

Research Article

NON-INVASIVE CONTINUOUS MONITORING OF GLUCOSE LEVEL ENABLED BY WEARABLE BIOSENSOR TECHNOLOGIES

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Abstract

Non-invasive continuous glucose monitoring has emerged as animportant solution for managing diabetes and maintaining metabolic health. Wearable biosensor technologies have contributed this field by offering real-time monitoring of glucose levelin minimally-invasive way, enabling improved patient compliance and enhanced disease management. This article reviews the latest advancements in wearable biosensor systems, especially focusing on sweat-based glucose monitoring method. We highlight clinical requirement in patient-care, essential approaches to develop the wearable biosensor seamlessly integrated with skin and principles of glucose monitoring from sweat. It highlights innovations in materials, device integration, considering sensor performance in terms of accuracy, stability, and biocompatibility. Finally, we explore future directions for wearable glucose sensors, emphasizing the potential for multi-analyte detection and personalized health management systems. By bridging cutting-edge research with clinical applications, this work underscores the transformative potential of wearable biosensors in revolutionizing diabetes care and beyond.

Keywords: Bladder Exstrophy, bladder plate, continence, surgical outcomes, ureteric reimplantation.

INTRODUCTION

The increasing prevalence of diabetes has emerged as a significant global health challenge, affecting hundreds of millions of individuals worldwide. The management of this chronic condition heavily relies on the ability to monitor blood glucose levels accurately and continuously. Traditional glucose monitoring methods, such as finger-prick blood tests, although widely adopted, are often invasive, inconvenient, and limited in their ability to provide real-time insights into glucose fluctuations. These limitations have propelled research and development into non-invasive and continuous glucose monitoring technologies that aim to transform diabetes management, enhancing patient compliance, quality of life, and health outcomes. Wearable biosensor technologies have drawn considerable attention as a promising solution to address these challenges. By integrating advanced materials, miniaturized electronics, and cutting-edge sensor technologies, these devices enable real-time, non-invasive monitoring of glucose levels with minimal discomfort to users (1,2). Such innovations align with the broader trends in personalized medicine, which seek to empower individuals with actionable health data while reducing the burden on healthcare systems. The adoption of wearable biosensors for glucose monitoring represents not only a technological advancement but also a paradigm shift in the way diabetes is managed, transitioning from reactive to proactive care. Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia due to impaired insulin secretion, action, or both. The World Health Organization (WHO) and the International Diabetes Federation (IDF) report alarming statistics that underscore the urgency of addressing this global epidemic. As of recent estimates, over 500 million adults are living with diabetes, with projections indicating a continued rise in prevalence over the coming decades (3).

Beyond its sheer prevalence, diabetes imposes significant economic and societal costs, including increased risks of cardiovascular diseases, neuropathy, retinopathy, and kidney failure, alongside reduced workforce productivity and heightened healthcare expenditures. Effective diabetes management is contingent upon maintaining glucose levels within a target range to minimize complications. Traditional self-monitoring of blood glucose (SMBG) using capillary blood sampling has been a cornerstone of diabetes care for decades. However, SMBG provides only discrete glucose measurements, failing to capture dynamic glucose trends that are critical for understanding individual glycemic patterns. Continuous glucose monitoring (CGM), on the other hand, offers a more comprehensive picture of glucose variations, enabling timely interventions and personalized therapeutic strategies. Yet, the invasive nature of existing CGM systems, which require subcutaneous sensor implantation, poses challenges to user acceptance and long-term adherence (4). The advent of wearable biosensor technologies has revolutionized the landscape of health monitoring by enabling the seamless integration of sensors into everyday life. Pioneering advances in materials science, microelectronics, and data analytics have facilitated the development of wearable devices that are lightweight, flexible, and capable of providing physiological measurements. For continuous glucose monitoring, wearable biosensors leverage non-invasive or minimally invasive techniques, including optical. electrochemical, and electromagnetic sensing, to detect glucose concentrations in interstitial fluid, sweat, saliva, or tears. Optical sensing methods, such as near-infrared (NIR) spectroscopy, Raman spectroscopy, and photoplethysmography (PPG), exploit the interaction of light with glucose molecules to estimate glucose levels. These techniques offer the advantage of non-invasiveness but face challenges related to signal interference and calibration accuracy. Electrochemical sensing, a widely adopted approach, relies on enzymatic or non-enzymatic reactions that produce

