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Non-invasive blood glucose sensors based on electromagnetic wave

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Abstract: Low-cost, reusable, highly compliant and non-invasive blood glucose sensors (NIBGS) are necessary for current and future medical systems. This review aims to introduce various NIBGS with wide application prospect and focus on electromagnetic wave-based NIBGS. The main introduction is based on Near-infrared spectroscopy-based, Raman spectroscopy-based and microwave-based sensors. The basic working principle of each type of sensor is explained, and their structure, detection accuracy, detection range and detection site are also summarized. The improvements and impacts made by various types of non-invasive testing applications are also analyzed. Several commonly used performance evaluation methods of non-invasive blood glucose monitoring (NIBGM) are introduced. With the development of electronic device and intelligent algorithms, NIBGM will continue to expand its advantages, and the creation of new practical applications will greatly improve the healthcare environment and bring great convenience to the lifestyle of patients with diabetes.

1. Introduction

Diabetes is an intractable, challenging health problem in the 21st century[1]. It is one of the most widely spread chronic diseases affecting millions of people and ranks among the leading causes of death globally[2-4]. There is 1.6 million people die from diabetes annually. People with diabetes cannot be completely cured by current medical treatments. The most important requirement is to take tight control of their blood glucose level[5-7]. Therefore, patients need to monitor blood glucose level regularly to reduce the incidence and risk of diabetes or complications from diabetes[8-10]. Most people with diabetes have pre-diabetic symptoms, and regular real-time monitoring can effectively prevent a high risk of death[11,12].

The most traditional indicator and the gold standard for diabetes diagnosis is glucose level in the blood[13-15]. However, traditional glucose detection is invasive and requires a blood sample, which cannot detect continuously and can cause great psychological stress in diabetic patients because of pain caused by invasive methods[8,16,17]. Moreover, invasive blood glucose testing methods can easily increase the risk of infection[18]. What's more, invasive blood glucose testing methods do not promptly reflect blood glucose fluctuations due to specific lifestyles and dietary habits[19]. For

diabetic patients, a comfortable NIBGM method can be greatly effective in improving the effectiveness of treatment[20]. Therefore, a real-time and NIBGM equipment is urgently needed[6,17,21]. Especially now COVID-19 is raging all over the world, people need to be isolated at home and cannot easily reach the hospital. The demand for efficient NIBGM is increasing[22,23]. After decades of development, the traditional blood glucose detection method also has great improvements, gradually changing to the minimally invasive method, but it is still unable to achieve real-time monitoring. Since then, many researchers have proposed the idea of continuous glucose monitoring (CGM). The implantable sensors used in the continuous glucose monitoring system can effectively avoid the burden of repeated blood sampling within a day or a period [24], but the implantable sensors still have a large disadvantage because of invasive[14,25,26], and the sensor needs to be replaced regularly. This process is also full of risks of infection. Due to certain defects, such as the risk of thromboembolic and protein contamination of electrode surfaces, the application of continuous glucose monitoring (CGM) is limited. Figure 1 shows the development routine of sensors for blood glucose monitoring. NIBGM system can overcome the limitations of continuous monitoring systems [27]. Most of the existing NIBGM methods can be simply divided into electrochemical methods (testing in body fluids such as sweet, tear and ISF) and electromagnetic wave methods (Near-infrared spectroscopy, Raman spectroscopy and microwave detection methods are the most representative). Sensor based on electromagnetic wave has a history of more than 60 years and has relatively mature technology. The use of spectroscopy in combination with other technologies is also very popular nowadays. The field of NIBGM involves biological relevance, long-term stability, linearity, calibration and miniaturization. In ref [28], N. K. Tiwari et al. clearly stated that sensitivity of sensor has an important role in the development of non-invasive sensors. In order to check the sensitivity of the sensor, some performance evaluation methods like Clarke error grid[23,29] and Correlation coefficient are often used. The currently known NIBGS are making efforts to get higher sensitivity. However, the accuracy of NIBGS cannot meet the clinical requirements now, which encounters a great challenge. Although NIBGM methods have been significantly improved because of the efforts of many researchers, only a few of them have realized commercial applications, and few of them have been used in clinical practice[30]. There are few sensors or devices that can achieve good linearity, accuracy and correlation of reference methods[31]. It has been repeatedly proven to be challenging to accurately retrieve glucose from the body using non-invasive methods[32]. NIBGM can also be needed for health monitoring for some special groups such as athletes and astronauts. Ryo Takeuchi et al. combined NIBGM with exercise therapy to promote health management in daily life[33]. This will also be a trend of NIBGM in the future. At present, wearable sensing devices with advanced machine learning and artificial intelligence methods are becoming more and more popular, and blood glucose monitoring may develop toward more intelligent and reliable.

The purpose of this review is to introduce various non-invasive blood glucose detection sensors with wide application prospect and focus on electromagnetic wave-based NIBGS. The main introduction of electromagnetic wave-based NIBGS is based on Near-infrared spectroscopy-based sensors, Raman spectroscopy-based sensors and microwave-based sensors. The basic working principle of each type of sensor is explained at the beginning. In the subsequent sections, the detection accuracy, detection range, and detection site of these sensors are summarized. The improvements and impacts made by various types of non-invasive testing applications are also analyzed. Several commonly used performance evaluation methods of NIBGM are summarized. The continuous development of non-invasive glucose technology and the creation of new practical applications have greatly improved the healthcare environment and bring great convenience to the lifestyle of diabetic patients. The effective observation of real-time glucose data also brings tremendous safety to patients.

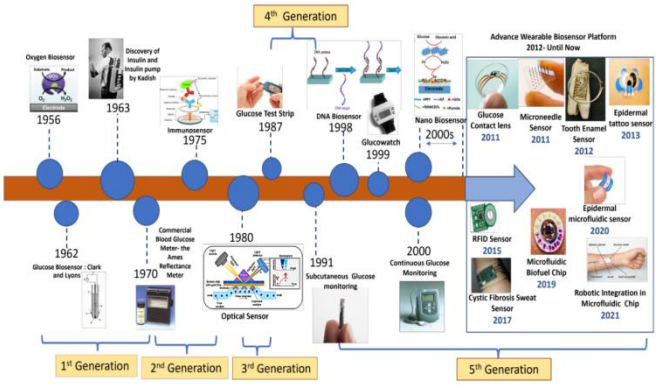

Figure 1: Development routine of sensors for blood glucose monitoring (taken from Ref. [8])

2. Electromagnetic wave-based NIBGS

Electromagnetic waves-based NIBGM has also been welcomed by many research workers[23]. Electromagnetic waves can be considered as a spectral method[29]. The use of spectral methods to detect compounds in living organisms has been around for over sixty years[34]. Several common spectral methods currently used for NIBGM are Raman spectroscopy[35,36], optical coherence tomography[37,38], Photoacoustic spectro-scopy[39,40], Impedance spectroscopy[41], Thermal emission spectroscopy[42], Near-infrared spectroscopy, Mid-infrared spectroscopy and microwave sensing technology. Optical sensors are very advantageous in monitoring biological processes. The optical method does not require the removal of any sample from the monitoring process, it allows the non-invasive detection of blood glucose levels through the absorption of light excited by vibration or rotation by glucose molecules[5,39,43]. In the following, the techniques of Near-infrared spectroscopy, Raman spectroscopy and microwave sensing which have more popular applications are mainly reviewed.

2.1. Principle of electromagnetic wave-based NIBGS

Changes in absorbance caused by the chemical composition of the blood can lead to changes in the spectrum. This principle can be used to extract rich information about glucose levels in the blood. The higher concentration of glucose, the less light is scattered and the more it is absorbed [44]. The applications of spectroscopy in non-invasive testing should follow the Beer-Lambert law[45]. According to Beer-Lambert law, the attenuation of light is only due to absorption analysis and proportional to the concentration of blood[46].

$$A = \log(\frac{I}{I_0}) = \varepsilon cd \tag{1}$$

Where I is the intensity of transmitted light, and I_0 is intensity of incident light. ε is molar extinction coefficient. c is concentration of chromophores, and d is path length.

