Current Status of Non-invasive Diabetes Monitoring

Sreedevi Paramparambath, Ishwar Maruti Islampure, T. Sabitakala, Muni Raj Maurya, Hajar Morsy, Swathi Yempally, Suresh Muthusamy, Senthil Kumar Ramu, Santhiya Pandiyan, Raghad Abuznad, Alaa Elsafiahmed, Aeshah Alruwaili, Muna Ibrahim, Peter Kasak, Ravikumar Ramlu Vidule, Ankanagari Srinivas, and Kishor Kumar Sadasivuni

Abstract In routine life, diabetes is usually measured by an invasive process. Although this technique is accurate, there are many drawbacks, especially if you need to take multiple readings regularly. Hence**,** it is necessary to develop a highly reliable non-invasive diabetes screening technology that is better than the pre-existing invasive technique**.**In recent investigations, human serums such as tears, saliva, urine,

M. Ibrahim · P. Kasak · K. K. Sadasivuni (B)

H. Morsy e-mail: hm1604839@qu.edu.qa

R. Abuznad e-mail: Ra1704974@qu.edu.qa

A. Elsafiahmed e-mail: sabithakalatatituri@jntuh.ac.in

A. Alruwaili e-mail: aa1604608@qu.edu.qa

M. Ibrahim e-mail: mi1701758@qu.edu.qa

P. Kasak e-mail: peter.kasak@qu.edu.qa

I. M. Islampure Robokidz Eduventures Pvt Ltd, Pune, Maharashtra, India

T. Sabitakala Department of Chemistry, Jawaharlal Nehru Technological University, Hyderabad, India e-mail: sabithakalatatituri@jntuh.ac.in

M. R. Maurya Department of Mechanical and Industrial Engineering, Qatar University, Doha, Qatar

S. Muthusamy

Department of Electronics and Communication Engineering, Kongu Engineering College, Erode, India

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S. Paramparambath · H. Morsy · S. Yempally · R. Abuznad · A. Elsafiahmed · A. Alruwaili ·

Center for Advanced Materials (CAM), Qatar University, 2713 Doha, Qatar e-mail: kishorkumars@qu.edu.qa

and respiratory secretions have been found to reflect the presence of glucose in it. These factors increase the possibility of non-invasive blood glucose level estimation. Diabetes was a rare condition in past years compared to recent times, but this has become more widespread in recent decades due to changes in the eating habits and lifestyles mismanagement of human beings. In some cases, there are chances of diabetes in newly born infants. When the body cannot produce enough insulin or cannot use its insulin, blood glucose levels rise in the body. As a result, invasive methods for measuring blood glucose levels are used, which may cause major or minor problems for patients in the long run of life. To address this issue, a low-cost, non-invasive approach for detecting diabetes is urgently required by our society. Many new technologies have been researched and implemented; each has its advantages and disadvantages. The present chapter gives a qualitative overview of various non-invasive glucose monitoring systems beneficial for diabetic patients.

Keywords Invasive · Non-invasive · Diabetes · Spectroscopy · NIR

1 Introduction

In contrast to typical invasive laboratory testing of the blood sample, self-monitoring of glucose level provides a current scenario of diabetes with a continuous, dependable, and reliable approach for determining blood glucose concentration. Checking glucose levels frequently using invasive methods is a critical process for the treatment of diabetes. This invasive technique assists patients in preventing and detecting hypoglycaemic and hyperglycaemic conditions. Many commercial blood glucose monitors present in the market require a small drop of blood to be taken by pricking the skin with a lancet, which is generally a fingertip (often called a fingertip test). These are the intrusive blood glucose monitors that cause the patients a huge amount of discomfort because they are likely to be punctured several times a day for checking their blood glucose level.

Depending upon the amount and condition of the sample, human inaccuracy during sample collections, calibration errors, humidity, and poor cleanliness in the testing region, might increase the proportion of mistakes while using invasive monitoring techniques [\[1\]](#page-18-0).

S. K. Ramu

R. R. Vidule (\boxtimes) Department of Chemistry, SSGM College, Loha, Dist. Nanded, Maharashtra, India

A. Srinivas

Department of Genetics & Biotechnology, Osmania University, Hyderabad, India

Sri Krishna College of Technology, Coimbatore, India

S. Pandiyan Computer Science and Engineering, Anna University, Chennai, India

Fig. 1 Flowchart of blood glucose monitoring techniques

The non-invasive approach, a recent technology, requires glucose signals from the body. Non-invasive methods avoid "finger pricking" and help continuously monitor blood glucose levels. Techniques such as applying fluorescent light to the body in a specific location, in addition to the techniques involving the implantation of a sensor in the subcutaneous tissue, lead to a major disadvantage: the interference of nearby signals such as ultraviolet and visible light with the process.

Another approach that uses optical beams to detect glucose signals is acoustic spectroscopy. However, this process suffers from scattering effects, resulting in insensitivity. Near-Infrared (NIR) spectroscopy is also one technique that can also be used to measure the level of glucose in blood [\[2\]](#page-18-1). The level of glucose can also be evaluated with the help of multi-modal spectroscopy IC which combines impedance spectroscopy (IMPS) and multi-wavelength near-infrared spectroscopy (fNIRS) [\[1\]](#page-18-0). In Fig. [1](#page-2-0) the flowchart of different blood glucose measurement techniques is shown.