detectable electrical signals proportional to glucose concentration. Advances in electrode design, including the use of nanomaterials and biocompatible coatings, have significantly enhanced the sensitivity and selectivity of electrochemical sensors. The integration of wearable biosensors into diabetes management encompasses several key dimensions, including sensor performance, data analytics, and user experience. High-performance sensors must exhibit accuracy, reliability, and stability over prolonged periods, even under varying environmental and physiological conditions. Data analytics play a critical role in translating raw sensor outputs into actionable insights, often leveraging machine learning algorithms to predict glucose trends and identify potential anomalies. Equally important is the user-centric design of wearable devices, which prioritizes comfort, aesthetics, and ease of use. Successful adoption of wearable glucose monitors depends on their ability to seamlessly integrate into users' lifestyles, whether as wristbands, patches, or other form factors. Emerging trends in this domain include the development of multi-analyte sensors that concurrently monitor glucose alongside other biomarkers, such as lactate or cortisol, to provide a holistic view of metabolic health. Despite their promise, wearable biosensor technologies for glucose monitoring face several challenges that must be addressed to achieve widespread clinical adoption. Technical hurdles include ensuring sensor accuracy across diverse populations, minimizing drift over time, and overcoming signal artifacts caused by motion or environmental factors. Regulatory approval processes, which demand rigorous validation of device safety and efficacy, also represent significant barriers to market entry. Future research directions are likely to focus on enhancing sensor performance through innovations in material science, such as the development of soft biocompatible materials for highly comfortable wearable biosensor. Additionally, the integration of biosensors with digital health ecosystems, including smartphone applications and cloudbased platforms, has the potential to enable real-time feedback, telemedicine consultations, and population-level health monitoring. Wearable biosensor technologies for non-invasive continuous glucose monitoring hold transformative potential in reshaping diabetes care. In this work, we will highlight the importance of continuous, real-time monitoring in patient-care and requirements of medical devices. Next, we will discuss glucose monitoring in sweat as a promising minimally invasive method. Finally, we will review potential advancements in material science and design aimed at enhancing the functionality of wearable technologies.