The reflection, transmission and absorption of microwave are closely related to the dielectric properties of human skin, and changes in glucose levels can alter the dielectric constant of the skin. When the operating frequency of the microwave device changes, the dielectric constant of the skin will change. At this time, Cole-Cole equation[47]can be used to describe this correspondence.

$$\varepsilon^*(w) = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1+(jw\tau)^{1-\alpha}} + \frac{\sigma_s}{jw\varepsilon_0} \tag{2}$$

Where ε_∞ is the permittivity at infinite frequency, and ε_s is static permittivity; ω is angular frequency; τ is relaxation time; σ_s is static conductance; ε_0 is permittivity of free space; α is index parameters and its value is between 0 and 1.

2.2. Near-infrared spectroscopy-based sensor

Near-infrared spectroscopy is considered to be one of the most effective or ideal testing methods for NIBGM[26,48,49]. It is widely used in the field of monitoring human physiological parameters due to its economic, simple and safe properties[50]. Near-infrared light has good penetration to the human body. It can penetrate human tissue to reach the dermis and subcutaneous tissue. Near-infrared spectroscopy also has an advantage of detecting several compounds at the same time [43]. Near-infrared spectroscopy in the first overtone and combination band region is composed of substances such as water and various proteins. Spectra of glucose in this region overlaps severely with the spectra of water and proteins. It is necessary to utilize some methods of measurement such as Partial Least Square Regression (PLSR) [44,51], Principal Component Regression (PCR) and Multiple Linear Regression (MLR). Besides, Deep Neural Networks (DNN) for NIBGM is also one of the current trends. Near-infrared light has a wavelength region between 750nm and 2500nm. The overtone band occurs between 780nm and 2000 nm, the first overtone band is 1400nm to 2000 nm, the second overtone band is 780nm to 1400 nm, and the combined overtone region is 2000 to 2500nm. In contrast, Mid-infrared spectroscopy works in the wavelength region of 2500-10000nm, so the required light source is more expensive. The transmission ability of Mid-infrared spectroscopy to human tissues is pretty poor. Therefore, Mid-infrared spectroscopy is not as widely used as Near-infrared spectroscopy in the field of NIBGM[52]. Near-infrared spectroscopy can be simply divided into the Near-infrared diffuse reflection [5,53,54]and the Near-infrared transmission [18]. Both diffuse Near-infrared light signals and transmitted Near-infrared light signals contain a lot of information about the glucose absorption spectrum. Near-infrared diffuse reflection or transmission can be chosen by researchers based on their design ideas and the directions of the study. The wavelength of the light used in Near-infrared spectroscopy is closely related to the accuracy of the detection. H. Ali et al. attempted to explore the correlation with blood glucose concentration using 650nm red visible light (light from a diode laser)[55]. Yasuhiro Uwadaira et al. did extensive researches on the correlation between blood glucose values and the intensity of light at a single wavelength, and found that the wavelength fluctuated at different moments in the same person[56]. Serhii Mamilov et al. studied the variation of the optical signal of a Near-infrared earlobe sensor at 660 and 940 nm, and a fingertip sensor at 660, 850 and 940 nm[18]. The results show a detection accuracy that is not up to the conditions for clinical application. Choosing the right measurement site is also one of the keys to improve the detection accuracy of Near-infrared spectroscopy for NIBGM[48,57]. Commonly test sites include fingertips, earlobes[48], palms[56]and forearms. Different sites have different capillary density and skin thickness. The most critical aspect of Near-infrared spectroscopy for the non-invasive detection of blood glucose concentrations is the extraction of specific blood glucose signals from complex or confounding background variations[18,54]. The vulnerability to human physiological activity, light source drift and time drift are the common background variations when using Near-infrared spectroscopy for NIBGM [58]. There are two important methods to eliminate background interference: relative measurement and reference position measurement. Reference position measurement is considered to be one of the most promising methods of spectroscopy for NIBGM. Guang Han et al. proposed a special source-detector separation method, in which the diffuse reflectance spectra are collected simultaneously at eight separation points, and the optimal reference position is determined using a calibration model[54]. Jingying Jiang et al. combined the floating

reference point theory and Monte Carlo model to find the optimal location for earlobe detection[48]. When the temperature and humidity around the detection site and the size of the pressure applied to the Near-infrared sensor are different, it will all cause interference in the detection[56]. Therefore, there are many variables in Near-infrared spectroscopy over a long period. The variables lead to a strong fluctuation in the accuracy of the measurement[59]. Y. Tanaka et al. proposed a sensor based on differential continuous wave photoacoustic spectroscopy (DCW-PAS)[39] (Figure2.a). Dual-wavelength (1382 and 1610 nm) amplitude modulation is used for this sensor to confirm changes in glucose levels, and detection site is irradiated by two laser beams of the same frequency (380 kHz). The two wavelengths have the same absorbance for water but different absorbance for glucose, which eliminates the background overlap between glucose and water molecules. L. Ben Mohammadi et al. designed a sensor based on differential Near-infrared spectroscopy technology[52]. The sensor includes a microfluidic channel, a light-coupled total mirror, two light sources and four photodetectors. The input and output of the optical signal are realized by the total reflector, and the first overtone absorption band of glucose is used for continuous differential measurement. The sensor can measure concentrations of glucose in the range of 0 to 400mg/dL, with an absolute error of 3 to 10mg/dL. However, the sensor exhibits a long-term drift, and the drift is reduced after the calibration model is added. R P Jenie et al. developed a finger-clip Near-infrared sensor[57] (Figure2.b) that consists of a pair of Near-infrared light-emitting diodes, a photodiode and an Analogue to a Digital Converter (ADC). Modulation spectrophotometry and fast Fourier transform are proposed for spectrum transformation of measurement of blood glucose level. Rachim et al. designed a wearable band-type visible Near-infrared optical biosensor[5] (Figure2.c) that uses diffuse reflection to extract effective information on blood glucose levels from multiple Near-infrared spectroscopy. The sensor contains four LEDs (two VIS- LEDs and two Near-infrared LEDs) and a photodiode with a spectrum operating range of 400-1100nm, and extracts Photo-plethysmography (PPG) signal corresponding to four wavelengths (950 nm,850 nm,660 nm,530nm) in 10 seconds. The characteristic value of the PPG signal is extracted to obtain information on human blood glucose levels. The standard error of prediction (SEP) of this sensor is $\mathrm{SEP}<6.16\mathrm{mg/dl}$, and correlation coefficient $R_p > 0.86$. Similarly, a Near-infrared sensor proposed by Chowdhury et al. obtains the concentration of glucose and insulin in blood by acquiring PPG signal corresponding to three different wavelengths of Near-infrared light[34]. At present, the method of obtaining human blood glucose information by extracting the PPG signal is very popular. PPG signal is composed of a DC steady-state component and an AC pulse component. Constant DC light is mainly absorbed by tissues such as bones, muscles. The absorption of variable AC light is mainly due to the pulsating volume of arterial blood. Helena Cano-Garcia et al. designed a novel multiwavelength sensor by combining RF signals and Near-infrared spectroscopy[60] (Figure2.d). The sensor consists of two patch antennas and two optical fibers, which can simultaneously collect data about glucose levels in the electromagnetic wave segment of 37-39 GHz and 900-1800 nm. In the RF band, water molecules cause serious attenuation to the signal, so the combination of Near-infrared spectroscopy and RF signal can effectively solve the problem that the spectrum of water overlap with glucose molecules in the condition of only Near-infrared light. The results of the measurement show that the combination of Near-infrared spectroscopy and RF signal can achieve a high precision detection. Chavis Srichan et al. proposed a multiple photonic bands Near-infrared sensor (mbNIR)[61] (Figure2.e) based on Shallow Dense Neural Networks (SDNN). The sensor emphasizes personalized medical features (PMF). It is the first time that personalized medical features (PMF) is utilized to improve the accuracy of Near-infrared sensor. Diya Wang made an improvement on a non-invasive glucose detection integrated sensor (ISNBGD)[62] based on the conservation of energy metabolism (COEM). The sensor integrates a dual-wavelength light source (660nm and 905nm), a temperature sensor and a humidity sensor. Blood glucose level is obtained by measuring hemoglobin saturation and pulse wave frequency through multiple linear