This technology employs indirect dielectric properties of the tissue surrounding the blood and the precision of the glucose levels obtained by the suggested microchip to eliminate various systemic sounds.

A recent method for identifying diabetes is to use the Gabor filter to analyze face contour features [\[3\]](#page-18-2). Human respiration can potentially be used to diagnose diabetes. This indicates a good link with blood sugar since human breath includes acetone, which can be analyzed simply by exhaling it directly into the monitoring device [\[4\]](#page-18-3). In Fig. [2,](#page-3-0) the non-invasive glucose monitoring techniques are shown.

Fig. 2 Different non-invasive glucose monitoring. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 by Gonzales et al., Licensee MDPI, Basel, Switzerland

2 NIR Spectroscopy

The spectroscopical region of 12,500–4000 cm⁻¹ belongs to Near-infrared (NIR) region, and its wavelength is 800–2500 nm. Both wavenumber and wavelength are being considered in the present chapter. The region in-between IR and the visible region is NIR spectroscopical region. Generally, NIR spectroscopy deals with reflection, emission, diffusion, and light absorption. NIR spectroscopy has advanced characteristics that have played a significant role in basic and applied science applications over the last two decades [\[6\]](#page-18-5). In the spectral range of near-infrared, the ability of light to penetrate soft tissues and biofluids is relatively high (>0.5 mm) as, compared to visible light and ultraviolet light, it scatters less. Apart from this, this technique can achieve both reflection and transmission for the sensing measurement of light [\[7\]](#page-18-6). The mathematical formulation for calculating sample absorption is done by Beer-Lambert law (Eq. [1\)](#page-3-1) from the already known thickness and concentration.

$$
I = I_o 10^{(-l.\varepsilon.c)} = I_o e^{-l.\mu_a}
$$
 (1)

where I is the intensity of light at depth within the absorption medium W/cm^2 , initial light intensity is represented by I₀ (W/cm²), absorption depth is represented by l, ε is the molar attenuation coefficient or molar extinction coefficient (L/mmol cm), it depends on the structure of absorbing molecules and the wavelength of incident light. Absorbing molecules concentration is represented by c (mmol/L). The absorption coefficient μ_a is proportional to the product of c and ε .

This model showcases the transmitted/reflected intensity of light as a function of concentration, the thickness of the sample, and absorption coefficient. In contrast, the scattered light effect is ignored in this phenomenon. $Log(I_0/I)$ is used to define absorbance [\[8\]](#page-18-7). NIR absorption spectroscopy can quantify the glucose absorbance and its dependence on wavelength in the aqueous medium. Incident light absorption by water must be considered as it is the most abundant species in biofluids. Two absorption peaks, one between 1350 and 1520 nm and the other in-between 1790 and 2000 nm, are revealed in the NIR spectrum range for water. To measure glucose in the NIR range, wavelength windows in the range of 700–1100 nm, 1500–1850 nm, and $2000-2400$ nm can be used $[9-11]$ $[9-11]$.

On the contrary, light absorption in a shorter wavelength range is lower for water. So to obtain selective NIR spectroscopic results with the minimization of interfering effects of water, one should essentially use shorter wavelengths [\[7,](#page-18-6) [12\]](#page-18-10). Figure [3](#page-5-0) shows the spectra recording equipment. The equipment consists of a NIR spectrometer, a light source, and a fiber optical measuring head. In NIR spectrometer, a 128 pixels InGaAs photodiode array detector is attached to a glass block, and it uses a polychromator with a holographic imaging diffraction grating. According to the modified Beer's equation, near-infrared diffused reflection difference spectra are obtained at the skin tissue to constantly forecast the blood glucose content, which is proposed and investigated without multivariate analyses. The difference spectra are presumed to be generated from four primary elements in the human skin (glucose, protein, fat, and water) and a scattering equivalent component called the baseline. As a result, the morphological similarity of the absorption spectrum between glucose and baseline is one of the roots of inaccuracies in predicting blood glucose levels in the near-infrared region. An artificial component integrated with baseline and fat is revealed when extracting the glucose components from the distinction spectra at baseline using fat's specific wavelength. It is predicated on the notion that a change in skin scattering induces both the variation in fat contribution and leads to baseline development.

We can reduce the blood glucose prediction mistakes by using the imaginary component. In contrast to multivariate analysis methods, the estimation procedure of blood glucose substances from observed reflection spectra is transparent, making it easier to evaluate the causes for fluctuations and contributions of the components in the observed reflection spectra. In Fig. [3,](#page-5-0) the typical blood glucose level profile is shown. Using radial-basis neutral networks (RBF) and partial least-squares regression (PLS), the calibration coefficient of matrices is calculated.