Importance of continuous monitoring from patients

The continuous monitoring of glucose levels has revolutionized the management of diabetes and is an essential aspect of modern healthcare, particularly for individuals living with type 1 and type 2 diabetes. Unlike traditional fingerstick glucose testing, which provides a snapshot of blood sugar levels at specific moments, continuous glucose monitoring (CGM) systems deliver real-time data throughout the day and night. This continuous stream of information enables patients and healthcare providers to gain a dynamic understanding of glucose trends, making it possible to optimize treatment, prevent complications, and improve overall quality of life. The importance of this technology cannot be overstated, as it addresses critical gaps in diabetes care while empowering individuals to take control of their health. One of the most significant advantages of CGM is its ability to provide realtime feedback on glucose levels, which is particularly important for managing diabetes. For example, a patient using a CGM device can immediately see the impact of meals, exercise, stress, or medication on their blood sugar levels. This instant feedback allows them to make informed decisions about their diet, physical activity, or insulin dosage, reducing the risk of extreme glucose fluctuations. For instance, if a CGM detects a rapid rise in blood sugar after a carbohydraterich meal, the patient can administer insulin promptly, preventing hyperglycemia. Conversely, if the device alerts the patient to a rapid drop in glucose, they can consume a fastacting carbohydrate to avoid hypoglycemia, a potentially lifethreatening condition.CGM is particularly invaluable for individuals with type 1 diabetes, who are at constant risk of both hyperglycemia and hypoglycemia. Unlike fingerstick tests, which are typically performed a few times a day, CGM provides a comprehensive picture of glucose trends, helping to identify patterns that might otherwise go unnoticed. For example, a CGM might reveal that a patient's blood sugar consistently drops during the night, a phenomenon known as nocturnal hypoglycemia. Armed with this knowledge, the patient and their healthcare provider can adjust their insulin regimen or bedtime snack to mitigate this risk. Such insights are critical for preventing dangerous episodes and ensuring more stable glucose control. Beyond individual benefits, CGM also has a broader impact on healthcare systems by reducing the need for emergency interventions and hospitalizations related to diabetes complications. Uncontrolled glucose levels are a major contributor to long-term complications, including cardiovascular disease, kidney failure, nerve damage, and vision loss. By providing continuous data, CGMs enable early intervention, reducing the likelihood of these complications and the associated healthcare costs. For instance, a patient whose CGM indicates consistently high post-meal glucose levels might be advised to modify their diet or adjust their medication, preventing the progression of diabetes-related complications over time. The integration of CGM data with digital health platforms and artificial intelligence further enhances its utility. Many CGM devices now connect to smartphone apps or cloud-based systems, allowing patients to share their glucose data with healthcare providers and caregivers. This feature is particularly beneficial for pediatric patients or elderly individuals who require additional support in managing their diabetes. For example, parents of a child with type 1 diabetes can receive alerts if their child's glucose levels drop dangerously low during school hours, enabling prompt action. Similarly, AI algorithms can analyze CGM data to predict glucose trends and provide personalized recommendations, improving the precision of diabetes management. One notable success story involves athletes with diabetes who rely on CGM to maintain optimal glucose levels during training and competition. Physical activity can significantly impact blood sugar, often leading to unpredictable fluctuations. For example, long-distance runners with type 1 diabetes have reported using CGM to monitor their glucose levels during marathons, allowing them to make real-time adjustments to their carbohydrate intake or insulin dosing (5). This capability not only enhances performance but also ensures safety, enabling individuals with diabetes to pursue active lifestyles without fear of severe glucose imbalances.CGM also plays a crucial role in gestational diabetes management, a condition that affects pregnant women and poses risks to both mother and baby if left uncontrolled. Continuous monitoring helps expectant mothers maintain tight glucose control, reducing the likelihood of complications such as macrosomia

(excessive fetal growth), preterm birth, or preeclampsia. For example, a pregnant woman using CGM can identify glucose spikes after meals and work with her healthcare provider to modify her diet or adjust insulin therapy, ensuring a healthier pregnancy outcome. Moreover, CGM has significant psychological benefits for individuals living with diabetes. The constant vigilance required for glucose management can be overwhelming, leading to "diabetes burnout." By automating much of the monitoring process and providing actionable insights, CGMs reduce the mental burden associated with diabetes care. For instance, individuals no longer need to perform frequent fingerstick tests, which can be painful and inconvenient, especially in public settings. Instead, they can rely on discreet CGM devices to keep track of their glucose levels, enhancing their confidence and independence. While the benefits of CGM are undeniable, its adoption still faces challenges, including cost and accessibility. Many CGM devices remain expensive, and not all insurance plans cover them, limiting their availability to certain populations. However, ongoing advancements in technology and increased advocacy for broader insurance coverage are gradually addressing these barriers. Additionally, newer, more affordable CGM models are entering the market, making this lifechanging technology more accessible to a wider range of patients. In conclusion, the continuous monitoring of glucose levels represents a groundbreaking advancement in diabetes care, offering patients unprecedented control over their condition. Whether by providing real-time feedback, preventing dangerous glucose fluctuations, or enabling early intervention, CGM systems empower individuals to lead healthier, more fulfilling lives. From athletes managing glucose during competitions to pregnant women ensuring a safe delivery, the applications of CGM are vast and transformative. As technology continues to evolve and become more accessible, the impact of continuous glucose monitoring on individual health and global healthcare systems will only grow, making it a cornerstone of diabetes management in the years to come.In this background, wearable devices for sweat glucose detection allow users to monitor their glucose levels discreetly and conveniently throughout the day, without the need for frequent calibration or manual data entry. We will address this technology in next section.

