International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 15 Issue 05 , May - 2026

Advances in Breath-Based VOC Analysis for Non-Invasive Diabetes Detection

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Abstract **- Diabetes Mellitus is a rapidly increasing metabolic disorder that requires continuous and reliable monitoring. Conventional diagnostic methods are mainly invasive and often inconvenient for frequent use, creating a need for more patient-friendly alternatives. Breath analysis has recently gained importance as a non-invasive method, using volatile organic compounds, especially acetone, to reflect metabolic conditions. Many studies have been done in this area, but they are often not connected.They focus on different parts of the system instead of giving a full understanding.This shows the need for a detailed survey.This paper provides a detailed review of breath based diabetes detection methods covering gas sensing, electronic nose systems and machine learning technqiues.It looks at how breath acteone levels relate to diabetic conditions and dicussess key performance measures along.**

Index Terms **- Breath Analysis, Volatile Organic Compounds (VOCs), Acetone, Diabetes Mellitus, Gas Sensors, Electronic Nose, Machine Learning**

I. INTRODUCTION

Diabetes Mellitus is a long term metabolic condition in which body is unable to properly control blood glucose due to either reduced insulin production or ineffective use of insulin.Over time,it has become one of the most widespread global health issues, making regular monitoring essential to avoid serious complications.Traditional diagnostic techniques,such as blood glucose testing are invasive and can be inconvenient for patients, especially when frequent checking is required.These limitations have encouraged to investigate alternative diagnostic techniques that are more comfortable and suitable for continuous monitoring [21], [30].

In recent years, non-invasive diagnostic techniques have gained significant attention, with breath analysis emerging as a promising solution. Human breath contains a complex mixture of volatile organic compounds (VOCs) that originate from metabolic processes within the body. These VOCs are transported through the bloodstream and released into the lungs, making breath a valuable medium for detecting physiological changes. Advanced analytical techniques such as gas chromatography–mass spectrometry (GC-MS) have demonstrated the presence of hundreds of VOCs in exhaled breath, indicating its importance for disease diagnosis [1], [29].

Among the various VOCs, acetone has been identified as a key biomarker for diabetes, as its concentration is closely related to metabolic processes such as fat oxidation. Higher levels of acetone in breath are commonly linked to poor glucose utilization making it a useful marker for diabetes detection and monitoring [18], [20]. This has led to increased research in the improvement of breath-based diagnostic systems that utilize gas sensors and electronic nose technologies for real- time analysis [3], [10], [15].

Recent advancements in sensing technologies, including metal oxide semiconductor sensors and nanostructured materials, have significantly improved the sensitivity and detection capabilities of breath analysis systems [8], [19], [25]. In parallel, machine learning techniques have been included with sensor systems to enhance classification accuracy and enable automated diagnosis based on breath patterns [2], [4], [6], [27]. These developments have led to more efficient and intelligent breath-based diagnostic solutions.

However, despite progress, existing research often focuses on isolated aspects such as sensor design, signal processing, or classification techniques, without providing a comprehensive and integrated system perspective. Additionally, challenges such as environmental interference, sensor variability, and lack of standardized methodologies remain unresolved [12], [26], [28]. This fragmentation highlights the demand for a structured and comprehensive survey that integrates different approaches and identifies key research gaps.

In this paper, a detailed survey of breath-based diabetes detection techniques is presented, focusing on the analysis of VOCs, particularly acetone, as a biomarker. The study reviews various gas sensing technologies, electronic nose systems and machine learning approaches, while also discussing performance parameters, challenges and future research directions. The objective is to provide a unified understanding that can support the development of reliable, non-invasive and practical breath analysis systems for diabetes monitoring.

II. BACKGROUND AND MOTIVATION

The worldwide spread of diabetes has created an immediate need for for diagnostic solutions that are both accessible and patient-friendly. Although conventional blood-based methods provide accurate measurements, their invasive nature often discourages frequent monitoring and early detection, particularly in long-term disease management [21], [30]. This drawback shows the importance of developing alternative methods that allow continuous and user friendly monitoring.

Recent advancements in sensor technology and biomedical engineering have led to non-invasive diagnostic approaches. Among these, breath analysis has gained significant attention due to its ease and potential for real-time monitoring. A variety of volatile organic compounds are present in human breath and they provide insight into metabolic processes making breath a valuable source of physiological information [1], [28].