Glucose measurements are interfered with by chemical and physical parameters such as albumin, triglyceride, temperature, and pressure variation. Environmental changes such as variations in humidity, carbon dioxide, atmospheric pressure, skin

Fig. 3 Schematic representation of the three modes of NIR spectroscopy. **a** Transmittance mode. **b** Reflectance mode. **c** Interactance mode. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 by Gonzales et al., Licensee MDPI, Basel, Switzerland

hydration, and temperature also cause errors. The proposed technique may become a convenient tool for interpreting non-invasive blood glucose monitoring using nearinfrared spectroscopy [\[13\]](#page-18-11).

Rolamjaya Hotmartua et al. used NIR spectroscopy for Glucose detection from the earlobe. They first carried out the test by varying glucose concentration from 50 mg/dl to 2 g/dl, and 2nd test was carried out directly in the earlobe [\[14\]](#page-18-12). Samman et al. researched glucose monitoring for about 169 days and analyzed the accuracy as well as stability of the calibration method $[15]$. In brief, it can be said that the application of NIR spectroscopy in combination with regression analysis helps quickly to detect the glucose levels in a non-invasive manner, thereby providing an additional tool for the early detection of diabetic problems [\[9\]](#page-18-8).

3 Raman Spectroscopy

The degree of scattering of monochromatic light is determined by Raman spectroscopy which is based on the Raman effect. Scattered light that travels in all directions is produced when a single wavelength light hits the target. Using the imaginary component can reduce the error in predicting the blood sugar level. Unlike multivariate analysis, this method makes it clearer to calculate blood sugar levels from the observed reflectance spectrum, making it easier to estimate the reason for the change and the component contribution in the reflectance spectrum. Rayleigh scattering occurs in visible radiation when the scattering is elastic. The phenomenon is known as Raman scattering if the scattering is not elastic [\[16\]](#page-18-14). The schematic representation of Raman scattering is shown in Fig. [4.](#page-6-0)

Raman shift is termed for such wavelength differences. The Raman shift represents the difference between the initial and final vibrational states of molecules under study [\[17\]](#page-18-15). The vibrational and rotational states of molecules are dependent on Raman spectroscopy. The functional group's vibrational modes are shown in the peaks of Raman spectra. It consists of a lens that seizes the scattered radiation. It also filters the radiation and allows the Raman scattered radiation to the detector for getting sensed. The signals are processed by computer and provide Raman shift correspondingly.

Raman spectroscopy is a favorable non-invasive biomedical method and analyses the problems associated with metabolism. For example, clinical tests and selfmonitoring of glucose levels based on a finger prick technique blood sample are no longer painful. Raman spectroscopy is based on the elastic scattering of photons by certain molecules in the sample. The energy shift of the scattered photons is determined by the bonds of the interacting molecule, thereby resulting in molecular fingerprints. The advantages and limitations of Raman scattering for glucose monitoring are shown in Table [1.](#page-7-0)

It also has important benefits in biomedical diagnostics, including noninvasiveness, a short procurement time, and the capability to offer quick results. It has been shown that Raman spectroscopy and principal component analysis (PCA)

Fig. 4 Schematic representation of Raman spectroscopy. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 by Gonzales et al., Licensee MDPI, Basel, Switzerland

Pros	Cons
• Less susceptible to variations in temperature • Moderate sensitivity to water • It can be used on any surface, including opaque substrates, to measure scattered light • The elevated degree of specificity	• Susceptible to interference by other molecules such as hemoglobin • Intensity and laser wavelength are unstable • The collection time is long • Prone to noise interference (low signal to noise ratio), fluorescence, and turbidity

Table 1 The pros and cons of glucose detection using Raman spectroscopy

paired with support vector machine (SVM) has proven to be effective in classifying glycated hemoglobin levels using in vivo techniques [\[18\]](#page-19-0).

4 Bio-impedance Spectroscopy

The bio-impedance analysis is a non-invasive, low-cost, and widely utilized method for determining body composition and assessing clinical status. There are numerous ways of interpreting the measured bio-impedance data. Apart from that, there are numerous applications of bio-impedance in the assessment of body composition and the evaluation of clinical status. In addition, bio-impedance spectroscopy is being used in various ways in healthcare institutions, including disease prognosis and monitoring of vital signs. Thus, we feel that this warrants a review of the most underlying facets and forecasts healthcare applications of bio-impedance spectroscopy [\[19\]](#page-19-1).

The bio-impedance analysis is a low-cost, non-invasive method for evaluating body composition and helps in monitoring of clinical state. There are varieties of techniques to interpret measured bio-impedance data and a variety of bio-impedance applications in body composition assessment and clinical status assessment.

A wrist glucose monitor based on impedance spectroscopy has been invented. It is shown in Figs. [5](#page-8-0) and [6.](#page-8-1) This monitor uses the skin as a dielectric to sample an LC resonance circuit data. There are numerous approaches for interpreting measured bio-impedance data and bio-impedance applications in body composition and clinical state assessment. The drawbacks and advantages are shown in Table [2.](#page-9-0) Bioimpedance is also used in healthcare facilities for various applications, such as disease prognosis and vital sign monitoring [\[20\]](#page-19-2).