regression processing. The correlation coefficient between ABA and the improved NIBGS could reach 0.8621. Yan Yu et al. innovatively used transfer learning to develop a handheld Near-infrared sensor[44]. The sensor is composed of a highly integrated DLP NIRscan Nano EVM, a grating and a single-point detector. High integration avoids the drawbacks of traditional spectroscopy systems such as large size and high cost. Kiseok Song et al. proposed a sensor by combining multiwavelength Near-infrared spectroscopy (850nm,950nm and 1300nm) and impedance spectroscopy[41]. The sensor makes use of the optical absorption characteristics of glucose molecules in the blood and the indirect dielectric properties of the measurement site to compensate for the estimation error of another way to achieve relatively high accuracy of NIBGM. The collected data are processed by a digital signal processor (DSP) combined with a neural network method, and the estimation error of the sensor is reduced to 8%.

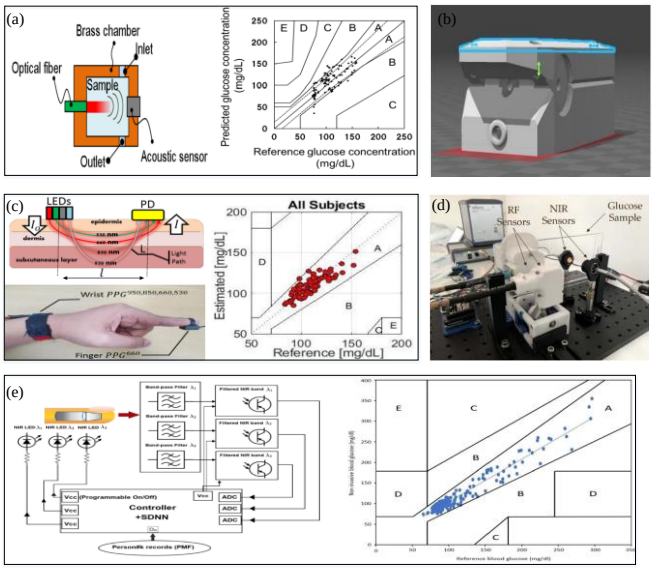

Figure 2: (a) Schematic diagram of the sensor based on differential continuous wave photoacoustic spectroscopy (DCW-PAS); the glucose data measured by the sensor based on differential continuous wave photoacoustic spectroscopy are compared with reference glucose concentration from FGM (taken from Ref.[39]). (b) Schematic diagram of finger-clip Near-infrared sensor (taken from Ref. [57]). (c) Photograph of wearable band type visible-near infrared optical biosensor and measurement depth of four wavelengths (950 nm,850 nm,660 nm,530nm); correlation coefficient and Clarke grid error of the system (taken from Ref.[5]). (d) Photograph of a near infrared sensor combining RF signals and Near-infrared spectroscopy technology (taken from Ref.[60]). (e) Schematic illustration of a sensor based on shallow density Neural network (SDNN) and the multiphoton band Near-infrared (mbNIR); the measurement capability of the sensor (Clarke error grid diagram and 95% confidence plot) (taken from Ref.[61]).

Near-infrared spectroscopy is usually not used alone at most of the time, but combined with other technologies to improve the accuracy of detection, such as impedance spectroscopy and radio frequency signals. There are more applications for multi-wavelength Near-infrared light than for just one wavelength of Near-infrared light. To overcome the interference of the background, various calibration models have been applied extensively. However, models of calibration for Near-infrared spectroscopy are more effective for single subjects, but no better model can be used for all subjects, i.e., models of calibration are significantly less effective when they are used for multiple subjects. A large number of research workers generally improve the stability and reliability of monitoring in terms of algorithms and hardware circuits. This can be considered the most effective method at present.

2.3. Raman spectroscopy-based sensor

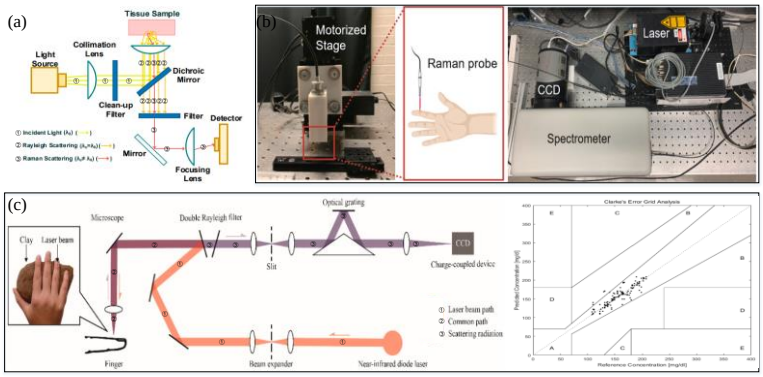

Figure 3: (a) Typical device based on Raman spectroscopy for the detection of blood analytes (taken from Ref.[63]). (b) A device based on time-resolved measurement technique (taken from Ref.[64]). (c) Confocal Raman spectrometer and Near-infrared diode laser for non-invasive blood glucose testing; Clark's error grid for predicted glucose concentration values (taken from Ref.[36]).

Raman spectroscopy has excellent chemical specificity and it can measure multiple components in blood simultaneously[35]. When it comes to Raman spectroscopy, the phenomenon of Raman scattering has to be mentioned. The Raman scattering phenomenon defines that the frequency of the scattered photon is different from the frequency of the incident photon. In Figure3.a, a typical device based on Raman spectroscopy[63] is shown. Compared with Near-infrared spectroscopy, Raman spectroscopy can change the polarity of molecules by vibrational leap and produce clear spectra. There is no light stability and spectral overlap of substances like water[36]. Collecting geometries and tissue modulation are common methods to enhance differential signals in blood when used for NIBGM[14]. But the intensity of signal of Raman spectroscopy in biological samples is very weak and on-analyte specificity variations in human tissues can severely affect calibration[64]. Raman spectroscopy for NIBGM is usually used to detect glucose concentrations in the ISF or stratum corneum. In ref[65], a new critical depth of detection is used to analyze the glucose level in the ISF, and the results show that the Raman signal is severely weakened when the depth of the detection is increased. It can be seen that the depth of detection has a non-negligible effect on the measurement of Raman spectroscopy. In ref[66], Narahara Chari Dingari et al. particularly emphasized that Raman spectroscopy cannot ignore the interfering concentration of glucose due to uncontrolled physiological changes. Apart from these, Rishikesh Pandey et al. proposed a portable Raman spectroscopic detector[14] based on a fiber probe by introducing non-imaging optical elements based on Raman spectroscopy. Nan Li et al. believe that glucose levels in ISF and epidermis have a physiological lag with glucose levels in the blood, so they changed the traditional detection site to focus on the nail fold of the human body. A confocal Raman spectrometer and a Near-infrared diode laser[36] (Figure3.c) are directly used to focus the laser on the microvessels of the nail fold, meaning that the spectrum came from the blood rather than the ISF. The predicted glucose concentrations are all in regions A and B of the Clarke error grid. Maciej S. Wrobel et al. proposed a time-resolved measurement technique[64] (Figure3.b) based on combination of Raman spectroscopy techniques and pulse frequency. Glucose concentration in blood can be measured by the dynamic changes in pulse frequency. It also enhances dynamic pulse correlation spectra and reduces the effect of static tissue by phase-sensitive detection and heart rate under natural conditions. The sensor consists of a Raman spectrometer with a laser wavelength of 830 nm and a fiber optic probe that continuously measures signals at high sampling frequencies within 10 minutes.

