distinction between the BG meter and the reference esteems is bigger than 20%, and the subsequent clinical choices are not right (zone A); however, uncrical.  

Figure 5(a), (b), (c),(d) and (e) shows different zone of Clarke Error Grid

**Figure 5(a):** zone A of the Clarke Error Grid

**Figure 5(b):** zone E of Clarke Error Grid
3. Current Trending Gadgets & Standards available In Market

As shown in figure 1, there is an n number of methods available for non-invasive blood sugar monitoring; not all the methods were able to produce the accurate result as the traditional methods. Some methods were sensitive to the environment, while others were sensitive to temperature. For example, the surface resonance method is highly affected by sweat and temperature, while coherent optical methods are...
affected by temperature and tissue inhomogeneity. The available methods can be considered for detecting blood glucose. However, the accuracy of the result and practicality of implementing the method into a commercial product supports only by a few methods. This section will discuss the methods that have proven supportive for the commercial market like Fluorescence, NIR Spectroscopy, Microwave method, Glucose pop test, saliva analyzer, SugarBeat & GlucoTrack.

3.1. Near-Infrared Spectroscopy
NIR technology uses the properties of absorption and scattering. It supports a wavelength ranging from 780 nm to 2500 nm since the bonds' rotation and vibrations can be obtained in the molecules. Here we adopt three modes of measurement, namely reflectance, transmittance, and interacting. Nevertheless, all these measurement methods depend on the dispersive spectrometer.

In the transmission stage, a polychromatic source is used on the tester. A deflection grating is used on the former side to split the communicated mission into required wavelengths earlier for sensing and detector analyzing. The detector and diffraction grating are present in the reflectance stage, and a source to detect the reflection is happening. Similarly, interactants mode uses a blocking in the middle of the source and the mirrored rays to view the detector from the source side. Transmittance mode helps analyze see-through samples, while reflectance and interactions are used for analyzing dense solids samples. The merits and demerits of near infrared are tabulated below. We may show several demerits, but due to its low cost and high resistance to interference, alternative ways under this topic are getting more attention. Table 1 shows Merits & Demerits of NIR spectroscopy and Fluorescence in Table 2.

| Table 1: Merits & Demerits of NIR spectroscopy |
|-----------------------------------------------|
| Advantages | Disadvantages |
|---|---|
| 1. This technique is not affected by materials like plastic or glass. | 1. High scattering level. |
| 2. Low-cost materials needed. | 2. Mixed distributions of glucose can give false readings |

3.2. Fluorescence
For Fluorescence technique on glucose fluorophores and receptors is much needed; some fluorophores can bind to the glucose molecule straight away. At the same time, many other need agent molecules named receptors as they help in binding with the glucose easily and also adopts reversible changes in their characteristic’s properties; this helps in allowing reformed fluorescence allowing the possibility of new fluorescence techniques monitoring from a wide range of the spectrum, ranging between UV to NIR spectrum.

Fluorescence resonant energy transfer (FRET) has got attention, as it can work with two different molecules, the fluorophore, and the receptor. In standards, when a link between glucose and acceptor happens, this link leads to the decrease of electrons and an increase in fluorescence. However, when the glucose molecules are high, the electron flow increases, leading to less illumination.

The advantages and disadvantages of fluorescence are tabulated below. We may show several demerits, but due to its low cost and high resistance to interference, alternative ways under this topic are getting more attention.
Table 2: Merits & Demerits of Fluorescence

| Advantages                                      | Disadvantages                                               |
|------------------------------------------------|-------------------------------------------------------------|
| _ Very sensitive to glucose concentrations.   | _ Highly affected by pH changes and oxygen levels.          |
| _ High optical properties of the molecule     | Foreign material in the blood may affect the inference.     |
| _ Its measurement depends on the concentration of glucose to Fluorescence intensity and time taken for decay | _ Short lifespan of the molecules illumines.                |
| _ Immune to light scattering                  | Local tissue damage may give a false reading.               |
|                                                | _ Autofluorescence property is high for donors and acceptors in blood. |