5 Thermal Emission Spectroscopy

Thermal Emission Spectroscopy (TES)—the based device is a novel, non-invasive hand-held BG monitor having the same dimensions and ease of use as an ear thermometer. Still, this technique is with more technological breakthroughs. The gadget

Fig. 5 Graphical abstract of glucose detection using bioimpedance spectroscopy. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 Gonzales et al., Licensee MDPI, Basel, Switzerland

Fig. 6 Bioimpedance model measurement and architecture of gain-phase detector

is passive, and, in this technique, chronic external radiation does not injure the human tissues.

This gadget will help individuals with diabetes to live better lives since it will boost patient BG testing, which will lead to improved glycaemic management and lesser complications related to diabetes. Thermal emission spectroscopy (TES) detects infrared signals produced by changes in glucose content in the human body. According to this technique, the natural mid-infrared emission of the human body, particularly the eardrum, is regulated by the state of the emitting tissue. Its selectivity is based on the same premise as the absorption spectroscopy technique used for measurement analysis [\[21\]](#page-19-3). Figure [7](#page-9-1) represents the pictorial representation of the principle of thermal emission spectroscopy for glucose detection.

The detection of glucose level using a non-invasive prototype based on thermal emission in the mid-IR spectral area was measured satisfactorily. Individual daily

Fig. 7 Principle of thermal emission spectroscopy. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 by Gonzales et al., Licensee MDPI, Basel, Switzerland

Pros	Cons
• It is a passive method • There is no threat of tissue damage • Excellent selectivity due to the well-defined glucose spectra at $9.4 \mu m$ • There is no need for calibrating	• Sensitive to changes in motion and temperature • Radiation intensity is vulnerable to tissue thickness • It may not be efficient for sensing sudden variations of glucose

Table 3 Pros and cons of glucose detection using thermal emission spectroscopy

calibrations are unnecessary with this technology, which is one of its benefits [\[21\]](#page-19-3). One disadvantage of this technique is that the strength of infrared radiation emitted by an eardrum is influenced by its thickness and temperature. The other drawbacks and advantages of this method for glucose detection are shown in Table [3.](#page-10-0) Although the clinical outcomes acquired with TES are encouraging, they do not yet meet clinical accuracy criteria [\[22\]](#page-19-4).

6 Optical Polarimetry

Optical polarimetry works on the principle of chiral molecules, i.e., the plane of polarization is rotated by the molecules. The chiral molecule glucose can rotate the plane of polarisation of a beam of light by an angle α in the clockwise direction. This glucose detection method is one of the basic techniques of non-invasive technology. When the beam of polarized light is incident on the glucose solution, the plane of polarization of the incident light is rotated by the presence of glucose.

At present, the sum of glucose level is comparative to the directional angle concerning the original incident direction formed by the polarisation direction [\[23–](#page-19-5) [27\]](#page-19-6). The rotation amount is proportional to the optical path length, the laser beam wavelength, the temperature, and the analyte concentration.

This wavelength will usually appear in the NIR upper region and the optical band is in the lower region (approximately 780–400 nm). The polarimeter measures the plane of polarised light when it passes through the sample. The pictorial representation of optical polarimetry is shown in Fig. [8.](#page-11-0) The maximum intensity of light is identified by a photodetector when the electric field rotation is comparable with the polarization axis of the analyzer. The photodetector cannot detect light when the polarization angle is perpendicular to the electric field rotation angle [\[28,](#page-19-7) [29\]](#page-19-8).

The application of optical polarimetry in the skin is not feasible as the scattering of light in tissue and skin is high, decreasing the glucose's optical rotation [\[30\]](#page-19-9). The optical polarimetry can be used in the eyes anterior chamber as it has a good optical property [\[30,](#page-19-9) [31\]](#page-19-10). Eye glucose monitoring is shown in Fig. [8.](#page-11-0) For this method, a satisfied error accuracy is not obtained even though this method can be detected by visible light, easy operation, and obtaining results [\[32](#page-19-11)[–34\]](#page-19-12). Currently,

there are two new mechanisms for resolving the interference issues of the birefringence of the polarization of glucose overlooked in blood. Dual-wavelength polarizer and birefringence compensator are the two mechanisms used to resolve this issue. Dual-wavelength polarimetric glucose detection is shown in Fig. [9.](#page-11-1)

Fig. 9 Dual-wavelength polarimetric glucose detection

7 Fluorescence

Fluorescence technology is associated with the principle of fluorescent light emission. This fluorescent light emission results in stock shift, wavelength difference due to the effect of the light emission.

Unlike optical approaches, this approach of utilizing fluorescence requires contact between sample and sensor. Recently, new techniques have been developed for analyzing glucose and vitamin A using field instruments. Pickup et al. [47] studied glucose monitoring using the intrinsic tissue fluorescence. This technique utilizes the product of glucose metabolism, nicotinamide adenine dinucleotide phosphate (reduced) (NAD(P)H), a fluorescent cofactor. The test was carried out in in-vivo analysis, and later they were studied in vitro. The fluorescence sensitivity is highly required as the glucose concentration in the fluid is in the micromolar range.