2.4. Microwave-based sensor

Microwave technology has been widely used in the field of NIBGM on account of the advantages of non-radiation and low cost. Compared with other ionizing radiation, the microwave band has the benefit of non-wave damage and does not pose a risk to the human body[67]. Different levels of blood glucose will lead to the changes in permittivity[47,67,68], so microwave technology can be applied in NIBGM. Qinwei Li et al. utilized microwave signals at a frequency of 500 MHz to obtain absorption spectra at blood glucose levels ranging from 0-500 mg/dl to verify the feasibility of microwave technology for NIBGM[20]. Pratik J. Mhatre et al. investigated the variation of antenna parameters at different blood glucose concentration by building a human model. The results show that the variation in blood glucose concentration directly affects the performance of the antenna[69]. Buford Randall Jean et al. first proposed an early microwave-based sensor whose sampling site is an open spiral-shaped microstrip line[70]. The sampled signal is generated by the standing wave produced by the microstrip transmission line coupled to the output trace. To ensure the stability of the pressure, the sensor is also fitted with a plastic thumb position locator. Resonators are often used for microwave sensing, such as microstrip open-ring resonators, split-ring resonators[71,72], complementary split-ring resonators[19,58]and metamaterial resonators[68,73], etc. Metamaterial resonators are favored because of their more compact structure and higher frequency resolution[28]. Material characterization theory is utilized by the resonator, which means that the permittivity of blood in the human body is influenced by glucose molecules. In addition to resonators, vector network analyzers (VNAs) are generally required. Microwave-based technology should focus on the selection of detection sites and working frequency. As same as Near-infrared spectroscopy, fingers and earlobes are the two commonly selected areas for microwave sensing. There is no fixed frequency choice for NIBGM and it is related to the practical purposes of the designer[74]. If sensors need higher tissue penetration, a low frequency band can be chosen. For example, microwave signals with a resonant frequency of 1GHz can penetrate several centimeters into the human body[72]. If the sensors need to avoid penetration, a higher frequency band can be chosen, because high frequencies do not have as strong penetration as low frequencies[67]. A new planar microwave-based sensor[75] (Figure4.a) is designed by Ala eldin omer et al. The sensor consists of four hexagonal complementary split-ring resonators integrated with a radar board in the frequency band of 2.4G~2.5G. The resonators are coupled to the radar board via microstrip, and the receive channel of the radar board acquires data related to blood glucose levels. The sensor has a frequency resolution of 94 MHz/(mg/mL), which can repeatedly detect glucose concentrations from 0 to 300 mg/dL, and it has an accuracy of 5 mg/dL. Ala Eldin Omer et al. reported a microwave-based sensor in the low cm band, operating from 1 to 6 GHz[19]. The sensor consists of three circular complementary split resonators, and the resonators are coupled on a planar microstrip transmission line. Glucose level is predicted from the frequency response of the harmonic reflections and transmission resonances collected by the sensor. This is because the changes in glucose concentration disrupt the effective resistance and capacitance of the complementary splitting resonators. However, the sensor is designed for type 2 diabetes and is not widely adaptable. Conventional microwave-based sensors are not particularly ideal for measuring liquids with large losses. Greeshmaja Govind et al. proposed a high-sensitivity microwave-based microfluidic control sensor[68] by adding an interdigital capacitor (IDC) to the gap of the resonant cavity of a conventional split-ring resonator (SRR). The microfluidic channel of the sensor is manufactured from polydimethylsiloxane (PDMS), and the test sample can be placed in a larger area of the resonator for higher overall sensitivity. Masoud Baghelani et al. reported a chip-free microwave tag sensor[71] (Figure4.b). The tag sensor consists of a split-ring resonator that consumes no power because it does not need to read data actively, and resonant frequency can be read by an embedded smartwatch. This split ring resonator has a relatively large feature. It does not have a substrate and

increases accuracy greatly. It can detect glucose concentrations in the range of 0~200 mm/L. Heungjae Choi et al. proposed a sensor[72] consisting of a double split-ring resonator, where one split-ring resonator is used to detect changes in glucose levels (sensing ring) and the other is used as a reference (reference ring). The two split-ring sensors are not coupled to each other. This purpose is to calibrate the effect of temperature on the detection of blood glucose concentration. The temperature in here refers to the temperature of the detection section rather than the temperature of the resonator. However, the sensor can only measure a relatively small range of blood glucose concentrations. Sina Kiani et al. proposed a dual resonant frequency microwave-based sensor[67] for NIBGM (resonant frequencies of 5.5 GHz and 8.5 GHz, respectively) and emphasized the importance of quality factors to prevent frequency shifts. The dual-frequency sensor has a protective chamber, a compact overall structure and a high concentration of electromagnetic fields in the sensing region. It is most noteworthy that the quality factor of the sensor is designed to be large enough. The measurement results show that the dual-frequency microwave-based sensor has only a 3% error with the glucose meter, which is still relatively impressive. The pressure applied to the sensor at the detection site is closely related to the prediction of blood glucose level, and inconsistent application of pressure results in frequency drift leading to incorrect blood glucose predictions. So Volkan Turgul et al. proposed an RF-based pressure sensor[76], which consists of a single-port microwave resonator and a laminate. If there is nothing on the sensor, the resonant frequency is 4.8GHz. Resonant frequency drops to 3.25GHz after the finger is put on it. The sensor transmits the pressure data to the MCU in real time to ensure the measurement site reaches the set value. When it comes to the future development trend of microwave technology, Qinwei Li et al. referred to wireless body area networks for microwave sensing[20].

However, most of the published resonators are short of sufficient frequency resolution for detecting glucose level in the blood. Moreover, microwave-based sensors can cause a certain degree of frequency shift due to the external environment and the structure of the instrument itself. The actual source of the frequency shift has to be paid attention to. In other words, the determination of the actual source of the frequency shift is a particularly important factor in improving detection accuracy.

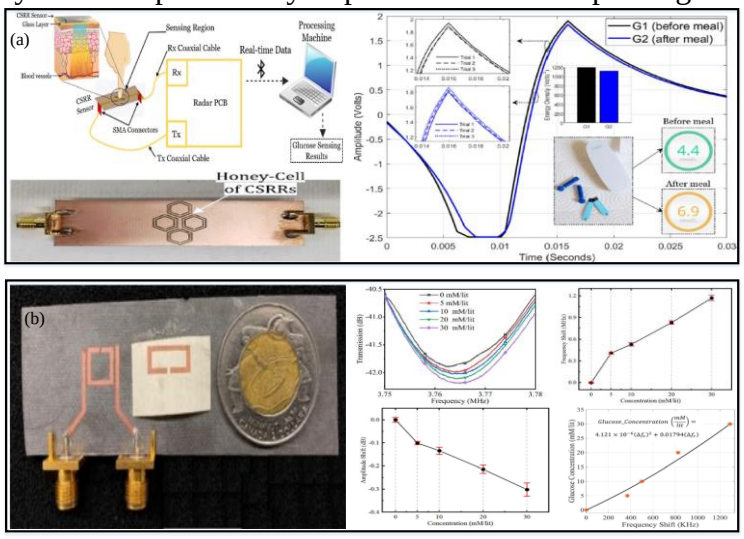

Figure 4: (a) Schematic diagram and working principle of this new planar microwave sensor; raw data is collected by the receiving channel of the radar board (taken from Ref.[75]). (b) Photograph of chip-free microwave tag sensor; variation of resonant frequency and amplitude with glucose concentration and calibration curve of resonant frequency versus glucose concentration (taken from Ref.[71]).