The goal of this work is to narrow the gap between research findings and practical use. While previous studies confirm that breath based detection is possible,they often deal with separate aspects like sensor development , data analysis instead of a complete system. This creates a need for integrated solutions that combine sensing, signal processing and advanced data interpretation for reliable monitoring

III. OVERVIEW OF DIABETES MELLITUS

A long term metabolic condition that leads to persistently high blood sugar levels is known as diabetes mellitus. This occurs due to issues in insulin production and its effectiveness or both. The condition is generally categorized into Type 1, Type2 and gestational diabetes each differs in causes and characteristics.

Type1 Diabetes is an autoimmune condition in which the pancreas produce a little or no insulin, requiring lifelong insulin therapy. In contrast,Type 2 Diabetes is mainly linked to reduced sensitivity to insulin and is more commonly seen in adults,often affected by lifestyle habits such as diet and physical activity. If not properly controlled, diabetes can result in serious complications including heat related problems, kidney damage and disorders affecting the nerves.

Given the progressive nature of the disease, early detection and consistent monitoring are crucial for proper management. Conventional diagnostic techniques, however, they are not practical for frequent use, increasing the demand for non-invasive and patient-friendly alternatives. This has led to growing research interest in breath-based diagnostic approaches that can offer real-time insights into metabolic conditions [18], [20].

IV. BREATH ANALYSIS AND VOC BIOMARKERS

Human breath is composed of a complex mixture of gases, including hundreds of volatile organic compounds (VOCs) generated as by-products of metabolic activities within the body. These substances travel through the bloodstream to the lungs and are expelled during respiration. Advanced analytical techniques such as gas chromatography–mass spectrometry (GC-MS) have confirmed the presence of numerous VOCs in exhaled breath, demonstrating its potential as a diagnostic medium [1], [29].

Studying VOCs in breath is providing to be a promising non invasive diagnostic approach because variations in metabolic process are often reflected in changes in VOC concentration level.Unlike traditional methods, breath based methods do not involve blood collection ,allowing for repeated and painless measurements. This makes it particularly suitable for continuous monitoring of chronic conditions such as diabetes [14], [30].

Recent progress in gas sensing has led to improved detection of VOCs at extremely low concentration levels, particularly with the use of metaloxide semiconductor based devices and nanostructured materials [8], [19].In addition, combining electronic nose systems with data driven algorithms has significantly enhanced the interpretation of complex breath signals and the identification of disease-related biomarkers [2], [3], [6].

As a result, breath analysis is increasingly being explored for the diagnosis and monitoring of various diseases, including diabetes, respiratory disorders, and cancer. However, challenges such as sensor variability, environmental interference, and absence of standardized methodologies still need to be dealt with to ensure reliable real-world implementation.

V. ACETONE AS A BIOMARKER FOR DIABETES

Acetone is one of the key significant volatile organic compounds present in human breath and is closely associated with metabolic processes, particularly fat metabolism. Under normal physiological conditions, the human body primarily relies on glucose as its main energy source. However, in individuals with impaired glucose utilization, such as diabetic patients, the body shifts toward fat oxidation, leading to the production of ketone bodies, including acetone [18], [20].

The generated acetone is transported through the bloodstream and eventually expelled via the lungs during respiration. Consequently, the concentration of acetone in exhaled breath provides vital information about metabolic activity and has been shown to correlate with blood glucose levels. Clinical studies indicate that healthy individuals typically exhibit low acetone concentrations, whereas diabetic patients may present significantly elevated levels, particularly under conditions such as diabetic ketoacidosis [18], [21].

TABLE I
BREATH ACETONE LEVELS FOR DIFFERENT CONDITIONS

Condition	Acetone Level (ppm)
Healthy	0.3 – 0.9
Diabetic	1.8 – 5.0
Ketoacidosis	≥ 10

Table I shows typical acetone levels under different conditions.

One of the key advantages of acetone as a biomarker is its non-invasive nature, which enables frequent and convenient monitoring without the need for blood sampling. In addition, advances in sensing technologies have made it possible to detect acetone at very low concentrations, supporting its use in real-time monitoring applications [8], [19], [25].