The fluorescence techniques can be categorized into affinity-binding and glucose oxidase (GOx) based sensors. GOx based sensors have a certain limitation as the results depend not only on the concentration of glucose but also on the oxygen tension under in-vivo conditions.

Fluorophores, a specialized molecule that release fluorescent light with certain characteristics, are proportional to the analyte concentration under study. Some fluorophore molecules can bind with glucose molecules directly, but they are associated with interference, irreversibility, analyte depletion, and low selectivity. Therefore, the use of intermediatory molecules like receptors binds with glucose molecules more effectively, leading to changes in their local properties reversibly. This results in fluorescence alteration [67]. Different types of receptors are used for this such as boronic acid derivatives, enzymes, and glucose binding proteins, which are nature-derived and fabricated synthetic materials such as quantum dots and carbon nanotubes.

Fluorescence resonant energy transfer (FRET) has gained much attention based on binding assays. The energy transfer in this technique occurs between the donor and acceptor molecules, the light-sensitive molecules. When the acceptor molecules bind with glucose, the bond between acceptor and donor gets disrupted, increasing fluorescence due to less electron sharing. This is shown in Fig. [10.](#page-12-0)

Fig. 10 Fluorescence glucose monitoring

The FRET and fluorescence lifetime techniques were used to measure glucose concentration by Lakowicz and co-workers [50]. They used reagents such as maltoseinsulin-malachite green and ruthenium-Con A to fabricate a similar sensor. The fluorescence lifetime and fluorescence intensity of ruthenium dye is increased with an increase in glucose concentration. The advantage of this type of fluorescence sensor is that they are highly specific and highly sensitive to the analyte under study. Apart from that, it also eliminates the potential interferences. The drawback of this technique is the short lifespan of the fluorophore, foreign materials in biological media which can cause potential toxicity, etc.

There are so many other techniques that can non-invasively detect glucose concentration, such as Metabolic Heat Conformation (MHC), Photoacoustic Spectroscopy (PAS), Optical Coherence Tomography (OCT), Millimeter and Microwave Sensing, etc. Table [4](#page-14-0) shows the list of recent research developments on MI and NI techniques in Glucose detection. Table [5](#page-16-0) compares non-invasive and minimally invasive glucose monitoring devices that are currently accessible or about to be released in the market soon. Figure [11](#page-17-0) depicts the position of non-invasive and minimally invasive methods and devices for monitoring glucose in the spectrum.

8 Conclusion

The scientific advancement of non-invasive glucose monitoring technologies in recent years is discussed in this chapter. Optical, microwave, and electrochemical methods are the three types of non-invasive blood glucose monitoring technologies available. The advantages of optical and microwave technologies, in general, are their non-invasive nature and ability to monitor continuously without causing discomfort to the human body. In terms of detection, there are still certain issues, such as sophisticated detection means, harsh detecting components, a time-consuming detection procedure, high detection equipment needs, and significant background signal interference. Future research will see if other physical characteristics and other indicators linked to blood glucose may be integrated to increase the accuracy of non-invasive skin glucose test results.

Institution	Technology	Comments	Target	
Polytechnic University of Catalunya	NIR spectroscopy Photoplethysmography	• Principle: the relationship between PPG waveform and glucose levels • No calibration needed • Linear response even in hypoglycemia and hyperglycemia	Finger	
Karunya University	NIR spectroscopy Photoplethysmography	• Blood viscosity, breathing, emotional state, and autonomous nervous system are linked to glucose levels • Analysis was done with machine learning	Forearm and finger	
Tohoku University	MIR spectroscopy Trapezoidal multireflection	• Suitable for areas without a thick skin layer • Tuned at 8658 nm • Sensitive to contact pressure	Oral mucosa Inner lips	
ETH Zurich	MIR spectroscopy Photoacoustic detection	• It uses Quantum Cascade lasers (QCLs) • Wavelengths: $8.47 - 10$ nm	Forearm	
RSP Systems	Raman spectroscopy	• Glucose sensing at a critical depth in the skin • Accuracy affected by time-lag \bullet λ : 830 nm	Hand Palm	
Electronics and Telecomm Research Inst. of Korea (ETRI)	Photoacoustic spectroscopy	• Insensitive to skin secretions • Acoustic signal: 47 kHz \bullet λ : 8-10.4 nm	Fingertip	
National Cheng Kung University (NCKU)	Optical coherence tomography	• It senses optical rotation angle (γ) and depolarization index (Δ) using the Mueller model • Increase in glucose increases γ and decreases Δ	Fingertip	

Table 4 List of recent research on MI and NI techniques for monitoring glucose levels

(continued)