2.5. Summary of Electromagnetic wave-based NIBGS

As is shown in Table 1, some of the NIBGS based on electromagnetic wave technology in recent years will be summarized here. The range, accuracy and measuring site of blood glucose detection by sensors have been paid more attention. NIBGS based on electromagnetic wave technology are very popular at present. With the continuous improvement of signal processing algorithms and calibration algorithms, the detection accuracy and stability are greatly improved. In addition, the simple circuit structure and relatively low cost make the NIBGS based on electromagnetic wave technology have great potential to capture the future NIBGM market.

Table 1: Summary of Electromagnetic wave based NIBGS

NO.	Measuring Method	Evaluation Object	Detection Range	Accuracy Sensitivity	Measuring Site	Ref.
1	NIR spectroscopy	Glucose water solution	50-300mg/dL (1382nm,1610 nm)	R_p 1=0.58~0.8	--	[39]
2	NIR spectroscopy	Glucose water solution in vitro	0~400mg/dL (1450nm,1550nm)	Absolute error is 3~10mg/dL	--	[52]
3	NIR spectroscopy	Glucose in blood	--	--	Finger	[57]
4	NIR spectroscopy	Glucose in blood	(PPG signal; 950,850,660,530nm)	SEP2<6.16mg/dL, R_p >0.86	Wrist	[5]
5	NIR spectroscopy	Glucose in blood	(PPG signal; 1070,950,935nm)	--	Finger	[34]
6	NIR spectroscopy	Glucose water solution	80~5000mg/dL (36.5GHz;900-1800nm)	0.00026 dB/(mg/dl)	--	[60]
7	NIR spectroscopy	Glucose in blood	60 ~ 400 mg/dL	15% error	Finger	[61]
8	NIR spectroscopy	Glucose in blood	3.5 ~ 6.5 mmol/L (660,905nm)	R_p =0.8621	Finger	[62]
9	NIR spectroscopy	Glucose in blood	-- (900~1700 nm)	RMSEP3= 0.13 mmol/L	Finger	[44]
10	NIR spectroscopy	Glucose in blood	-- (850,950,1300nm)	100% accuracy in CEG4 analysis	Wrist and hand	[41]
11	Raman spectroscopy	Glucose in ISF	--	--	Finger or arm	[14]
12	Raman spectroscopy	Glucose in blood	-- (830nm)	RMSEP= 0.27 mmol/L, R^2 5=0.98	Finger	[36]
13	Raman spectroscopy	Blood pulse	-- (830nm)	--	Finger	[64]
14	Microwave	Glucose in blood	-- (100 MHz to 5 GHz)	--	Thumb	[70]
15	Microwave	Glucose in blood	0 ~ 300 mg/dL (2.4~2.5GHz)	0.94 MHz/ (mg/dL)	Finger	[75]
16	Microwave	Glucose water solution	70–120 mg/dL (1~6GHz)	6.2 dB/(mg/ml)	Finger	[19]
17	Microwave	Glucose in biological liquids	0~5000 mg/dl (1~5GHz)	2.60E-02 $MHz / mgdl^{-1}$	--	[68]
18	Microwave	Glucose in ISF	0~200mm/L (38 kHz)	~ 1 mM/l	--	[71]
19	Microwave	Glucose in blood	-- (1.4GHz)	3.287 kHz per mM in resonant frequency.	Abdominal skin	[72]
20	Microwave	Glucose in blood	89~262 mg/dL (5.5,8.5GHz)	3.53 and 3.58 MHz/ (mg/dL)	Finger	[67]
21	Microwave	Glucose in blood	-- (4.8 or 3.25GHz)	standard deviation= 0.366 MHz	Finger	[76]

1) R_p : correlation coefficient.
2) SEP: standard error of prediction.
3) RMSEP: root mean square error prediction.
4) CEG: Clarke error grid.
5) R^2 : squared correlation coefficient.

3. Performance evaluation methods of NIBGM

In order to evaluate the performance of NIBGM technology and equipment, the measured blood glucose data are often calibrated and compared to data measured by highly reliable NIBGM devices. Based on clinical and statistical knowledge, several indicators are usually used to evaluate the detection accuracy of NIBGM devices[29]. The first is the Clarke Error Grid (CEG)(Figure5) [77], which describes the clinical accuracy of non-invasive blood glucose monitors using scatter plots. It is usually divided into five areas, where area A indicates deviation from the reference value of the blood glucose measurement within 20%. Area B indicates an error larger than 20% from the reference value, but does not lead to inappropriate processing. Data in areas A and B are clinically acceptable. Area C indicates that it leads to overcorrection of the blood glucose value. While area D and E indicate failure to detect abnormal blood glucose levels and incorrect processing, respectively. The second is root mean square error (RMSE), which can be used to evaluate the deviation between the predicted value of blood glucose and the reference value. Correlation coefficient R_p is also a common evaluation method, which can reflect the predictive ability of a model. The value of R_p between 0.7 and 1 indicates that the two variables are highly correlated. In addition, there is a coefficient of determination R^2, which measures the goodness of the linear regression equation fitted to the predicted blood glucose values.

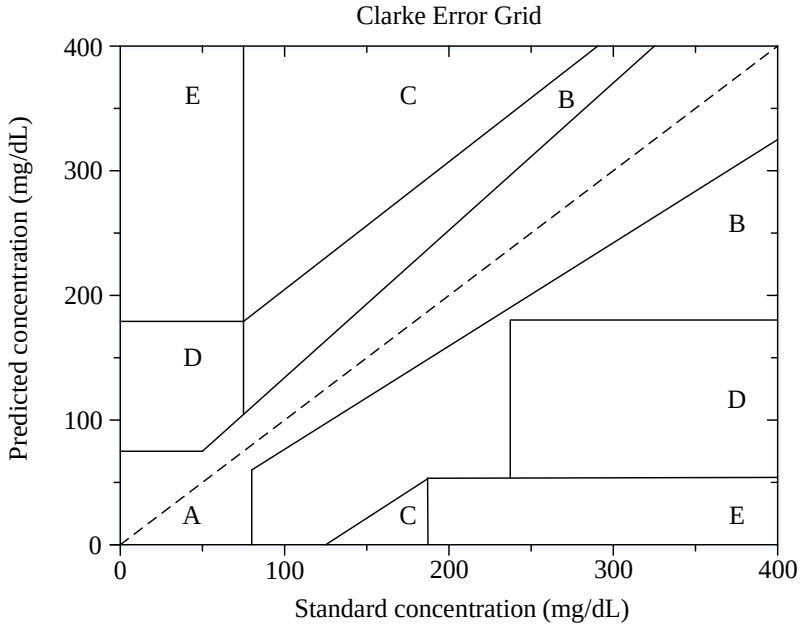

Figure 5: Clarke error grid analysis of reference and measured blood glucose data.

4. Conclusions and outlook

We systematically review the applications of electromagnetic wave based NIBGS with wide application prospect, such as Near-infrared spectroscopy-based, Raman spectroscopy-based and microwave-based NIBGS. Their sensing principles, structure and the materials or devices used are summarized. For Near-infrared spectroscopy-based NIBGS, combination with other technologies for calibration is current trend, and it involves simple structures of circuit and relatively inexpensive sensing devices. For sensors based on Raman spectroscopy, its excellent chemical properties make it possible to detect multiple components in blood simultaneously, but the weak Raman signal is also a difficulty that plagues its development. As for microwave-based NIBGS, there is no clear and

recognized optimal operating frequency for NIBGM, and the choice often needs to be made under different penetration requirements depending on the purpose of design. The use of the above three different electromagnetic waves for NIBGM have a common feature: they are committed to improving the hardware structure and signal processing algorithms constantly to improve the accuracy of detection.

As research continues, the requirements for accuracy and repeatability of NIBGS will become higher and higher, and more efficient circuit structure and intelligent algorithms will be considered. In the future, the stability and repeatability of NIBGS need to be enhanced to a greater extent. It is believed that a NIBGM device that meets clinical requirements will be developed in the future, which will be a milestone breakthrough. At that time, NIBGM will continue to expand its advantages in the field of health monitoring for athletes and astronauts, etc. More importantly, it will greatly improve the healthcare environment and bring great convenience to the lifestyle of diabetic patients.