3.3. Microwave

Microwave and millimeter radiation has very low energy and less scattering in the tissues, which helps in deeper penetration of the tissues, helps in more exact glucose measurements, so to make use of this property, microwave techniques have started to emerge in many fields, including the medical field. Feeding on the reflective property like transmission and absorption in the blood capillaries, glucose concentration in the patient body can be identified. The microwave technique adopts four techniques, namely: radar, transmission, resonant perturbation, and reflection. Table 3 explains about merits & demerits of microwave spectroscopy and few non-invasive methods in Table 4. Table 5 and 6 discusses about Comparison Table of Gas Detection Techniques. Table 7 explores the List of Sample-based Methods for Blood Glucose Checking.

Table 3: Merits & Demerits of Microwave spectroscopy

| Penetration properties are much high to reach sufficient glucose. | Merits | Demerits                                                               |
|----------------------------------------------------------------------|--------|------------------------------------------------------------------------|
| _ ionization is not needed.                                           |        | AFFECTED BY ORGANIC VARIATION IN BLOOD.                                 |
| _ Even small variations in glucose can also be detected.             |        | _ Even affected by breath level, sweat level and cardiac activity.      |

Table 4: Merits & Demerits of few non-invasive methods

| Technology used                      | Exposed area     | Merits                                       | Demerits                                                                 |
|--------------------------------------|------------------|----------------------------------------------|--------------------------------------------------------------------------|
| Polarization change                  | Eye              | uses visible light                           | sensitive to eye vary from individual and not suitable for all skin types |
| Bioimpedance spectroscopy            | Skin             | keeps track of changes in glucose level       | Poor penetration                                                         |
| Mid-infrared spectroscopy            | Skin             | better then NIR                              | Instability, time-consuming for spectral acquisition                     |
| Raman spectroscopy                   | Skin             | The fixed wavelength of lasers, low cost     |                                                                          |
| Thermal emission spectroscopy        | Ear, forearm skin, fingertip | Decent availability for detecting glucose present | disturbed by body heat and physique motion                              |
### Table 5: Comparison Table of Gas Detection Techniques

| Technique | Highlights | Challenge |
|-----------|------------|-----------|
| Elected Ion Flow Tube - mass spectroscopy | It is a type of bulk spectroscopy where substance ionization reactions are used to evaluate unpredictable natural mixes. Recognition of the unpredictable natural mixes should be possible continuously, and the exactness of identification is seen as high. | Significant expense, low movability, complex utilization. |
| Gas chromatography-mass spectroscopy | isolates unstable natural segments because of the variety in the substance in the middle of these atoms in a vaporous blend and their qualified fondness for the segment's fixed period. This technique is exceptionally precise and shows high affectability and selectivity in the glucose observation. | Significant expense, low convey ability, complex utilization, practice is impossible during the continuous investigation. |
| E-Nose | The innovation is a detecting innovation that utilizes various synthetic sensors that distinguish and perceive the unstable natural mixes because of their concoction properties. These strategies are reasonable, compact, and have a quick reaction time. Continuous investigation of the mixes is conceivable. | High-temperature activities and sensors are touchy to moist. |
| Cavity Ringdown Spectroscopy | This visual spectroscopic strategy gauges the convergence of unstable natural multiple foundations on the measure of retained or dispersed light. The method is exceptionally effective, and it very well may be continuously investigat | ed. The requirement for alignment strategy. |

### Table 6: Comparison Table of Gas Detection Techniques

| Sensing Technique         | Response Time | Detection in mm | Drawback                                      |
|---------------------------|---------------|-----------------|-----------------------------------------------|
| Carbon Nanotubes          | ~500sec       | 0.5–5ppm        | moisture affects sensitivity                  |
| Electrochemical           | 3-5min        | 0.2-10ppm       | Interference of moisture in the breath        |
| Metal Oxide Semiconductors| 3-4min        | >0.5ppm         | The occurrence of wetness and hotness disturb the performance. |
Acoustic 20-30mins 443.2 mg/dl and 90.29 mg/dl Interfering of moisture in the breath

Conducting Polymers 5min 1-10ppm Long recovery time

CMOS-MEMS 7-8min 0.05 -5ppm Frequency drift and sensitivity are less.