Despite its potential, accurate detection of breath acetone remains challenging. Environmental factors such as humid- ity, temperature fluctuations, and the presence of interfering volatile compounds can significantly affect sensor performance. Furthermore, variations in individual physiology can introduce additional complexity in interpreting breath data. These challenges highlight the importance of robust sensor design, proper calibration techniques, and advanced data processing methods [12], [26].

Overall, acetone continues to be a promising biomarker for diabetes detection. However, achieving reliable and practical implementation requires a careful balance between sensing accuracy, environmental adaptability, and system integration. Fig. 1 illustrates the variation in breath acetone concentration across different physiological conditions, showing a clear increase from healthy individuals to diabetic and ketoacidosis cases.

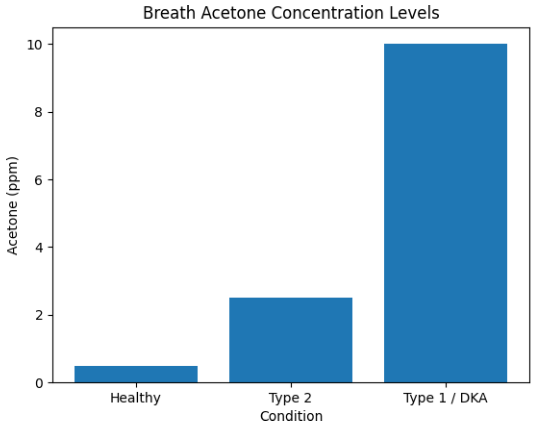

Fig. 1. Breath acetone concentration levels for different conditions

VI. GAS SENSING TECHNOLOGIES FOR VOC DETECTION

Building on the role of acetone as a key biomarker, the effective detection of volatile organic compounds (VOCs) in human breath depends heavily on the performance of gas sensing technologies. Since VOCs are typically present in trace concentrations, often in the ppm or ppb range, highly sensitive and dependable sensors are required for accurate detection [8], [19].

Over the years, significant advancements in sensor materials and fabrication techniques have improved the capability of gas sensors to detect low concentrations of biomarkers such as acetone. The choice of sensing technology is influenced by several factors, including sensitivity, selectivity, response time, cost, and suitability for portable applications. Therefore, understanding the operating principles and limitations of different sensor types is essential for designing efficient breath-based diagnostic systems.

Fig. 2 presents a comparison of different gas sensing technologies, highlighting variations in detection accuracy and indicating the relative performance of each sensor type.

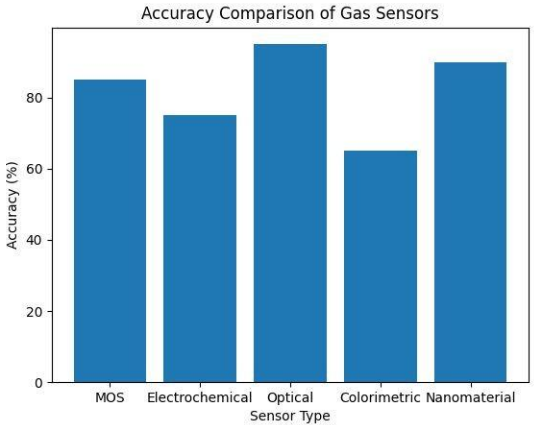

Fig. 2. Accuracy comparison of different gas sensing technologies

A. Metal Oxide Semiconductor (MOS) Sensors

Metal Oxide Semiconductor (MOS) sensors are among the most commonly used technologies for VOC detection due to their high sensitivity, robustness, and cost-effectiveness. These sensors work based on the change in electrical resistance of a metal oxide material, such as tin oxide (SnO_2), when exposed to target gases [8], [19].

At high temperatures, oxygen molecules attach to the sensor and form ions that capture electrons from the conduction band. When a reducing gas such as acetone interacts with the sensor, it reacts with these oxygen ions, releasing electrons back into the material and causing a measurable change in resistance. This change is directly related to the concentration of the target gas.

MOS sensors are suited to breath analysis applications because they can detect acetone at very low concentrations and can be easily integrated into compact and portable systems. Additionally, recent developments in nanostructured materials have further enhanced their sensitivity and response characteristics [25].

However, MOS sensors also have certain limitations. Their performance is influenced by environmental conditions such as humidity and temperature, and they often exhibit cross-sensitivity to other gases present in breath. These factors can lead to inaccuracies in measurement if not properly addressed. As a result, calibration techniques and compensation algorithms are essential to improve sensor reliability and ensure consistent performance [12].