Institution	Technology	Comments	Target
Caltech	Millimeter-wave transmission	• Based on waveguides and patch antennas \cdot f: 15-25 GHz, 16-36 GHz	Ear lobe
Cardiff University	Microwave split-ring resonance	• Glucose level change shifts resonant frequency • Up to 17.5 mm depth penetration	Abdomen
University of Bath	Reverse iontophoresis	• Based on the electro-osmotic flow principle • ISF extracted through hair follicles • Independent from skin characteristics variance • Some skin irritation is associated	Skin
Ulsan National Inst. of Science and Technology (UNIST)	Contact lenses—enzymatic detection	• Measures the level of glucose in tears • Electrodes embedded in the contact lens • The lag time is between 10 and 30 min • Interference from other electroactive species	Tears
University of Maryland	Contact lenses fluorescence	• Based on a glucose-silicone hydrogel • Decrease of fluorescence with the increase of glucose • It works with fluorophore Quin-C18 • Long storage seems not to affect the lens' response	Tears
KTH Royal Institute of Technology	Microneedle-enzymatic detection	• The measurement taken within the dermis • Based on passive fluid extraction • Microneedle length: 700 µm	Forearm

Table 4 (continued)

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Device	Technology	Target	Type	Accuracy	Status
Combo glucometer (Cnoga Medical)	NIR spectroscopy (combination of four LEDs and four sensors to analyze absorption and scattering pattern) λ : 625, 740, 850, 940 nm	Finger	NI NCGM	PEG Zone A:96.6% Zone B: 3.4% MARD: 14.4%	Available
NBM-200G* (OrSense)	NIR spectroscopy (occlusion spectroscopy) λ : 610, 810 nm	Finger	NI Point-of-care	CEG Zone A: 69.7% Zone B: 25.7%	Dropped
HELO Extense (world global network)	NIR spectroscopy	Finger	N _I NCGM	N/A	Available
GlucoTrack (integrity applications)	Combination of: • Ultrasound • Thermal • Electromagnetic sensing	Earlobe	NI NCGM	PEG Zone A: 62.4% Zone B: 37.6% MARD: 19.7%	Available
GlucoWise (MediWise)	mm-wave transmission spectroscopy $f: 60$ GHz	Hand	N _I NCGM	N/A	Under development
SugarBEAT (NemauraMedical)	Reverse iontophoresis	Upper arm	MI NCGM	MARD:13.76%	Waiting for CE approval
Symphony (echo therapeutics)	Sonophoresis	Skin	MI CGM	CEG Zone A: 81.7% Zone B: 18.3% MARD: 12.3%	Unknown
WizmiTM (Wear2b Ltd)	NIR spectroscopy	Arm wrist	N _I NCGM	CEG Zone A: 93% Zone B: 7% MARD: 7.23%	Proof of concept
LTT (light touch technology)	MIR spectroscopy/optical parametric oscillation λ : 6–9_m	Finger	N _I NCGM	N/A	Under development
K'Watch (PK vitality)	Enzymatic detection/microneedles	Arm wrist	MI CGM	N/A	Pre-clinical tests
Eversense® (Senseonics)	Fluorescence	Upper arm	MI CGM	MARD: 14.8%	Available

Table 5 Comparison table of non-invasive and minimally invasive glucose monitoring devices

(continued)

Device	Technology	Target	Type	Accuracy	Status
GlucoGenius	Metabolic heat conformation λ : 660, 760, 850, 940 nm	Finger	NI NCGM	N/A	Unknown

Table 5 (continued)

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Fig. 11 The chart with location of non-invasive and minimally invasive methods and devices for glucose in the frequency spectrum. Reproduced with permission from [\[5\]](#page-18-4) CC By © 2019 Gonzales et al., Licensee MDPI, Basel, Switzerland

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Ms. Sreedevi Paramparambath is working as Research Assistant at the Center for Advanced Materials (CAM), Qatar University. She joined CAM in September 2020. She completed her master's in chemistry from Amrita University in 2019 and her bachelor's degree in chemistry from Calicut University in 2017 from India. During her masters, she has published 2 journal papers in the Materials today journal and has participated in two international conferences. After joining CAM, she is currently working on 3D printed Biosensors, Corrosion etc. she is a meticulous, focused, hardworking, keen learner who assists students and executes it well. She has a keen interest in the field of scientific research. She completes tasks diligently and focuses on quality and not only achieving but exceeding in the research works. She possesses good skills, making the researchers' job easier and more efficient.

Ishwar Maruti Islampure is working as System Engineer at Infosys Ltd., Pune Maharashtra. Having core interest in writing different topics related to use of information technology for the betterment of human beings and to keep environment ecofriendly.

Dr. T. Sabithakala is working as Assistant Professor in Dept. of Chemistry, Jawaharlal Nehru Technological University, Hyderabad, India. Dr. T. Sabithakala works in the areas of Inorganic and Organic Synthesis, synthesis of ligands and its binary and ternary metal complexes and characterization methods, the use of a wide array of spectroscopic and electrochemical tools to understand the biological, electrochemical and magnetic properties, synthesis of coordination polymeric complex and study of its Crystal structure, magnetic properties, DNA binding and electrochemical studies, separation of Regio isomers by using preparative HPLC.

Dr. Muni Raj Maurya received his Ph.D. in Engineering Science (2020) from CSIR-National Physical Laboratory, New Delhi, India. He is currently a staff researcher at the Centre for Advanced Materials, Qatar University. His research interests include investigation of the optical properties of nanocomposites semiconductor materials and the development of optically active nanostructures. His current research is mainly focused on nanomanufacturing, and device designs for sensor and nanophotonic applications.