Microwave ~5min 0-265ppm Interference of other gases.

Photo-ionized Detector <10sec 0-1500ppm The sensor shows a non-lined reaction to high concentrations.

| Table 7: List of Sample-based Methods for Blood Glucose Checking |
|---------------|-------|-----------------|----------------|
| Method                    | Equipment                                      | Benefits                                      | Drawbacks                                      |
| Salivary examination     | biosensor                                     | Delicate, pain-free, convenient, fast.       | Saliva thickness can vary for different persons. |
| Breath examination,       | Metal oxide semiconducting sensors             | Free of environmental conditions and low cost | can be performed only in the laboratory         |
| Salivary analysis         | Optical paper biosensor, strip                 | Cost-effective                                | Not affected by low glucose levels             |
| tear and salivary test   | Biosensor                                     | Pain-free, highly sensitive                   | Extra sample volume is needed due to proteins presence |
| Saliva Analysis           | Disposable biosensor                          | ease of use, cost-effective                   | Disturbed by motion artifacts.                |
| Salivary analysis         | Cavities sensors                              | module for telemetry, customized mouthpiece | Hence data noise occurs. Uncomfortable to use |
| Tear examination          | sensor present in Contact lens,               | Reduced risks of getting infected, time effective | harmful effects of the equipment cause vision problem, increase in eye temperature |
| Breath examination        | E-nose                                        | Better precision, pain-free                   | Not fit for clinical use                      |
| Breath analysis           | E-nose                                        | humidity and alveolar air are taken into account | Model not precise enough for real use.        |
4. New Technologies That Are Understudy

(Goestom Budianto et al., 2018) [1] The excreted urine is a very good indicator of a patient’s health condition, which is achieved by testing the urine. There is a number of methods available for a urine test, of which the easiest and quickest result yielding method is the strip test. In the strip test, once the strip surface touches the sample, the reagent's color starts to change. Strip test helps us analyze the urine sample's substance, such as ketones, glucose, nitrite, urobilinogen, blood, and bilirubin. This paper creates an image processing system to analyze the strip by capturing the strip image and processing it through an algorithm on the smartphone. From the observed results, we can say that 93.4% accuracy was observed in the sample to recognize kidney stones and 90% correctness for glucose monitoring without any medical staff assistance.

(Lincy Alice Philip A et al., 2017) [3] The photoplethysmography signal is noted from the body, and numerous factors that help estimate the value of blood glucose are taken from this signal. Scientific parameters and observed parameters are analyzed using a machine learning algorithm, and the inference is charted and compared.

(Sahnius Usman, et al., 2017) [4] We use the second derivative of the photoplethysmography waveform technique to monitor the states of diabetic HbA1c. The proposed method is simple and cost-effective. Results indicated the patient might be at risk of having high HbA1c, which can be estimated by analyzing the PPG signal's information.

(B. Lakshmi Priya et al., 2018) [5] Visible red laser light of wavelength 650 nm is used to penetrate the blood capillaries and tissues. The refractive index of laser light is more vulnerable to glucose concentration changes resulting in quicker response when compared to NIR make it more reliable than NIR or MIR methods. The data obtained from the hardware is sent to the Thing Speak cloud server; the proposed system analyzed the blood glucose level in in-vitro vessels, and the results were compared with standard measurements made.

(Heungjae Choi et al., 2014) [7] a new glucose sensor design using microwave split-ring resonators with an operating frequency of 1.4 GHz is designed. The sensing rings are prepared from copper wire coated with silver, and the reference ring functions at a greater frequency. In this method, the temperature effect on the ring is considered, and calibration is made depending on the temperature effect. The sensing device is directly attached to the stomach area by using a bonding agent patch. For authentication, the proposed sensor was tested with two market available sensors for 12 hours and after three meals of a day.

(Mohammed Shahriar Arefin et al., 2018) [8] a novel was used by combining the available two standard methods near Infra-Red absorption and bio-impedance measurements. Separate tests were made to check the methods' accuracy than by using Artificial Neural Network and least squares regression techniques. The two methods were combined, and their results were tabulated. The hybrid technique is constructed using linear regression, which shows the correctness of 90% and 10% of data in the A&B region of the Clarke error grid, which falls under the acceptable region.