B. Electrochemical Sensors

Electrochemical sensors detect gases through chemical reactions occurring at the electrode surface. These sensors typically consist of a sensing electrode, a counter electrode, and an electrolyte, where the interaction between the target gas and the electrode leads to oxidation or reduction reactions. This process generates a current proportional to the gas concentra- tion, enabling quantitative analysis [11].

One of the key advantages of electrochemical sensors is their high selectivity, as they can be specifically designed to respond to particular gases such as acetone. In addition, they operate at relatively low temperatures compared to MOS sensors, resulting in lower power consumption and making them convenient for portable and battery-operated devices [20].

However, these sensors also present certain limitations. Their performance tends to degrade over time due to electrode aging and electrolyte instability, which reduces their lifespan. Furthermore, they require periodic calibration and controlled operating conditions to maintain accuracy. These constraints can limit their long-term reliability in real-world breath analysis systems.

C. Optical and Spectroscopic Sensors

Optical and spectroscopic sensing techniques offer highly accurate and selective detection of VOCs by analyzing the interaction between light and gas molecules. Techniques such as infrared (IR) absorption spectroscopy, photoacoustic spectroscopy, and laser-based detection is largely used due to their ability to identify gases based on their unique spectral signatures [18], [28].

Light interacts with gas molecules differently depending on their composition and this property is used to identity compounds like acetone with good precision. These methods are highly sensitive and can detect very small concentrations, even at parts per billon levels, which makes them useful is both clinical and laboratory settings.

However,even though they are accurate, optical and spectroscopic systems are usually complex and costly. They use parts like light sources, detectors and optical chambers, which make the system bigger and more expensive. Because of this, they are mostly used in labs and are not suitable for portable or real-time use.

D. Colorimetric Sensors

Gas detection using colorimetric sensors works by chemical reactions that produce color changes,offering a convenient and afforable method. In the presence of acetone, the sensing material undergoes a chemical transformation that alters its color intensity, which can be measured and correlated to gas concentration [17], [24].

These sensors are easy to use and do not require complex electronic circuitry, making them suitable for low-cost and portable diagnostic applications. In breath analysis systems, the color change can be captured using optical sensors or imaging devices and processed to estimate acetone levels.

However, the performance of colorimetric sensors can be affected by external factors such as lighting conditions, humidity, and subjective interpretation of color changes. These limitations can reduce measurement accuracy, and therefore, colorimetric sensors are often used together with other sensing techniques to improve system reliability.

VII. ELECTRONIC NOSE SYSTEMS FOR BREATH ANALYSIS

While individual sensors provide valuable information about specific gases, real-world breath analysis often involves complex mixtures of VOCs. To address this challenge, electronic nose (e-nose) systems have been designed to mimic the human olfactory system by using arrays of gas sensors combined with pattern recognition techniques [3], [10], [16].

In an e-nose system, multiple sensors with varying sensitivities respond to different VOCs, generating a collective response pattern or “fingerprint.” This pattern is then analyzed using computational algorithms to classify the sample. With reference to diabetes detection, e-nose systems can identify characteristic patterns associated with elevated acetone levels along with other metabolic markers.

One of the major benefit of electronic nose systems is their ability to analyze complex gas mixtures rather than focusing on a single biomarker. This enables a better understanding of breath composition and improves diagnostic accuracy [26]. Additionally, the inclusion of machine learning techniques further enhances classification performance and system adaptability.

However, e-nose systems also face several challenges. Sensor drift, variability in sensor responses, and sensitivity to environmental conditions can affect system stability over time. Moreover, maintaining consistent calibration across multiple sensors is a complex task. These limitations highlight the need for robust system design and advanced data processing techniques to ensure reliable real-world performance [12], [13].

Fig. 3 demonstrates the concept of an electronic nose system, where multiple sensors work together to analyze complex breath patterns and improve detection reliability.