Author Contributions

Conceptualization, W.W. and Y.Y.; validation, W.W., Y.Y. and J.Q.; writing—original draft preparation, X.X. and J.Q.; writing—review and editing, W.W and Y.Y.; visualization, W.W. and J.Q.; supervision, Y.Y.; project administration, Y.Y.; funding acquisition, Y.Y. All authors have read and agreed to the published version of the manuscript.

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References

[1] Johnston, L., Wang, G., Hu, K., Qian, C., Liu, G. Advances in Biosensors for Continuous Glucose Monitoring Towards Wearables. Front Bioeng Biotechnol 2021, 9, 733810, doi:10. 3389/fbioe. 2021. 733810.

[2] Kim, J., Campbell, A. S., Wang, J. Wearable non-invasive epidermal glucose sensors: A review. Talanta 2018, 177, 163-170, doi:10. 1016/j. talanta. 2017. 08. 077.

[3] Chen, Y., Lu, S., Zhang, S., Li, Y., Qu, Z., Chen, Y., Lu, B., Wang, X., Feng, X. Skin-like biosensor system via electrochemical channels for noninvasive blood glucose monitoring. Science Advances 2017, 3, doi: 10. 1126/ sciadv. 1701629.

[4] Lin, X., Xu, Y., Pan, X., Xu, J., Ding, Y., Sun, X., Song, X., Ren, Y., Shan, P. F. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep 2020, 10, 14790, doi:10. 1038/s41598-020-71908-9.

[5] Rachim, V. P., Chung, W. -Y. Wearable-band type visible-near infrared optical biosensor for non-invasive blood glucose monitoring. Sensors and Actuators B: Chemical 2019, 286, 173-180, doi:10. 1016/j. snb. 2019. 01. 121.

[6] Bandodkar, A. J., Jia, W., Yardimci, C., Wang, X., Ramirez, J., Wang, J. Tattoo-based noninvasive glucose monitoring: a proof-of-concept study. Anal Chem 2015, 87, 394-398, doi:10. 1021/ac504300n.

[7] Lee, H., Song, C., Hong, Y. S., Kim, M., Cho, H. R., Kang, T., Shin, K., Choi, S. H., Hyeon, T., Kim, D. H. Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module. Sci Adv 2017, 3, e1601314, doi:10. 1126/sciadv. 1601314.

[8] Zafar, H., Channa, A., Jeoti, V., Stojanovic, G. M. Comprehensive Review on Wearable Sweat-Glucose Sensors for Continuous Glucose Monitoring. Sensors (Basel) 2022, 22, doi:10. 3390/s22020638.

[9] American Diabetes, A. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013, 36 Suppl 1, S67-74, doi:10. 2337/dc13-S067.

[10] Alberti, K. G. M. M., Zimmet, P. Z. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. Diabetic Medicine

1998, 15, 539-553, doi:10. 1002/(sici)1096-9136(199807)15:7<539::Aid-dia668>3. 0. Co, 2-s.
[11] Donelli, M., Espa, G., Feraco, P., Manekiya, M. Wearable non-invasive blood glucose monitor system based on galvanic skin resistance measurement. Electronics Letters 2021, 57, 901-902, doi:10. 1049/ell2. 12315.
[12] Aggidis, A. G., Newman, J. D., Aggidis, G. A. Investigating pipeline and state of the art blood glucose biosensors to formulate next steps. Biosens Bioelectron 2015, 74, 243-262, doi:10. 1016/j. bios. 2015. 05. 071.
[13] Lee, H., Hong, Y. J., Baik, S., Hyeon, T., Kim, D. H. Enzyme-Based Glucose Sensor: From Invasive to Wearable Device. Adv Healthc Mater 2018, 7, e1701150, doi:10. 1002/adhm. 201701150.
[14] Pandey, R., Paidi, S. K., Valdez, T. A., Zhang, C., Spegazzini, N., Dasari, R. R., Barman, I. Noninvasive Monitoring of Blood Glucose with Raman Spectroscopy. Acc Chem Res 2017, 50, 264-272, doi:10. 1021/acs. accounts. 6b00472.
[15] Makaram, P., Owens, D., Aceros, J. Trends in Nanomaterial-Based Non-Invasive Diabetes Sensing Technologies. Diagnostics (Basel) 2014, 4, 27-46, doi:10. 3390/diagnostics4020027.
[16] Zhang, S., Zeng, J., Wang, C., Feng, L., Song, Z., Zhao, W., Wang, Q., Liu, C. The Application of Wearable Glucose Sensors in Point-of-Care Testing. Front Bioeng Biotechnol 2021, 9, 774210, doi:10. 3389/fbioe. 2021. 774210.
[17] Xuan, X., Yoon, H. S., Park, J. Y. A wearable electrochemical glucose sensor based on simple and low-cost fabrication supported micro-patterned reduced graphene oxide nanocomposite electrode on flexible substrate. Biosens Bioelectron 2018, 109, 75-82, doi:10. 1016/j. bios. 2018. 02. 054.
[18] Mamilov, S., Velyhotskyi, D., Yesman, S., Mysiura, A., Bekh, I., Gisbrecht, A. Non-Invasive Assessment of Blood Glucose Changes with Near Infrared Sensor. In Proceedings of the 2020 IEEE 40th International Conference on Electronics and Nanotechnology (ELNANO), 2020, pp. 536-540.
[19] Omer, A. E., Shaker, G., Safavi-Naeini, S., Alquie, G., Deshours, F., Kokabi, H., Shubair, R. M. Non-Invasive Real-Time Monitoring of Glucose Level Using Novel Microwave Biosensor Based on Triple-Pole CSRR. IEEE Trans Biomed Circuits Syst 2020, 14, 1407-1420, doi:10. 1109/TBCAS. 2020. 3038589.
[20] Li, Q., Xiao, X., Kikkawa, T. Absorption spectrum for non-invasive blood glucose concentration detection by microwave signals. Journal of Electromagnetic Waves and Applications 2019, 33, 1093-1106, doi: 10. 1080/ 09205071. 2019. 1596168.
[21] Zheng, L., Liu, Y., Zhang, C. A sample-to-answer, wearable cloth-based electrochemical sensor (WCECS) for point-of-care detection of glucose in sweat. Sensors and Actuators B: Chemical 2021, 343, doi:10. 1016/j. snb. 2021. 130131.
[22] Guo, S., Wu, K., Li, C., Wang, H., Sun, Z., Xi, D., Zhang, S., Ding, W., Zaghloul, M. E., Wang, C., et al. Integrated contact lens sensor system based on multifunctional ultrathin MoS2 transistors. Matter 2021, 4, 969-985, doi: 10. 1016/ j. matt. 2020. 12. 002.
[23] Xue, Y., Thalmayer, A. S., Zeising, S., Fischer, G., Lubke, M. Commercial and Scientific Solutions for Blood Glucose Monitoring-A Review. Sensors (Basel) 2022, 22, doi:10. 3390/s22020425.
[24] Elsherif, M., Hassan, M. U., Yetisen, A. K., Butt, H. Wearable Contact Lens Biosensors for Continuous Glucose Monitoring Using Smartphones. ACS Nano 2018, 12, 5452-5462, doi:10. 1021/acsnano. 8b00829.
[25] Kownacka, A. E., Vegelyte, D., Joosse, M., Anton, N., Toebes, B. J., Lauko, J., Buzzacchera, I., Lipinska, K., Wilson, D. A., Geelhoed-Duijvestijn, N., et al. Clinical Evidence for Use of a Noninvasive Biosensor for Tear Glucose as an Alternative to Painful Finger-Prick for Diabetes Management Utilizing a Biopolymer Coating. Biomacromolecules 2018, 19, 4504-4511, doi:10. 1021/acs. biomac. 8b01429.
[26] Yadav, J., Rani, A., Singh, V., Murari, B. M. Prospects and limitations of non-invasive blood glucose monitoring using near-infrared spectroscopy. Biomedical Signal Processing and Control 2015, 18, 214-227, doi: 10. 1016/ j. bspc. 2015. 01. 005.
[27] Sabu, C., Henna, T. K., Raphey, V. R., Nivitha, K. P., Pramod, K. Advanced biosensors for glucose and insulin. Biosens Bioelectron 2019, 141, 111201, doi:10. 1016/j. bios. 2019. 03. 034.
[28] Tiwari, N. K., Singh, S. P., Mondal, D., Akhtar, M. J. Flexible biomedical RF sensors to quantify the purity of medical grade glycerol and glucose concentrations. International Journal of Microwave and Wireless Technologies 2019, 12, 120-130, doi:10. 1017/s1759078719001089.
[29] Zhang, R., Liu, S., Jin, H., Luo, Y., Zheng, Z., Gao, F., Zheng, Y. Noninvasive Electromagnetic Wave Sensing of Glucose. Sensors (Basel) 2019, 19, doi:10. 3390/s19051151.
[30] Shende, P., Sahu, P., Gaud, R. A technology roadmap of smart biosensors from conventional glucose monitoring systems. Ther Deliv 2017, 8, 411-423, doi:10. 4155/tde-2017-0012.
[31] Scognamiglio, V., Arduini, F. The technology tree in the design of glucose biosensors. TrAC Trends in Analytical Chemistry 2019, 120, doi:10. 1016/j. trac. 2019. 115642.
[32] Villena Gonzales, W., Mobashsher, A. T., Abbosh, A. The Progress of Glucose Monitoring-A Review of Invasive to Minimally and Non-Invasive Techniques, Devices and Sensors. Sensors (Basel) 2019, 19, doi:10. 3390/s19040800.
[33] Takeuchi, R., Nagao, K., Miyamoto, H. Proposal of Blood Glucose Control and Exercise Therapy Support System Using Non-invasive Blood Glucose Meter. Pertanika Journal of Science and Technology 2020, 28, doi:10. 47836/pjst. 28. s2. 02.
[34] Chowdhury, S. R., Nandi, B., Mondal, P. A Non-Invasive Blood Insulin and Glucose Monitoring System Based on