(RA. Buda et al., 2014) [9] portable non-invasive infrared sensors are developed for the measurement of blood glucose. The observed glucose concentration is displayed, but the required insulin level depending on the patient's body mass index, is also calculated and displayed. Several tests were made to prove the reliability of the device.
(Hui Zheng et al., 2018) [13] the application engineering of Nar-line Band Internet of Things (NB-IoT) is utilized in non-intrusion sugar hardware. Likewise, a functioning sensor gathers and studies the internal heat level, pulse, heartbeat, and strolling status just as individuals' glucose and their comparing NB-IoT designs. At that point, our estimation can screen the entire state of an individual and check the deliberate estimation of blood glucose with the other physiological highlights. This framework adjusts a person's degree of blood glucose without a blood test [14].

An implantable glucose sensor may keep up a key good way from the heaviness of reiterated blood groupings. However, it is exceptionally prominent and requires intermittent replacement of the sensor inferable from biofouling and its short lifetime; particularly, the progression of non-invasive sensors regardless of everything has a chance to show signs of improvement [15] to the extent of immobilizing impetuses, growing the affectability, and fortifying the drawn-out unfaltering quality of the sensors. Close by the mechanical points for single contraption level pending further investigation, the beneficial structure of the non-invasive glucose [16] watching system and show related with the obtainment of biofluid model may in like manner be refined to propel tolerant appropriateness [17]. Numerous scientists have utilized counterfeit intelligence (AI). Artificial intelligence-based estimation of how many more choice models hold the eventual fate of non-obtrusive glucose observing as far as precision, cost viability, convey ability and productivity [18], and so on. The essentialness of this work is twofold: 1. To overcome any issues among IT and clinical field and 2. To overcome any barrier between end clients and the arrangements, equipment and programming are shown.

5. **Future Prospective**

   Improvement of non-noticeable diabetes analytic methods in a wise and clinically conceivable manner is chief to regulate the interminable affliction's quick advancement. As referenced already, diabetes addresses one of the greatest basic problems concerning today. Sniff evaluation non-intruding framework has shown uncommon limits concerning diagnosing this infection. On examining the different gas appraisal advancements, the e-nose strategy is the possible unequivocal instrument for the sickness's clinical affirmation. Regardless of how different frameworks for breath-based methods for diabetes checking are proposed and made. There are sure hindrances that end its effective use.

6. **Research Gaps**

   From the above studies, we can conclude that the problem addressed is the pain-free, non-invasive method. However, considering some of the studies, they use a minimally invasive mechanism or sensors attached to the body by binding agents. Even these suggested methods are fully unable to overcome the preliminary problem of Pain-free monitoring technique. The first gap that can be identified is that a 100% clinically effective non-intruding method to measure the blood glucose level is not available in the market. The second consideration is the steps involved in the detection process; without proper technical knowledge and assistance from the medical expert, the above-mentioned methods are not effective. The next gap is that we need to develop a system that uses minimal steps and user-friendly methods to self-assess blood glucose levels. As given in the introduction, the growth of the diabetic patient population is increasing rapidly [19]. If this growth retains the testing time and duration will increase, we need a system that uses less testing time and less analytical time to process the sample. Even if the processing and testing time is to consider the precision, the result must not be affected due to this time constraint.

7. **Conclusion**

   This review has provided a detailed view of the current available glucose monitoring device and techniques without blood from the patient. The tools, devices, equipment’s, and electromagnetic spectrum...
region, which have shown good results in finding accurate blood glucose values, are well explained in all the above sections. Connecting all the sections by illustrating its merits and demerits and the future devices that are to be formulated will lead a new way in non-invasive blood sugar monitoring. As new frameworks and technological development are happening rapidly, the main obstacle of low sensitivity, low specificity, and interference can be overcome in no time, and a genuine model for non-invasive blood sugar monitoring can happen in no time.