Wearable biosensor technology: principles and design

Wearable biosensor technology is a rapidly evolving field that integrates principles of bioengineering, electronics, and materials science to enable real-time monitoring of physiological and biochemical parameters. At its core, these sensors operate by detecting specific analytes or signals in bodily fluids, such as sweat, saliva, or interstitial fluid, and converting them into measurable electrical, optical, or mechanical signals. The performance and usability of wearable biosensors depend on four critical factors: sensitivity, selectivity, stability, and user comfort. Sensitivity refers to the sensor's ability to detect low concentrations of analytes with high precision, enabling accurate monitoring even at trace levels. This capability is achieved through advanced materials and detection mechanisms that amplify responses to target biomarkers. Selectivity is equally vital, ensuring the biosensor can accurately distinguish the desired analyte from similar substances or environmental interferences. This is often accomplished using specific enzymes, molecular recognition elements, or engineered nanostructures. Stability pertains to the device's capacity to maintain consistent performance over time, even under varying physiological conditions or prolonged use. It is especially critical for real-time, continuous monitoring applications, where sensor degradation can compromise data reliability. Lastly, user comfort plays a key role in the adoption of wearable biosensors, as long-term adherence depends on minimizing discomfort. Advanced materials, including flexible substrates, conductive polymers, and nanostructured elements, play a crucial role in ensuring device biocompatibility and seamless integration with the human body. A biosensor consists of several interconnected components that work synergistically to detect and quantify analytes (Figure 1). The bioreceptor serves as the recognition element, typically composed of biological materials such as enzymes, antibodies, nucleic acids, or cells, which interact selectively with the target analyte to ensure specificity. These receptive materials capture the target analytes, leading chemical reactions. For example, in sweat-based glucose detection method, glucose is detected using enzymes such as glucose oxidase (GOx) or glucose dehydrogenase (GDH) immobilized on an electrode surface. When glucose in sweat interacts with these enzymes, it undergoes a catalytic reaction that generates byproducts such as hydrogen peroxide or electrons. These byproducts produce an electrical signal proportional to the glucose concentration, which is then processed and analyzed (Figure 2) (6).

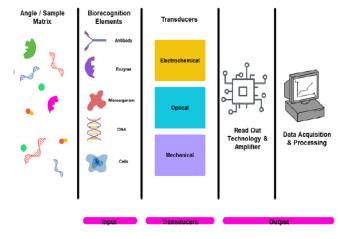


Figure 1. Schematics showing components of biosensor

The transducer then converts this biological interaction into a measurable signal, with mechanisms that can be optical, electrochemical, piezoelectric, or thermal, depending on the biosensor type. As the raw signal from the transducer is often weak, a signal processor amplifies and filters it to ensure accuracy and reliability. Finally, the processed signal is presented through a display or output interface, which may include digital readouts, graphical displays, or wireless data transmission to external devices for real-time visualization and analysis. Together, these components enable biosensors to deliver precise and actionable data in various applications.

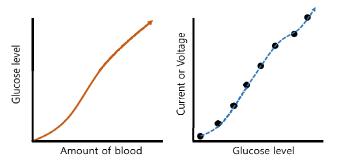
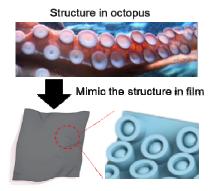


Figure 2. Data trends calibrated from glucose level

Material and mechanical design for seamless integration on skin

Material and mechanical design play an essential role in ensuring the seamless integration of wearable biosensors on the skin, enhancing both functionality and user comfort. Flexible and stretchable materials, such as silicone elastomers polydimethylsiloxane, PDMS), thermoplastic (e.g., polyurethanes (TPU), and conductive polymers (e.g., PEDOT: PSS), are commonly employed to accommodate the dynamic movements of the skin without compromising sensor performance (7-9). Mechanical designs often mimic the properties of human skin, such as low modulus and high elasticity, to reduce mechanical mismatches that could lead to discomfort or device detachment. For example, ultrathin films and serpentine structures are widely used to maintain device functionality under bending, stretching, and twisting(10-12). Materials like hydrogels provide not only flexibility but also excellent adhesion and hydration, enabling prolonged skin contact with minimal irritation. Additionally, microfluidic platforms integrated with these materials allow for the efficient collection and analysis of biofluids, such as sweat. Innovations like epidermal electronics and bio-inspired adhesive designs, including those modeled after gecko feet or octopus suckers, further improve the adhesion and conformability of wearable devices (13) (Figure 3). Together, these material and mechanical advancements facilitate the development of skinintegrated biosensors that are unobtrusive, reliable, and suitable for long-term use in real-world settings.