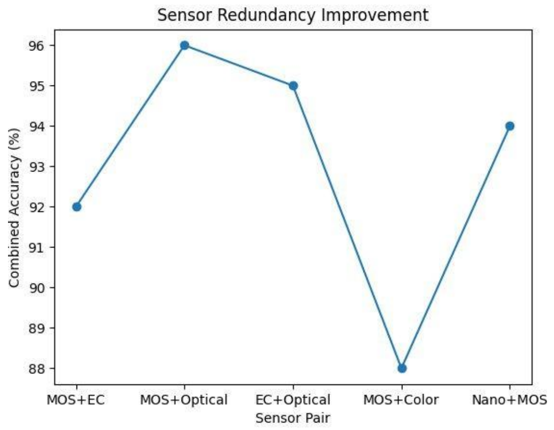

Fig. 3. Multi-sensor electronic nose (e-nose) system illustrating improved detection through combined sensor responses and pattern recognition.

VIII. MACHINE LEARNING TECHNIQUES IN BREATH ANALYSIS

Following the acquisition of sensor responses through gas sensing technologies and electronic nose systems, the interpretation of this data becomes a critical step in breath-based diagnostics. Sensor outputs are often non-linear, noisy, and influenced by multiple environmental and physiological factors. As a result, traditional analytical methods are not sufficient to extract meaningful patterns from such data. Machine learning techniques have therefore become essential for processing and interpreting breath analysis data [2], [6].

Machine learning algorithms enable the identification of complex relationships between sensor responses and underlying metabolic conditions. By learning from labeled datasets, these algorithms can classify breath samples and support the detection of diseases such as diabetes. The inclusion of machine learning with sensor systems significantly enhances diagnostic accuracy and enables automated decision-making in breath analysis applications [4], [27].

A. *Classification Algorithms*

Classification algorithms form the foundation of data interpretation in breath analysis systems. These methods are designed to distinguish between different physiological conditions based on patterns in sensor data. Commonly used algorithms include k-nearest neighbors (KNN), support vector machines (SVM), and decision trees [2], [5].

TABLE II
COMPARISON OF MACHINE LEARNING METHODS

Algorithm	**Strength**	**Limitation**
KNN	Works well for small data	Slow for large datasets
SVM	Handles complex data	Needs tuning
Decision Tree	Easy to understand	Overfitting possible

Table II summarizes commonly used classification methods.

KNN works well for small datasets, while SVM handles more complex sensor data and gives accurate results. Decision trees are easy to follow and show how each feature affects the final decision.

For diabetes detection, these methods use changes in sensor signals, especially due to acetone and other VOCs, to classify samples. But many models are built without considering real-world factors. Things like sensor drift, changes in environment, and real-time limits are often ignored.

Because of this, there is a clear gap between sensor systems and the models used for classification, which affects practical use. Future work should focus on combining better hardware with reliable and adaptable models.

B. *Deep Learning Approaches*

Deep learning is an advanced form of machine learning that is useful for processing complex and large sensor data. Neural networks are capable of automatically extracting relevant features from raw sensor signals, reducing the need for manual feature engineering [4], [27].

Models such as artificial neural networks (ANNs), convolutional neural networks (CNNs), and hybrid architectures have been applied to breath analysis systems. These models can capture intricate patterns in multi-sensor data, making them especially effective for electronic nose systems where multiple VOCs contribute to the overall response.

Deep learning approaches are particularly useful in addressing challenges such as sensor drift, noise, and variability in breath samples. By learning from large and diverse datasets, these models can achieve improved generalization and robustness across different conditions [6].

However, the use of deep learning introduces additional challenges. These models require large datasets for effective training and often involve high computational complexity, which can limit their deployment on embedded systems such as microcontrollers or single-board computers. Moreover, the lack of interpretability in deep models can make it difficult to understand the decision-making process.

Therefore, there is a growing need to develop optimized and lightweight deep learning models that balance accuracy with computational efficiency. Such approaches will be essential for enabling real-time, portable, and scalable breath-based diagnostic systems. Refined technical content, improved clarity, and enhanced structure of literature review. Added diagrams and supporting explanations where required.

IX. CHALLENGES AND LIMITATIONS

While breath-based diabetes detection has shown promising results, several challenges continue to limit its practical implementation. One of the primary concerns is the variability in sensor response caused by environmental factors such as humidity, temperature fluctuations, and the presence of interfering gases. These factors can significantly affect sen- sor readings, leading to inconsistencies and reduced system reliability [12], [26].