References

[1]. Tri Harsono, Goestom Budianto, Henry Yuniarti, "Strip Test Analysis Using Image Processing for Diagnosing Diabetes and Kidney Stone Based on Smartphone” International Electronics Symposium on Knowledge Creation and Intelligent Computing (IES-KCIC) 2018.

[2]. MD, FACP, David C. Klonoff “Overview of Fluorescence Glucose Sensing: A Technology with a Bright Future”

[3]. Journal of Diabetes Science and Technology Volume 6, Issue 6, November 2012.

[4]. K. Rajasekaran, Smily Jeya Jothi E., Lincy Alice Philip “Continuous Monitoring Of Blood Glucose Using Photophlythesmograph” Signal Proceedings of IEEE International Conference on Innovations in Electronic, Electronics, Instrumentation and Media Technology ICIEEIMT 17.

[5]. Sahnius Usman, Rudzidatul Akham Dzijauddin, Norhaslinda Harun, Nurul Aini Bani “Estimation of HbA1c Level Among Diabetic Patients using Second Derivative of Photoplethysmography” IEEE 15th Student Conference on Research and Development (SCoReD) 2017

[6]. B.Lakshmi Priya, R. Bhuvaneshwar, S. Jayalakshmy "Non-Invasive Blood Glucose Monitoring based on Visible LASER Light” Proceedings of the International Conference on Communication and Electronics Systems (ICCES 2018)

[7]. Riccardo Favilla, Marcus Larsson, Tomas Strömberg “Assessment of advanced glycated end-product accumulation in the skin using multispectral autofluorescence imaging” 2015, Computers in Biology and Medicine.

[8]. Jack Nylon, Stephen Luzio, Heungjae Choi, Jan Beutler, and Adrian Porch, “Design of Continuous Non-Invasive Blood Glucose Monitoring Sensor Based on a Microwave Split Ring Resonator” 2014 IEEE

[9]. Adnan Hossain Khan, Mohammed Shahriar Arefin and Rabiul Islam “Non-invasive Blood Glucose Determination using Near-Infrared LED in Diffused Reflectance Method” 10th International Conference on Electrical and Computer Engineering

[10]. M. Mohd. Addi and R.A. Buda – IEEE-EMBS Member “A Portable Non-Invasive Blood Glucose Monitoring Device” IEEE Conference on Biomedical Engineering and Sciences, 8-10 December 2014

[11]. Ahmed Toaha Mobashsher Wilbert Villena Gonzales and Amin Abbosh “The Progress of Glucose Monitoring—A Review of Invasive to Minimal and Non-Invasive Techniques, Devices and Sensors” Sensors 2019, 19, 800; DOI:10.3390/s19040800

[12]. Yitong Guo, Zheng Li, Qiuliang Ye, Zikang Tian, and Bingo Wing-Kuen Ling Ringo Wai-Kit Lam “Wearable Non-invasive Blood Glucose Estimation via Empirical Mode Decomposition Based Hierarchical Multiresolution Analysis and Random Forest” IEEE 2018

[13]. Meng Xia, Yuhang Liu, Zedong Nie, Member, IEEE, Jingzhen Li1, Yicheng Zeng2, and Lei Wang In vivo “wearable non-invasive glucose monitoring based on dielectric spectroscopy” 2016 IEEE
[17]. Jing He, Hui Zheng, Peng Li, Mengjiao Guo, Hui Jin, Jie Shen, Zhijun Xie, Chihung Chi "Glucose Screening Measurements and Noninvasive Glucose Monitor Methods" Procedia Computer Science 139 (2018) 613–621

[18]. S. Lekha and Suchetha.M, Member, IEEE, “Recent Advancements and Future Prospects on E-Nose Sensors Technology and Machine Learning Approaches for Non- Invasive Diabetes Diagnosis: A Review” DOI 10.1109/RBME.2020.2993591

[19]. L.-H. Chieng, C.-H. Li, I. S. Thimmaraju, and D.-J. Yao, “Using td- GC-ms to analyze coffee beans aromas of different roast levels,” in Nano/Micro Engineered and Molecular Systems (NEMS), 2014 9th IEEE International Conference on, pp. 507–512, IEEE, 2014.