Ms. Hajar yosry Morsy is a student at Qatar University, College of Science, Department of Chemistry. She has published two research articles on both journals on molecules and healthcare. She worked for two years in the Research & Graduate Studies Office-Center for Advanced Materials, also worked on two UREP projects at Qatar University. She got many certificates for academic excellence at Qatar University, as well as voluntary certificates.

Swathi Yempally M.Sc. (Physics) India. She received a bachelor's degree from Osmania University College for Women specializing in electronics. She has graduated with master's in physics from Osmania University with a specialization in Solid State Physics. She has two years of teaching experience after her graduation in INDIA. She is interested in designing and developing Volatile Organic Compounds (VOC) Sensors and advanced materials for various applications. She has assisted undergraduate students in UREP (Undergraduate Research Experience Program) and contributed to the development of VOC sensors to detect diabetes at Centre for Advanced Materials (CAM) QATAR UNIVERSITY.

Suresh Muthusamy received the bachelor's degree in Electrical and Electronics Engineering and the master's degree in Power Electronics and Drives from 2009 and 2011 from Anna University, Chennai and Anna University, Coimbatore, respectively. Currently, he is working towards his Ph.D. degree in Electrical Engineering at Anna University, Chennai, in Hybrid Renewable Energy Systems. Since 2011, he has been working as Assistant Professor Senior Grade in the Department of Electronics and Communication Engineering at Kongu Engineering College, Perundurai, Erode. He published more than 65 research articles in reputed international journal publications like Elsevier, Springer, Taylor and Francis, Wiley, ASME, etc. and indexed in SCI, SCIE, Scopus and Web of Science. His interests include hybrid renewable energy systems, power electronic converters, hybrid electric vehicles and battery management systems.

Senthil Kumar Ramu received the bachelor's degree in Electrical and Electronics Engineering from Anna University, India, in 2011. He got the master's degree in Power Electronics and Drives in 2013 from Anna University, Chennai, India. Also, he obtained his Ph.D. degree in 2021 from Anna University, Chennai, India. He is presently working as Assistant Professor at Sri Krishna College of Technology, Coimbatore, India. He published 37 research articles in various reputed international journal publications, including Elsevier, Wiley, Taylor, Francis, etc. His current research interests include power electronics and drives, soft computing techniques, Renewable energy systems, Electric vehicles, and signal processing Techniques.

Santhiya Pandiyan received the bachelor's degree in Computer Science and Engineering and the master's degree in Computer Science and Engineering during 2013 and 2015 from Anna University, Coimbatore and Anna University, Chennai, respectively. Currently, she is working towards the Ph.D. degree in Computer Science and Engineering at Anna University, Chennai, in Machine Learning. She worked as Assistant Professor in the Department of Computer Science and Engineering at Paavai Engineering College (Autonomous), Namakkal, for about 5 years 7 months. Since August 2021, she has been working as Assistant Professor in the Department of Computer Science and Engineering at Kongu Engineering College (Autonomous), Perundurai, Erode. She published 7 research articles in various international journals like Taylor & Francis and presented 5 papers in international conferences. Her areas of interest include Machine Learning, deep Learning, Internet of Things, Data structures, etc.

Ms. Raghad Abuznad is under bachelor's degree in Qatar University doing major Chemistry and Earth sciences. Her area of interest working in Material science and electrochemistry, she is doing her graduation project on the effects of temperature on smart material. She attended an interview with the Nobel prize winner in chemistry 2016, Prof. Fraser Stoddart was held at Texas university. She entered two UREP with different topics. She is a hard worker.

Ms. Alaa Elsafiahmed is a senior undergraduate student in Qatar University doing major in Chemistry and Earth Sciences. Her area of interest is working in Electrochemical sensors, and she is doing her graduation project on Catalytic Oxidation of Carbon Monoxide. She participated with two posters in Qatar University Annual Research Forum & Exhibition, and she is a member of the American chemical society. She met the winner of the Noble prize in chemistry 2016, prof. Frasr Stoddart in an interview held on Texas A&M University. She aims to present her research in international conferences and work in Center for Advanced Materials.

Ms. Aeshah Alruwaili is a senior student at Qatar University. Alruwaili, is a Chemistry major student. She is currently applying her internship as a chemistry teacher in Qatar schools. Alruwaili was known by her contributions in the chemistry group events and workshops in the science collage. As well as her interest in research specifically in physical chemistry and organic chemistry departments over her studying years, in addition to her knowledge related to computer science programming languages as a part of her interest and contribution in the university studying years, as well as her peer tutoring experience in chemistry courses.

Ms. Muna Ibrahim is under bachelor's degree in Qatar University doing major Chemistry and Earth sciences. Her area of interest working in Nanotechnology and electrocatalysts, she is doing her graduation project on electrocatalysts for oxygen evolution reaction. She participated on competition for the best Research poster, she also attended an interview with the winner of Nobel prize in chemistry 2016 Prof. Fraser Stoddart was held on Texas university. She aims to present her Research in international conferences by American chemical society as she is a member of this society.