Near-Infrared Spectroscopy with Remote Data Logging. In Proceedings of the 2018 IEEE 31st International Symposium on Computer-Based Medical Systems (CBMS), 2018, pp. 274-279.
[35] Barman, I., Singh, G. P., Dasari, R. R., Feld, M. S., Vaidyan, V. K., Jayakumar, V. S. Transcutaneous Measurement of Blood Analyte Concentration Using Raman Spectroscopy. In Proceedings of the AIP Conference Proceedings, 2008, pp. 33-37.
[36] Li, N., Zang, H., Sun, H., Jiao, X., Wang, K., Liu, T. C., Meng, Y. A Noninvasive Accurate Measurement of Blood Glucose Levels with Raman Spectroscopy of Blood in Microvessels. Molecules 2019, 24, doi:10. 3390/molecules24081500.
[37] Izatt, J. A., Fujimoto, J. G., Tuchin, V. V., De Pretto, L. R., Yoshimura, T. M., Ribeiro, M. S., de Freitas, A. Z. Optical coherence tomography for blood glucose monitoring through signal attenuation. In Proceedings of the Optical Coherence Tomography and Coherence Domain Optical Methods in Biomedicine XX, 2016.
[38] Esenaliev, R. O., Larin, K. V., Larina, I. V., Motamedi, M. Noninvasive monitoring of glucose concentration with optical coherence tomography. Opt Lett 2001, 26, 992-994, doi:10. 1364/ol. 26. 000992.
[39] Tanaka, Y., Tajima, T., Seyama, M., Waki, K. Differential Continuous Wave Photoacoustic Spectroscopy for Non-Invasive Glucose Monitoring. IEEE Sensors Journal 2020, 20, 4453-4458, doi:10. 1109/jsen. 2019. 2962251.
[40] Sim, J. Y., Ahn, C. G., Jeong, E. J., Kim, B. K. In vivo Microscopic Photoacoustic Spectroscopy for Non-Invasive Glucose Monitoring Invulnerable to Skin Secretion Products. Sci Rep 2018, 8, 1059, doi:10. 1038/s41598-018-19340-y.
[41] Song, K., Ha, U., Park, S., Bae, J., Yoo, H. -J. An Impedance and Multi-Wavelength Near-Infrared Spectroscopy IC for Non-Invasive Blood Glucose Estimation. IEEE Journal of Solid-State Circuits 2015, 50, 1025-1037, doi:10. 1109/jssc. 2014. 2384037.
[42] Mueller, M., Grunze, M., Leiter, E. H., Reifsnyder, P. C., Klueh, U., Kreutzer, D. Non-invasive glucose measurements in mice using mid-infrared emission spectroscopy. Sensors and Actuators B: Chemical 2009, 142, 502-508, doi:10. 1016/j. snb. 2009. 08. 048.
[43] Landgrebe, D., Haake, C., Hopfner, T., Beutel, S., Hitzmann, B., Scheper, T., Rhiel, M., Reardon, K. F. On-line infrared spectroscopy for bioprocess monitoring. Appl Microbiol Biotechnol 2010, 88, 11-22, doi:10. 1007/s00253-010-2743-8.
[44] Yu, Y., Huang, J. -P., Zhu, J., Liang, S. -L. An Accurate Noninvasive Blood Glucose Measurement System Using Portable Near-Infrared Spectrometer and Transfer Learning Framework. IEEE Sensors Journal 2020, 1-1, doi:10. 1109/jsen. 2020. 3025826.
[45] Yang, W., Liao, N., Cheng, H., Li, Y., Bai, X., Deng, C. Determination of NIR informative wavebands for transmission non-invasive blood glucose measurement using a Fourier transform spectrometer. AIP Advances 2018, 8, doi:10. 1063/1. 5017169.
[46] Peng, X., Yan, Y. -X., Liu, H. On the use of fiber lasers in non-invasive blood glucose monitoring. Optical Fiber Technology 2022, 68, doi:10. 1016/j. yofte. 2022. 102822.
[47] Turgul, V., Kale, I. Permittivity extraction of glucose solutions through artificial neural networks and non-invasive microwave glucose sensing. Sensors and Actuators A: Physical 2018, 277, 65-72, doi:10. 1016/j. sna. 2018. 03. 041.
[48] Tuchin, V. V., Jiang, J., Duncan, D. D., Zou, D., Min, X., Larin, K. V., Leahy, M. J., Ma, Z., Xu, K., Wang, R. K. Monte Carlo simulation on the effect of dermal thickness variances on noninvasive blood glucose sensing. In Proceedings of the Dynamics and Fluctuations in Biomedical Photonics X, 2013.
[49] Han, G., Chen, S., Wang, X., Wang, J., Wang, H., Zhao, Z. Noninvasive blood glucose sensing by near-infrared spectroscopy based on PLSR combines SAE deep neural network approach. Infrared Physics & Technology 2021, 113, doi:10. 1016/j. infrared. 2020. 103620.
[50] Ionescu, M., Doctorala, S. Measuring and detecting blood glucose by methods non-invasive. In Proceedings of the 2018 10th International Conference on Electronics, Computers and Artificial Intelligence (ECAI), 2018, pp. 1-7.
[51] Tuchin, V. V., Min, X., Duncan, D. D., Jiang, J., Zou, D., Larin, K. V., Leahy, M. J., Liu, R., Xu, K., Wang, R. K. Simulation on how to customize glucose adjustment method for non-invasive blood glucose sensing by NIRS. In Proceedings of the Dynamics and Fluctuations in Biomedical Photonics X, 2013.
[52] Popp, J., Ben Mohammadi, L., Drexler, W., Sigloch, S., Frese, I., Tuchin, V. V., Matthews, D. L., Stein, V., Welzel, K., Schmitz, F., et al. A minimally invasive chip based near infrared sensor for continuous glucose monitoring. In Proceedings of the Biophotonics: Photonic Solutions for Better Health Care III, 2012.
[53] Cot é, G. L., Ooi, E. T., Priezzhev, A. V., Zhang, X. Q., Chen, J. H., Soh, P. H., Ng, K., Yeo, J. H. Noninvasive blood glucose measurement using multiple laser diodes. In Proceedings of the Optical Diagnostics and Sensing VII, 2007.
[54] Luo, Q., Li, X., Gu, Y., Tang, Y., Han, G., Liu, J., Liu, R., Xu, K. Determination of the reference position in the near-infrared non-invasive blood glucose measurement in vivo. In Proceedings of the Optics in Health Care and Biomedical Optics VII, 2016.
[55] Ali, H., Bensaali, F., Jaber, F. Novel Approach to Non-Invasive Blood Glucose Monitoring Based on Transmittance and Refraction of Visible Laser Light. IEEE Access 2017, 5, 9163-9174, doi:10. 1109/access. 2017. 2707384.
[56] Uwadaira, Y., Ikehata, A., Momose, A., Miura, M. Identification of informative bands in the short-wavelength NIR