Octopus-inspired nano structure for adhesive

Figure 3. Octopus-inspired nanostructured film for wearable adhesives

Conclusion

In this review, we review the recent technologies regarding non-invasive continuous monitoring of glucose levels through wearable biosensor technologies representing a transformative advancement in diabetes management and broader healthcare applications. These devices combine innovative sensing mechanisms, especially electrochemical sensing method with diverse essential components, with cutting-edge materials and mechanical designs to provide accurate, real-time data in a user-friendly format. By eliminating the discomfort and inconvenience associated with traditional glucose monitoring methods, wearable biosensors enhance patient compliance and enable personalized health monitoring. Despite challenges such as sensor stability, motion artifacts, and environmental interferences, ongoing research in material science, miniaturization, and data analytics continues to address these limitations, paving the way for clinically reliable solutions. As wearable biosensors evolve, their integration with multi-analyte detection and digital health platforms holds the potential to revolutionize not only diabetes care but also preventive and precision medicine, marking a significant leap toward accessible and continuous healthcare monitoring

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REFERENCES

- 1. Bamgboje D. et al., Continuous Non-Invasive Glucose Monitoring via Contact Lenses: Current Approaches and Future Perspectives. 2021, *Biosensors*, 11, 189.
- Md. H.-O.-Rashid, M. N. Aktar, V. Preda and N. Nasiri, Advances in electrochemical sensors for real-time glucose monitoring. 2024, *Sensors and Diagnostics*, 3, 893–913.
- 3. Forouhi N. G., N. J. Wareham, Epidemiology of diabetes. 2022, *MEDICINE* 50, 10.
- 4. Lee I., D. Probst, D. Klonoff, K. Sode, Continuous glucose monitoring systems Current status and future perspectives of the flagship technologies in biosensor research. 2021, *Biosensors and Bioelectronics*, 181, 11305.
- Bowler A.L.M. et al., The Use of Continuous Glucose Monitors in Sport: Possible Applications and Considerations. 2023, International Journal of Sport Nutrition and Exercise Metabolism, 33, 121-132
- Jeon W.Y., H.-H. Kim and Y.-B. Choi, Development of a Glucose Sensor Based on Glucose Dehydrogenase Using Polydopamine-Functionalized Nanotubes. 2021, *Membranes*, 11, 384.
- Wang L., H. Wang, Q. Wan, J. Gao, Recent development of conductive polymer composite-based strain sensors. 2023, *Journal of Polymer Science*, 61, 3167–3185.
- 8. Gillan L., J. Hiltunen, M. H. Behfar, and K. Rönkä, Advances in design and manufacture of stretchable electronics. 2022, *Japanese Journal of Applied Physics*. 61, SE0804.
- 9. Xi Fan et al., PEDOT:PSS materials for optoelectronics, thermoelectrics, and flexible and stretchable electronics. 2023, *Journal of Materials Chemistry*, 11, 18561.
- 10. Yihao Shi et al., Freestanding Serpentine Silicon Strips with Ultrahigh Stretchability over 300% for Wearable Electronics. 2024, *Advanced Materials*, 36, 2313603.
- Sabrina M. Curtis et al., Thin-Film Super elastic Alloys for Stretchable Electronics. 2023, Shape Memory and Super elasticity, 9, 35–49.
- Li Y., A. Veronica, J. Ma, and H. Y. Y. Nyein, Materials, Structure, and Interface of Stretchable Interconnects for Wearable Bioelectronics. 2024, *Advanced Materials*, 2408456.
- Abraham A. P., J. Krahn and C. Menon, Recent advances in nanostructured biomimetic dry adhesives. 2013, *frontiers in Bioengineering and Biotechnology*, 1, 1.