Dr. Ravikumar Ramlu Vidule Asst. Professor, Dept. of Chemistry, & working as IQAC Coordinator, Shri Sant Gadge Maharaj Mahavidyalaya, Loha, Dist. Nanded. (MS)-431708, India. Mail id: ravidule@gmail.com, 80007840827. Published Fifteen Research papers in Reputed Journals. Participant in Academics and co-curricular activities. Actively engage and participating on environmental awareness programs by writing articles and delivering talks on All India Radio. Delivered talk in National and International conference, workshops, Refresher and Orientation courses. Currently started the campaign in India and abroad for the awareness of use of, MICROBEADS in PCCP (personal care cosmetic products). Writing articles to stop the use of single used plastic in newspapers. Wrote the chapters in the book: Blended Classroom: A Method for Encouraging Effective Global Education Learning Environment", Impact of Covid-19: In Teaching Learning Process in India. Challenges to The Academic Domain In The Aftermath Of Covid-19. Impact Of Covid-19 On Higher Education, Impact of COVID-19 on Textile Industry. Also, a core interest in Microbeads and other aspects been invited for the lecture. Invited as a speaker in Sacred Heart College, Kochi "Microbeads: A Threat for life on Earth" In Flasgship programme Prof. K.V. Thomas Endowment "National Seminar on New Frontiers in Materials and Environmental Sciences." 28th Jan. 2020, Invited as a Resource person in Pratibha College of Commerce and Computer Studies Pune College as "State Level Seminar on Emerging Environmental Challenges and its sustainable Approaches." 7–8th Feb. 2020, Given Short Presentation as a young researcher at Dr. T R Ingle memorial National Symposium, "Trends, Research

and Innovation in Chemical Sciences (TRI-2020), Feb 14–15, 2020, Organized by Dept., of Chemistry, SP College, Pune., An invited lecture (Webinar) "Nehur Yuva Kendra Ministry of Youth affair and Sports, Dist. Thiruvanthpuram, Kerala" conducting an internship for MSW students "Blended Learning as a new approach to social work." Given talk dated on 30 Mar 2021: Talk title: Microbeads: A Threat for Life on Earth in the International conference on Materials of the Future: Smart Applications in Science and Engineering, Qatar University, Qatar, Emergent Materials Journal and Chemistry Africa Journal, Springer.

Dr. Ankanagari Srinivas Dept. of Genetics & Biotechnology, Osmania University, Hyderabad, Telangana 500007. India. He obtained his Master's in Genetics from Osmania University and did his Doctorate in Life Sciences from University of Hyderabad. He had carried out several regulatory and non-regulatory pharmaceutical bioavailability and bioequivalence of drugs in Phase I and Phase II clinical trial projects of pharmaceutical industry. He was involved in analysis of biological samples for drugs/metabolites concentration and development, validation, and implementation of bio-analytical methods. He is currently engaged in academic and research activities at Department of Genetics & Biotechnology, Osmania University.

Dr. Kishor Kumar Sadasivuni is currently working as a group leader of Smart Nano Solutions at Center for Advanced Materials, Qatar University. Dr. Kishor's research has its roots from the analytical chemistry he mastered during his Master's degree in Andhra University, India. He received his Ph.D. in Materials Science and Engineering from the University of South Brittany at Lorient, France, in 2012 under Professor Yves Grohens and Professor Sabu Thomas. He has enormous knowledge and valuable experience in his field owing to over 12 years of active research experience of 12 years. Dr. Kishor has more than 250 research articles published in international peer-reviewed journals with a total citation of 5500 and h-index 41. He is also the author of 20 book chapters and the editor of 8 books. Dr. Kishor is an expert in nanomaterials engineering, especially sensing and flexible electronics. He has a keen interest in developing different devices based on smart materials by engineering IoT. Some of Dr. Kishor's inventions are protected by 2 US patents and 2 Indian patents, and presently 5 patent disclosures have been submitted by him. His strong academic background and passion for research are remarkable and reflected in his fast-paced career growth. Dr. Kishor's enthusiastic and sincere approach towards research works is reflected in the forms of various grants and awards offered to him. He is a group leader and is presently the lead principal investigator for 11 research projects, covering the NPRP, UREP, IRCC grants of Qatar National Research Fund and the

Qatar University. He is also involved in three other research grants as the principal investigator, summarizing a total grant amount of 3M\$. Dr. Kishor is a team player and has collaborated actively with researchers (more than 450 co-authors as evident from the Scopus data) in several disciplines of computer science, biomedical sciences, industrial engineering, and electrical engineering from all over the world (USA, France, South Korea, Oman, Spain, Italy, Australia, Malaysia). Dr. Kishor's achievements have been recognized by several awards such as Tyre & Rubber Industry Leadership Acknowledgement Awards (TRILA); Young Research Scholar of the Year 2017. He has been included in the world's top 2% scientists according to a list compiled by Stanford University in the year 2019, and for this, he was recently honored by the QU.