region for non-invasive blood glucose measurement. Biomed Opt Express 2016, 7, 2729-2737, doi: 10. 1364/ BOE. 7. 002729.
[57] Jenie, R. P., Iskandar, J., Kurniawan, A., Rustami, E., Syafutra, H., Nurdin, N. M., Handoyo, T., Prabowo, J., Febryarto, R., Rahayu, M. S. K., et al. Proposed Application of Fast Fourier Transform in Near Infra Red Based Non Invasive Blood Glucose Monitoring System. IOP Conference Series: Earth and Environmental Science 2017, 58, doi: 10. 1088/ 1755-1315/58/1/012011.
[58] Zapasnoy, A. S., Belichenko, V. P., Yakubov, V. P., Gorst, A. V., Mironchev, A. S., Klokov, A. V., Zavyalova, K. V. Application of Broadband Microwave Near-Field Sensors for Glucose Monitoring in Biological Media. Applied Sciences 2021, 11, doi:10. 3390/app11041470.
[59] Luo, Q., Li, X., Gu, Y., Tang, Y., Guo, C., Han, T., Zhang, Z., Sun, D., Liu, J. Optimization on source detector distance for the glucose sensing in a tissue phantom using near-infrared diffuse spectra. In Proceedings of the Optics in Health Care and Biomedical Optics VII, 2016.
[60] Cano-Garcia, H., Kshirsagar, R., Pricci, R., Teyeb, A., O'Brien, F., Saha, S., Kosmas, P., Kallos, E. Enhancing the Accuracy of Non-Invasive Glucose Sensing in Aqueous Solutions Using Combined Millimeter Wave and Near Infrared Transmission. Sensors (Basel) 2021, 21, doi:10. 3390/s21093275.
[61] Srichan, C., Srichan, W., Danvirutai, P., Ritsongmuang, C., Sharma, A., Anutrakulchai, S. Non-invasively accuracy enhanced blood glucose sensor using shallow dense neural networks with NIR monitoring and medical features. Sci Rep 2022, 12, 1769, doi:10. 1038/s41598-022-05570-8.
[62] Wang, D. An improved integration sensor of non-invasive blood glucose. In Proceedings of the The 7th IEEE/International Conference on Advanced Infocomm Technology, 2014, pp. 70-75.
[63] Shokrekhodaei, M., Quinones, S. Review of Non-invasive Glucose Sensing Techniques: Optical, Electrical and Breath Acetone. Sensors (Basel) 2020, 20, doi:10. 3390/s20051251.
[64] Wrobel, M. S., Kim, J. H., Raj, P., Barman, I., Smulko, J. Utilizing pulse dynamics for non-invasive Raman spectroscopy of blood analytes. Biosens Bioelectron 2021, 180, 113115, doi:10. 1016/j. bios. 2021. 113115.
[65] Lundsgaard-Nielsen, S. M., Pors, A., Banke, S. O., Henriksen, J. E., Hepp, D. K., Weber, A. Critical-depth Raman spectroscopy enables home-use non-invasive glucose monitoring. PLoS One 2018, 13, e0197134, doi:10. 1371/journal. pone. 0197134.
[66] Dingari, N. C., Barman, I., Singh, G. P., Kang, J. W., Dasari, R. R., Feld, M. S. Investigation of the specificity of Raman spectroscopy in non-invasive blood glucose measurements. Anal Bioanal Chem 2011, 400, 2871-2880, doi:10. 1007/s00216-011-5004-5.
[67] Kiani, S., Rezaei, P., Fakhr, M. Dual-Frequency Microwave Resonant Sensor to Detect Noninvasive Glucose-Level Changes Through the Fingertip. IEEE Transactions on Instrumentation and Measurement 2021, 70, 1-8, doi:10. 1109/tim. 2021. 3052011.
[68] Govind, G., Akhtar, M. J. Metamaterial-Inspired Microwave Microfluidic Sensor for Glucose Monitoring in Aqueous Solutions. IEEE Sensors Journal 2019, 19, 11900-11907, doi:10. 1109/jsen. 2019. 2938853.
[69] Mhatre, P. J., Joshi, M. Human body model with blood flow properties for non-invasive blood glucose measurement. Biomedical Signal Processing and Control 2022, 72, doi:10. 1016/j. bspc. 2021. 103271.
[70] Jean, B. R., Green, E. C., McClung, M. J., Ieee. A microwave frequency sensor for non-invasive blood-glucose measurement. In Proceedings of the 3rd IEEE Sensors Applications Symposium, Atlanta, GA, Feb 12-14, 2008, pp. 4-7.
[71] Baghelani, M., Abbasi, Z., Daneshmand, M., Light, P. E. Non-invasive continuous-time glucose monitoring system using a chipless printable sensor based on split ring microwave resonators. Sci Rep 2020, 10, 12980, doi:10. 1038/s41598-020-69547-1.
[72] Choi, H., Naylon, J., Luzio, S., Beutler, J., Birchall, J., Martin, C., Porch, A. Design and In Vitro Interference Test of Microwave Noninvasive Blood Glucose Monitoring Sensor. IEEE Trans Microw Theory Tech 2015, 63, 3016-3025, doi:10. 1109/TMTT. 2015. 2472019.
[73] Vrba, J., Vrba, D., Díaz, L., Fišer, O. Metamaterial Sensor for Microwave Non-invasive Blood Glucose Monitoring. In World Congress on Medical Physics and Biomedical Engineering 2018, IFMBE Proceedings, 2019, pp. 789-792.
[74] Yilmaz, T., Foster, R., Hao, Y. Radio-Frequency and Microwave Techniques for Non-Invasive Measurement of Blood Glucose Levels. Diagnostics (Basel) 2019, 9, doi:10. 3390/diagnostics9010006.
[75] Omer, A. E., Shaker, G., Safavi-Naeini, S., Kokabi, H., Alquie, G., Deshours, F., Shubair, R. M. Low-cost portable microwave sensor for non-invasive monitoring of blood glucose level: novel design utilizing a four-cell CSRR hexagonal configuration. Sci Rep 2020, 10, 15200, doi:10. 1038/s41598-020-72114-3.
[76]Turgul, V., Kale, I., Ieee. A Novel Pressure Sensing Circuit for Non-invasive RF/Microwave Blood Glucose Sensors. In Proceedings of the 16th Mediterranean Microwave Symposium (MMS), Abu Dhabi, U ARAB EMIRATES, Nov 14-16, 2016.
[77] Clarke, W. L., Cox, D., Gonder-Frederick, L. A., Carter, W., Pohl, S. L. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care 1987, 10, 622-628, doi:10. 2337/diacare. 10. 5. 622.