TABLE III
KEY CHALLENGES IN BREATH ANALYSIS SYSTEMS

Challenge	**Impact**
Humidity	Affects sensor response accuracy
Temperature Variation	Causes drift in sensor readings
Sensor Drift	Reduces long-term stability
Gas Interference	Leads to incorrect detection

Another major issue is sensor drift, where the characteristics of gas sensors change over time due to continued exposure to environmental conditions. This affects long-term stability and necessitates frequent calibration, which can be impractical for real-world and portable applications. Additionally, commonly used sensors such as metal oxide semiconductor sensors suffer from cross-sensitivity, making it difficult to selectively detect acetone in the presence of other VOCs [8], [19].

From a system-level perspective, many existing studies focus either on sensor development or data analysis independently, without considering a fully integrated approach. This lack of coordination between hardware and data processing leads to systems that perform well under controlled laboratory conditions but struggle in real-world environments.

Furthermore, machine learning models used in breath analysis often require large and diverse datasets for effective training. However, such datasets are limited in medical applications due to variability in human breath composition and differences across individuals. This creates challenges in model generalization and reduces the reliability of classification results [6], [27].

These limitations highlight a critical research gap in the development of robust, adaptive, and integrated systems that can operate reliably under real-world conditions.

X. RECENT ADVANCEMENTS

Recent advancements in breath analysis have significantly improved the feasibility of non-invasive diabetes detection. One of the key developments is the use of nanostructured materials in gas sensors, which has enhanced sensitivity and selectivity, enabling the detection of acetone at very low concentrations [19], [25].

The integration of electronic nose systems with machine learning algorithms has further improved system performance. Multi-sensor arrays combined with pattern recognition techniques allow for more accurate classification of complex breath samples, addressing the limitations of single-sensor systems [3], [10], [16]. In particular, deep learning models have demonstrated improved accuracy by capturing intricate patterns in sensor data [4], [27].

Another important advancement is the development of MEMS-based sensors and portable sensing platforms. These technologies have enabled the miniaturization of breath analysis systems, making them more suited to real-time and point-of-care applications [22], [23].

Using a mix of sensing techniques and data processing methods has led to the development of hybrid systems that handle the drawbacks of single methods. This improves both accuracy and reliability.

XI. FUTURE SCOPE AND RESEARCH DIRECTIONS

Future work should focus on building complete systems that combine reliable sensors, efficient processing, and real-time analysis. Bridging the gap between research and real-world use is still a challenge.

Improving sensor design, reducing interference, and using lightweight models that can run on small devices are important steps. Using shared datasets and combining systems with IoT and cloud platforms can also support better monitoring and data use.

Overall, the goal is to balance accuracy, efficiency, and portability to make these systems practical for real healthcare use.

XII. CONCLUSION

This study presents a comprehensive analysis of breath based diabetes detection using volatile organic compounds, with a primary focus on acetone as a reliable biomarker. The findings from Table I clearly demonstrate a significant increase in breath acetone concentration from healthy individuals to diabetic and ketoacidosis conditions, reinforcing its strong correlation with metabolic imbalance.

The comparative evaluation of sensing technologies (Fig. 2) indicates that while metal oxide semiconductor sensors offer a balance between sensitivity and cost, optical and nanomaterial-based sensors provide higher accuracy at the expense of complexity and cost. This highlights that no single sensing technology is universally optimal, and system design must consider application-specific trade-offs.

Furthermore, the integration of multi-sensor electronic nose systems (Fig. 3) combined with machine learning techniques (Table II) significantly improves classification accuracy by capturing complex VOC patterns rather than relying on a single biomarker. However, the analysis also reveals that existing models often lack robustness in real-world conditions due to limited datasets and insufficient consideration of environmental variations.

The challenges summarized in Table III, including humidity effects, temperature variations, sensor drift, and gas interference, remain critical barriers to practical implementation. These factors directly impact system stability, accuracy, and long-term reliability, indicating that current solutions are still largely constrained to controlled environments.

Overall, the key finding of this work is that the major limitation in current research is not sensor capability or algorithm performance individually, but the lack of an integrated system level approach. Future developments must focus on combining advanced sensing technologies with adaptive, lightweight machine learning models and robust calibration techniques to ensure reliable operation in real world conditions.

With continued advancements in sensor materials, embedded systems and intelligent data processing, breath-based diabetes detection has strong potential to evolve into a practical, non-invasive and real-time healthcare solution.

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